



## Research Literatures of New Ideas in Cancer Treatment

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**Abstract:** Cancer is the general name for a group of more than 100 diseases. Although there are many kinds of cancer, all cancers start because abnormal cells grow out of control. Untreated cancers can cause serious illness and death. The body is made up of trillions of living cells. Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries. This article introduces recent research reports as references in the related studies.

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**Key words:** cancer; life; research; literature; cell

### 1. Introduction

Cancer is the general name for a group of more than 100 diseases. Although there are many kinds of cancer, all cancers start because abnormal cells grow out of control. Untreated cancers can cause serious illness and death. The body is made up of trillions of living cells. Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries.

The following introduces recent reports as references in the related studies.

Aas, A. T., et al. (1994). "Chlorpromazine in combination with nitrosourea inhibits experimental glioma growth." *Br J Neurosurg* **8**(2): 187-192.

Modern cancer therapy has improved the prognosis for several tumour types. This, however, does not apply to the largest group of brain tumours, the malignant astrocytomas grades III-IV. Hence, there is need for new ideas to improve treatment. Ca<sup>2+</sup> and the Ca(2+)-binding protein calmodulin have been shown to be involved in the processes conferring stability to DNA in proliferating neoplastic cells. We have combined the calmodulin-inhibiting neuroleptic drug chlorpromazine (CPZ), with the anti-neoplastic drug 1,3-bis(2-chloroethyl-1)-nitrosourea (BCNU) in a treatment regime for rats with glioma cells implanted in the brain. A highly significant inhibiting effect upon the tumour growth was noticed, not by CPZ or BCNU as single drugs, but with their combination.

Agostini, M., et al. (2015). "An integrative approach for the identification of prognostic and predictive biomarkers in rectal cancer." *Oncotarget* **6**(32): 32561-32574.

**INTRODUCTION:** Colorectal cancer is the third most common cancer in the world, a small fraction of which is represented by locally advanced rectal cancer (LARC). If not medically contraindicated, preoperative chemoradiotherapy, represent the standard of care for LARC patients. Unfortunately, patients shows a wide range of response rates in which approximately 20% has a complete pathological response, whereas in 20 to 40% the response is poor or absent. **RESULTS:** The following specific gene signature, able to discriminate responders' patients from non-responders, were founded: AKR1C3, CXCL11, CXCL10, IDO1, CXCL9, MMP12 and HLA-DRA. These genes are mainly involved in immune system pathways and interact with drugs traditionally used in the adjuvant treatment of rectal cancer. **DISCUSSION:** The present study suggests that new ideas for therapy could be found not only limited to studying genes differentially expressed between the two groups of patients but deepening the mechanisms, associated to response, in which they are involved. **METHODS:** Gene expression studies performed by: Agostini et al., Rimkus et al. and Kim et al. have been merged through a meta-analysis of the raw data. Gene expression data-sets have been processed using A-MADMAN. Common differentially expressed gene (DEG) were identified through SAM analysis. To further characterize the identified DEG we deeply investigated its biological role using an integrative computational biology approach.

Alba Conejo, E. and J. Exposito Hernandez (2000). "[Physiopathologic knowledge and clinical practice. A case of high dose chemotherapy in breast cancer]." Med Clin (Barc) **114 Suppl 2**: 74-78.

Breast cancer is the major cause of death from cancer in women. This causes a great activity in oncological investigation in this field. During the 80s preclinical data and retrospective analysis suggested a dose-response relationship both for adjuvant treatment and metastatic disease. Technical advances in collection and administration of peripheral stem cells and the development of hematological growth factors permitted the use, in this and other diseases, of high dose chemotherapy, usually with hematological support. All these things produced the widespread use of this technique with the only scientific support of phase II studies usually performed in only one center and with highly selected patients. Most of the randomized trials performed afterwards did not show a clinically important relationship between dose and response. This makes us think that this technique should not be used as routine treatment. From a methodological point of view it would be interesting to investigate the evolution of this modality of treatment and why, its use has been so generalized without good quality scientific support. This could be due to predetermined ideas in relation to what is the evolution and treatment of this disease, the neglect in the use of scientific methodology and the pressures coming from different directions trying to adopt new (and presumably better, treatments). It is evident that if most of the patients who have received high dose treatment for breast cancer had participated in randomized trials the question would probably have already been answered.

Allen, M. R. and S. L. Ruggiero (2014). "A review of pharmaceutical agents and oral bone health: how osteonecrosis of the jaw has affected the field." Int J Oral Maxillofac Implants **29**(1): e45-57.

Just a decade ago, the outlook appeared limitless for the use of bisphosphonates for the treatment of a large number of metabolic bone diseases ranging from osteoporosis to cancer-related bone alterations to oral bone loss. Soon thereafter, however, osteonecrosis of the jaw (ONJ) emerged as a rare but significant condition associated with bisphosphonate treatment. Although many questions remain concerning ONJ, some significant knowledge has been gained over the past decade. Ideas have emerged regarding how to stage and treat the condition, and a number of preclinical models have been developed that will soon begin to speed progress toward understanding the pathophysiology of this condition. Researchers have also discovered that ONJ is not specific to bisphosphonates, as other potent antiremodeling agents have now been associated with

the condition. While antiremodeling agents remain essential tools in medicine, ONJ has somewhat slowed the momentum for this drug class, especially as it relates to new and emerging applications. Until more effective prevention or treatment regimens for ONJ are developed, this side effect of remodeling suppression will continue-for better or worse-to have a significant impact on the field. One potential treatment option may be in the form of osteoanabolics. Exciting new data have emerged demonstrating the efficacy of teriparatide (parathyroid hormone) in reversing oral cavity bone loss and even as a potential therapy for ONJ.

Amano, S. (2017). "[The Framework of the Amended Cancer Control Act]." Gan To Kagaku Ryoho **44**(11): 963-966.

The Cancer Control Act approved in 2006 was amended in December 2016 by the nonpartisan federation of the National Assembly, while meeting the requests from cancer patient groups. In the chapter on the basic ideas, it is said that cancer control needs to advance the development of the social environment that enables cancer patients to run a smooth social life and employment support for cancer patients and promotion of cancer education are newly stated. In the chapter on the basic measures, palliative care, rehabilitation, the research on rare cancer and intractable cancer, the treatment of childhood cancer patients and the improvement of educational environment for those patients, and the support for private organizations and cancer patient groups are newly stated. Regarding cancer genome medical care, new legislation is expected.

Ang, C. Y., et al. (2014). "Recent advances in biocompatible nanocarriers for delivery of chemotherapeutic cargoes towards cancer therapy." Org Biomol Chem **12**(27): 4776-4806.

Cancer is currently one of the major diseases that has gained a lot of scientific attention. Conventional cancer therapeutics involve surgical removal of tumors from patients followed by chemotherapeutic treatment. In the use of anticancer drugs during the chemotherapy process, patients often suffer from a variety of undesirable side effects including damage to normal organs. Thus, there is an urgent need for the development of novel strategies to overcome these side effect issues. Among several strategies, the utilization of nanocarriers for anticancer drug delivery has shown improved therapeutic efficiency of the drugs with minimization of the undesirable side effects. In this review, we discuss various types of nanocarriers recently reported in the literature for application in cancer therapy. We introduce some targeting ligands that have been functionalized on nanocarriers in order to impart specificity to the nanocarriers for targeted drug

delivery. We also highlight some therapeutic cargoes that are commonly used and their therapeutic mechanisms in cancer treatment. Finally, we summarize some interesting stimulus strategies for controlled release of therapeutic cargoes at tumor sites. This review is expected to inspire new ideas and create novel strategies in advancing efficient cancer therapy using nanomedicine approaches.

Assimakopoulos, D., et al. (2003). "Highlights in the evolution of diagnosis and treatment of laryngeal cancer." *Laryngoscope* **113**(3): 557-562.

**OBJECTIVES:** To present selected highlights from the evolution of diagnosis of laryngeal disease and treatment of laryngeal cancer from ancient Greece until the 20th century. **STUDY DESIGN:** Historical study of diagnosis of laryngeal disease and treatment of laryngeal cancer from the ancient Greek medical scriptures until the most recent evolutionary steps in the 20th century. **METHODS:** Original Greek-language texts of ancient and Byzantine medical writers were studied and literature on history of medicine was investigated to reveal early knowledge of diagnostic and therapeutic techniques for laryngeal disease and cancer of the larynx. **RESULTS:** Diseases of the upper aerodigestive tract were known and treated by ancient Greek physicians, and, later, Byzantine doctors, apart from preserving ancient medical concepts, contributed their own ideas, mainly about surgery and postoperative care. The initial therapeutic approach for the disorders caused by laryngeal tumors was either tracheotomy or endotracheal intubation in an attempt to prevent suffocation. In more recent times, construction of the laryngoscope and other modern examination instruments, as well as the final acceptance of histological diagnosis based on tissue biopsy, has allowed for accurate diagnosis and successful treatment of laryngeal lesions. Preoperational biopsy, application of pharyngoesophageal speech and advanced vocal devices for the laryngectomees, and invention of antibiotic and anesthetic agents had led, by the middle of the 20th century, to the establishment of extended and radical surgical techniques as optional treatment for laryngeal cancer. In addition, the discovery of x-rays and radium introduced radiotherapy as an alternative in the treatment procedure for cancer of the larynx. **CONCLUSION:** Progress in the evolution of laryngological diagnosis and practice demanded efforts by many daring and courageous investigators and surgeons, contributing new ideas and techniques in the development of modern laryngology.

Battista, G., et al. (2010). "Latest developments in imaging of bladder cancer." *Expert Rev Anticancer Ther* **10**(6): 881-894.

Despite the development of optic cystoscopy and new imaging techniques, the diagnostic process for bladder cancer is still a matter of debate and imaging management remains a work in progress. This article focuses on imaging of bladder cancer, from cornerstone modalities to new proposals and ideas. The discussion aims to point out and to stress whether techniques are sufficient in the diagnosis, staging and treatment evaluation of bladder cancer, as well as during the follow-up. Advantages, pitfalls and limits of every imaging method used or proposed will be analyzed, not to find 'the truth', but to allow the best optimization of the diagnostic tools available today in clinical practice.

Beuzebec, P. and S. Scholl (2014). "Prevention of Bone Metastases in Breast Cancer Patients. Therapeutic Perspectives." *J Clin Med* **3**(2): 521-536.

One in four breast cancer patients is at risk of developing bone metastases in her life time. The early prevention of bone metastases is a crucial challenge. It has been suggested that the use of zoledronic acid (ZOL) in the adjuvant setting may reduce the persistence of disseminated tumor cells and thereby might improve outcome, specifically in a population of patients with a low estrogen microenvironment. More recently, the results of a large meta-analysis from 41 randomized trials comparing a bisphosphonate (BP) to placebo or to an open control have been presented at the 2013 San Antonio Breast Cancer Meeting. Data on 17,016 patients confirm that adjuvant BPs, irrespective of the type of treatment or the treatment schedule and formulation (oral or intra-venously (IV)), significantly reduced bone recurrences and improved breast cancer survival in postmenopausal women. No advantage was seen in premenopausal women. BPs are soon likely to become integrated into standard practice. Published data on the mechanisms involved in tumor cell seeding from the primary site, in homing to bone tissues and in the reactivation of dormant tumor cells will be reviewed; these might offer new ideas for innovative combination strategies.

Blundell, T. L. (2017). "Protein crystallography and drug discovery: recollections of knowledge exchange between academia and industry." *IUCrJ* **4**(Pt 4): 308-321.

The development of structure-guided drug discovery is a story of knowledge exchange where new ideas originate from all parts of the research ecosystem. Dorothy Crowfoot Hodgkin obtained insulin from Boots Pure Drug Company in the 1930s and insulin crystallization was optimized in the company Novo in the 1950s, allowing the structure to be determined at Oxford University. The structure of renin was developed in academia, on this occasion in London, in response to a need to develop antihypertensives in pharma. The idea

of a dimeric aspartic protease came from an international academic team and was discovered in HIV; it eventually led to new HIV antivirals being developed in industry. Structure-guided fragment-based discovery was developed in large pharma and biotech, but has been exploited in academia for the development of new inhibitors targeting protein-protein interactions and also antimicrobials to combat mycobacterial infections such as tuberculosis. These observations provide a strong argument against the so-called 'linear model', where ideas flow only in one direction from academic institutions to industry. Structure-guided drug discovery is a story of applications of protein crystallography and knowledge exchange between academia and industry that has led to new drug approvals for cancer and other common medical conditions by the Food and Drug Administration in the USA, as well as hope for the treatment of rare genetic diseases and infectious diseases that are a particular challenge in the developing world.

Bray, G. A. (2002). "The underlying basis for obesity: relationship to cancer." *J Nutr* **132**(11 Suppl): 3451S-3455S.

An increase in the risk of cancer is one of the consequences of obesity. The predominant cancers associated with obesity have a hormonal base and include breast, prostate, endometrium, colon and gallbladder cancers. As the basis for understanding the problem of obesity has advanced, a number of new ideas have emerged about the relationship of obesity to cancer. The conversion of androstenedione secreted by the adrenal gland into estrone by aromatase in adipose tissue stroma provides an important source of estrogen for the postmenopausal woman. This estrogen may play an important role in the development of endometrial and breast cancer. Of interest is that experimental animals lacking aromatase or the estrogen receptor alpha are obese. Leptin is one of the many products produced by fat cells and has given rise to the ideas that the fat cell is an endocrine cell and that adipose tissue is an endocrine organ. The increased release of cytokines from this tissue may play a role in the inflammatory state that is associated with obesity. The gut also plays an important role in signaling satiety in response to food intake. Colon cancer is an important human disease, and experimental mice lacking gastrin are obese and have an increased risk of developing colon cancer in response to carcinogenic drugs. Efforts to control obesity through preventive strategies and treatment can be expected to have a benefit in reducing the risk of cancer.

Brodin, N. P., et al. (2015). "Photodynamic Therapy and Its Role in Combined Modality Anticancer Treatment." *Technol Cancer Res Treat* **14**(4): 355-368.

Photodynamic therapy (PDT) is a relatively new modality for anticancer treatment and although the

interest has increased greatly in the recent years, it is still far from clinical routine. As PDT consists of administering a nontoxic photosensitizing chemical and subsequently illuminating the tumor with visible light, the treatment is not subject to dose-limiting toxicity, which is the case for established anticancer treatments like radiation therapy or chemotherapy. This makes PDT an attractive adjuvant therapy in a combined modality treatment regimen, as PDT provides an antitumor immune response through its ability to elicit the release of damage-associated molecular patterns and tumor antigens, thus providing an increased antitumor efficacy, potentially without increasing the risk of treatment-related toxicity. There is great interest in the elicited immune response after PDT and the potential of combining PDT with other forms of treatment to provide potent antitumor vaccines. This review summarizes recent studies investigating PDT as part of combined modality treatment, hopefully providing an accessible overview of the current knowledge that may act as a basis for new ideas or systematic evaluations of already promising results.

Browne, D., et al. (1998). "Oncology services: the Department of Defense perspective." *Cancer* **82**(10 Suppl): 2010-2015.

The Department of Defense (DoD) military health system has responsibility for providing medical care for more than 8 million beneficiaries. This article discusses initiatives related to both the providing and purchasing of oncology services. A description of health care coverage under TRICARE, the Department's managed care program, which utilizes military treatment facilities and civilian health care providers, is provided. Participation in clinical trials by the DoD beneficiaries, oncology services in military treatment facilities, quality management programs, cancer research, and the development of new technologies to enhance early cancer detection are presented. Access to research trials and new technologies is necessary for a comprehensive approach to cancer care. Clinical trials have been the vehicle by which the oncology community developed most of its formal clinical evidence for the efficacy of various treatment approaches. The Department participates in clinical trials through cooperative group membership or affiliation. Through an interagency agreement with the National Cancer Institute, DoD beneficiaries have available the option of participating in NCI-sponsored clinical trials through the direct military care system or through civilian care with reimbursement for approved protocols nationwide. The DoD has been actively involved in breast cancer research since 1992 and prostate and ovarian cancer research since 1997. The goals of the cancer research programs are to expedite and facilitate breakthroughs in research, support innovative, and exploratory ideas with

a vision to foster new directions, address neglected issues, and bring new investigators into the research arena. The program incorporates the consumer perspective by involving consumers in the decision-making process. The DoD health care system trains experts in the management of cancer patients and provides a multidisciplinary approach to care through the direct military health care system or through network providers as part of the TRICARE system. Although cost containment is key, the delivery of high quality health care that is easily accessible is a primary goal of the military health system. Provision of a comprehensive benefits package that includes a spectrum of care and employing outcomes measurements to evaluate care that is appropriate for the patient's disease is essential.

Buyse, M., et al. (2000). "The validation of surrogate endpoints in meta-analyses of randomized experiments." *Biostatistics* **1**(1): 49-67.

The validation of surrogate endpoints has been studied by Prentice (1989). He presented a definition as well as a set of criteria, which are equivalent only if the surrogate and true endpoints are binary. Freedman et al. (1992) supplemented these criteria with the so-called 'proportion explained'. Buyse and Molenberghs (1998) proposed replacing the proportion explained by two quantities: (1) the relative effect linking the effect of treatment on both endpoints and (2) an individual-level measure of agreement between both endpoints. The latter quantity carries over when data are available on several randomized trials, while the former can be extended to be a trial-level measure of agreement between the effects of treatment of both endpoints. This approach suggests a new method for the validation of surrogate endpoints, and naturally leads to the prediction of the effect of treatment upon the true endpoint, given its observed effect upon the surrogate endpoint. These ideas are illustrated using data from two sets of multicenter trials: one comparing chemotherapy regimens for patients with advanced ovarian cancer, the other comparing interferon-alpha with placebo for patients with age-related macular degeneration.

Canderelli, R., et al. (2007). "Benefits of hormone replacement therapy in postmenopausal women." *J Am Acad Nurse Pract* **19**(12): 635-641.

**PURPOSE:** To provide an overview of current research regarding hormone replacement therapy (HRT) and to assist healthcare providers to better educate patients about potential benefits of this therapy. **DATA SOURCES:** A systematic review of healthcare literature was conducted with 602 articles selected from CINAHL, Medscape, Pubmed, and Medline databases. Keywords directing the search included hormone replacement therapy, benefits of hormone replacement therapy and

trends, hormone replacement therapy and osteoporosis, hormone replacement, and menopause symptoms. **CONCLUSIONS:** According to the literature, HRT can assist women with postmenopausal symptoms. In addition, research shows that HRT can help some postmenopausal women with selected comorbid conditions such as osteoporosis, type II diabetes, certain cardiovascular pathologies, and colorectal cancer. The decision as to who should use any form of HRT needs to be based on the individual woman's needs, quality of life, and potential risks versus benefits. **IMPLICATIONS FOR PRACTICE:** HRT has been a benefit to many women in the treatment of postmenopausal symptoms. Recent studies have shown that HRT, whether it is combined estrogen and progestin therapy, or estrogen-only therapy, can help postmenopausal women with osteoporosis and some selected comorbid conditions. Recent research indicates that some women are dying from comorbid conditions rather than breast cancer. Although the research regarding HRT in some areas may be limited, further research adds to existing knowledge and offers new ideas and possibilities in the treatment of postmenopausal symptoms and selected comorbid conditions. Certainly HRT can improve quality of life and possibly longevity for selected women. Ongoing research is needed to further validate such benefits, as well as to further explore the risks and benefits of long-term HRT. Increased knowledge about HRT will help healthcare providers better educate patients about the potential benefits of HRT, while providing documentation about who should take selected types of HRT or whether alternative treatment is preferred.

Caruso, R., et al. (2013). "Report on the 2013 European Multidisciplinary Cancer Congress-ECC 17, Amsterdam, 27 September-1 October 2013: nursing highlights." *Ecancermedicalscience* **7**: 367.

The European Cancer Organisation (ECCO) was founded on the ideas of the former Federation of European Cancer Societies (FECS). The ECCO was officially announced at the European Cancer Conference in Barcelona in September 2007, replacing the FECS as a dynamic new entity. Through its members, the ECCO represents the interests of over 50,000 professionals in oncology. The ECCO continues to expand its outreach and education through its prestigious biennial series of Congresses. This report highlights the nursing contributions at the seventeenth ECCO Congress in Amsterdam. At the congress, there were more than 17,000 professionals involved in the struggle against cancer. A record number of abstracts (3306) were submitted, almost 40% more than the 2011 conference. Related topics during nursing sessions were often aimed at investigating the meaning of the multidisciplinary approach and what it implies for daily

practice under different profiles. The debates showed that the multidisciplinary approach primarily means 'new challenges' for all the practitioners involved. The main challenge for nurses is to meet the needs of a rapidly changing society with some European peculiarities, such as the ageing population, the escalating costs of healthcare in a period of economic crises, fast changing treatments, changes in cancer services and the way nurses deliver care, and multidisciplinary empowerment as a modern concept of care. In this landscape, we also have to consider that cancer often becomes a chronic disease with an increasing number of treatment lines, an increasing number of survivors, and more conscious and exigent patients. We also have to consider the importance of diversity in cancer care.

Caudell, J. J., et al. (2017). "The future of personalised radiotherapy for head and neck cancer." Lancet Oncol **18**(5): e266-e273.

Radiotherapy has long been the mainstay of treatment for patients with head and neck cancer and has traditionally involved a stage-dependent strategy whereby all patients with the same TNM stage receive the same therapy. We believe there is a substantial opportunity to improve radiotherapy delivery beyond just technological and anatomical precision. In this Series paper, we explore several new ideas that could improve understanding of the phenotypic and genotypic differences that exist between patients and their tumours. We discuss how exploiting these differences and taking advantage of precision medicine tools-such as genomics, radiomics, and mathematical modelling-could open new doors to personalised radiotherapy adaptation and treatment. We propose a new treatment shift that moves away from an era of empirical dosing and fractionation to an era focused on the development of evidence to guide personalisation and biological adaptation of radiotherapy. We believe these approaches offer the potential to improve outcomes and reduce toxicity.

Celik, S., et al. (2015). "A Dilemma in Staging of Esophageal Cancer: How Should We Stage ypT0 N2 M0 Esophageal Cancer after Neoadjuvant Therapy?" Case Rep Pathol **2015**: 158626.

Background. Since neoadjuvant treatment in esophageal cancer began to become popular, a complete pathological response at the primary tumour site has been commonly reported. An issue of conflict is whether complete response in the esophageal lumen means that the esophagus is completely tumour-free. Another important issue is whether lymph nodes that are retrieved from pathologically complete response cases are also tumour-free or not. There is a gap in the esophageal cancer staging system for ypT0 N2 M0

tumours that have received neoadjuvant therapy. Here, we will discuss the problem about staging of esophageal cancer associated with neoadjuvant therapy. Case. A female aged 40 years complaining of dysphagia was diagnosed as having locally advanced thoracic esophageal cancer. Neoadjuvant therapy decision was taken by oncology committee. Six weeks after neoadjuvant therapy, with a curative intention, minimal invasive surgery was performed. The pathology report was as follows. "There were no neoplastic cells in the suspected area of the esophageal mucosa upon examination with all staining. There was no cancer at resection margins. Four metastatic lymph nodes were infiltrated with squamous cell cancer." Conclusion. Despite the growing use of neoadjuvant treatment in locally advanced esophageal cancer in world, we do not have a protocol for the evaluation of these patients' pathology reports. We believe that new studies and new ideas are needed to resolve this dilemma associated with neoadjuvant therapy.

Chen, H., et al. (2014). "[Research progress on mechanisms of modern medicine in cancer metastasis]." Zhongguo Zhong Yao Za Zhi **39**(15): 2823-2828.

Cancer metastasis is the most dangerous stage of tumorigenesis and evolution, the primary cause of death in cancer patients. Clinically, more than 60% of cancer patients have found metastasis at the time of examination. Modern medicine has made significant progress on the mechanisms of cancer metastasis in recent years, from the simple "anatomy and machinery" theory forward to the "seed and soil" theory, then to the "microenvironmental" theory and the "cancer stem cell" theory. The emerging "cancer stem cell" theory successfully explains phenomenon such as tumor genetic heterogeneity, anoikis resistance, tumor dormancy, providing more new targets and ideas for the diagnosis and treatment of cancer metastasis.

Chen, T., et al. (2009). "[Therapeutic effect and toxicity of compound vincristine liposome on breast cancer in nude mice]." Sheng Wu Yi Xue Gong Cheng Xue Za Zhi **26**(1): 127-129, 143.

This study was intended to assess the therapeutic effect and toxicity of Compound vincristine liposome on breast cancer in nude mice. The mammary cancer models of BALB/c nude mice were set up using MCF-7 cells, and were divided into seven groups: MTO-VCR-LP, MTO-VCR-Soln, VCR-LP, VCR-Soln, MTO-LP, MTO-Soln and 0.9% NaCl. After the first treatment in the same day of transplantation, different treatments were given respectively. According to the design, the BLAB/c nude mice were given the therapy, the weight of nude mice and tumor volume were measured, and the tumor growth inhibitory rate was calculated. Bone marrow smears and extravasation

injury were observed. The tumor growth inhibitory rates were higher in MTO-VCR-LP and MTO-VCR-Soln groups than in other groups. MTO-VCR-Soln, VCR-Soln and MTO-Soln led to severe local extravasation injury. MTO-VCR-Soln cause serious bone marrow inhibition of nude mice. The average weight of nude mice in the three liposome groups was higher than that in the three solution groups. So the use of liposome as the carriers of the two anticancer drugs could improve the cure rate of cancer and decrease the side-effects. This work, which not only expanded the research field of liposome but also brought in new ideas and new methods to treat cancer. Furthermore, the findings in this research may have the potential for use in clinical practice.

Cheng, J., et al. (2016). "Study on the relationship between the structure and functions of anti-human cervical cancer single-chain antibody and the lengths of linkers." *Eur J Gynaecol Oncol* **37**(2): 171-177.

**BACKGROUND:** This study aimed to find the linker with minimal impact among chains to fight against the structure and function of cervical cancer (CC) single-chain antibody. **MATERIALS AND METHODS:** The original variable region of heavy chain (VH) and variable region of light chain (VL), and the single-chain antibody with linkers of different lengths ( $n = 1-8$ ) were modeling by homologous modeling, while the peptide chain structure of  $(\text{Gly}_4\text{Ser})_n$  was utilized by the linkers. Comparison of the similarity of original VH/VL and  $\text{VH}_n/\text{VL}_n$  was carried out by applying the algorithm of spatial hierarchical alignment based on the spherical coordinates. The fore and aft distance and diffusion radius of alpha ( $\alpha$ ) were also calculated. The stability of antibody with different linker length was then compared. ELISA method was adopted to evaluate the immunological activity of single-chain antibody with different linkers. MTT assay was used to analyze the inhibition effect of ScFv- $n$  on CC cells. **RESULTS:** When  $n = 4$ , the structures were the most similar between ScFv and the original VH/VL. When  $n = 3$ , the influence of adding connecting peptide on the stability of single-chain antibody was the least. The result of ELISA and MTT methods indicated that when  $n = 3$ , single-chain antibody gained the highest activity. **CONCLUSION:** The optimum length of linker of anti-human CC single-chain antibody was  $n = 3$  from the point of mathematical modeling and biology experiments. This study provided new ideas for the design and constructions of single-chain antibody, and theoretical basis for the treatment of CC.

Cheng, X. Y. and H. Shen (2018). "[Circular RNA in Lung Cancer Research: Biogenesis, Functions and Roles]." *Zhongguo Fei Ai Za Zhi* **21**(1): 50-56.

Lung cancer is the most commonly diagnosed cancer and the leading cause of cancer death in China. In recent years, therapies for oncogenedriviers and immune checkpoints have proved inspiring. Circular RNA (circRNA), which is a kind of RNA with covalent ring structure relating to stages and metastasis of cancer, has many special biological functions in physiological processes, diseases and so on. Thus, circRNA is expected to be a potential biomarker for cancer prediction and treatment in view of its high conservation and tissue-specific. However, function analysis and regulatory mechanism of circRNA in lung cancer come so far remains unclear and limited literatures are available. In this review, we highlight the research history, formation mechanism, biological function of circRNA and research progress in cancer, especially in lung cancer. We mean to provide theoretical evidences and new ideas for researches on circRNAs in lung cancer.

Chopra, S., et al. (2012). "Robotic radical prostatectomy: The new gold standard." *Arab J Urol* **10**(1): 23-31.

**OBJECTIVES:** Open radical prostatectomy (RP) has been the standard and primary treatment for focal prostate cancer. However, in recent years this view has changed, as robot-assisted laparoscopic RP has gained acceptance among urologists. In this review we evaluate the importance and place of robotics in laparoscopic urological surgery, discussing several techniques that are currently being used and potentially new techniques that might be used in the future. **METHODS:** We systematically reviewed papers published between 1998 and 2011 using the keywords 'robotic prostatectomy' 'gold standard' and the Medline database. In addition, after selecting relevant reports we searched 'related citations' of the documents to find further supporting published papers. **RESULTS:** In all, 50 original papers were identified using the search criteria; we also found 28 through 'related citations' browsing. Papers were selected according to their relevance to the current topic (i.e. RP, original articles) and incorporated into this review. These papers were used for their information on the advantages of using robotics, as well as innovative ideas being used in the field of robotic urological surgery. **CONCLUSION:** Almost a decade after the first robotic RP many reports show the benefits and advantages of incorporating robotics into urological surgery. Robotic surgery decreases the learning curve necessary for surgeons when compared with laparoscopic techniques. In addition, patients prefer robotics, as the procedure is less invasive, diminishes the duration of hospitalisation and speeds the return to function.

Cinieri, S., et al. (2007). "Adjuvant strategies in breast cancer: new perspectives, questions and reflections at the end of 2007 St Gallen International Expert Consensus Conference." *Ann Oncol* **18 Suppl 6**: vi63-65.

Breast cancer detection and staging are constantly evolving as technologies improve. Breast cancer surgery is also undergoing continuous refinement, with the objective being to achieve optimal cosmetic results. Surgery has been combined with intraoperative radiation therapy to achieve the best local-disease control with minimal side-effects. The adjuvant strategy of treatment is a 'hot' issue in this 'scenario'. Every 2 years at St Gallen, a nice and cold town in the north of Switzerland, more of 4000 breast cancer experts arrive from every part of the world, to improve their knowledge in this issue. The Consensus Conference with the discussion of 40 international panelists is the zenith of the conference. This report provides a brief presentation and reflections, immediately at the end of the conference, with the objective being to stimulate ideas regarding what should be done tomorrow.

Clarke, N. S., et al. (2006). "Chemo-prevention in superficial bladder cancer using mitomycin C: a survey of the practice patterns of British urologists." *BJU Int* **97(4)**: 716-719.

**OBJECTIVE:** To assess the use of mitomycin C, by urologists within the UK, as a single-dose intravesical agent. Current European recommendations are to use one dose after any new tumour resection. **METHODS:** We assessed the current patterns of mitomycin C usage amongst British urologists, particularly with reference to one instillation after resecting a new bladder tumour, hypothesizing that British urologists would use mitomycin C in line with current guidelines. A one-page questionnaire was mailed to 527 consultant urologists in the UK enquiring about their use of mitomycin C in superficial bladder cancer. A second mailing was sent to encourage nonresponders. **RESULTS:** Of the 527 consultants, 320 (61%) replied, of which 313 (59%) questionnaires were evaluable. Of these 313 respondents, 299 (95%) used mitomycin C; 244 respondents (82%) advocated the use of one dose of mitomycin C after resecting a new tumour, but only 10 (4%) would use it immediately after tumour resection and 155 (64%) use it within 24 h. Most (98%) respondents favoured the use of a mitomycin C course after resecting multiple tumours or after multiple recurrences. Interestingly, 20 respondents (7%) would use mitomycin C as a first-line therapy for carcinoma in situ and a further 23 (8%) would use it for G3T1 tumours. A minority (14%) would use it after nephrectomy for upper tract transitional cell carcinoma. Almost all respondents indicated a dose of 40 mg in 40

mL of diluent. Maintenance treatment with mitomycin C was advocated by 44 (15%) of respondents, mainly for recurrent multifocal Ta/T1 tumours. The perception of the side-effects of mitomycin C was favourable, with 69% of respondents judging mitomycin C to be well tolerated with mild side-effects. **CONCLUSION:** Urologists adopt new ideas rapidly, as shown by the wide acceptance of the UK Medical Research Council study. The prompt use of mitomycin C needs to be reinforced, as efficacy is optimum within 6 h of resection. A few consultants persist in continuing with established practices, which have little evidence base. The publication of such survey results, with guidelines for treatment, should encourage those urologists whose practice is at variance from the norm to reflect on and change their practice.

Comanescu, M. and G. Bussolati (2014). "Cancer stem cells biomarkers in triple negative invasive carcinoma of the breast and associated in situ lesions." *Rom J Morphol Embryol* **55(2 Suppl)**: 569-574.

Triple negative breast cancer (TNBC) [negative for expression of estrogen and progesterone receptors (ER, PR) and HER2/neu protein] represent a subtype of breast cancer associated with poor prognosis and highly aggressive behavior. The characterization of stem cell in this type of carcinoma could determine the appearance of new ideas concerning origin and evolution. There is an impressive amount of data in the literature related to TNBC and a growing interest for stem cell research during the past years, but there are no data concerning the genetic characterization of stem cells in the context of cell biology of TNBC as compared with associated DCIS. We performed immunohistochemical studies for the expression and distribution of several stem cell-related antigens, focusing on the association of TNBC with DCIS and comparing the presence of stem cells in the invasive and in the in situ component. Optimization of detection, identification and characterization of tumorigenic breast cancer stem cells might permit further identification of targeted treatment.

Conti, A. (2000). "Oncology in neuroimmunomodulation. What progress has been made?" *Ann N Y Acad Sci* **917**: 68-83.

In 1987 in Dubrovnik, Yugoslavia, N.H. Spector named a new discipline: Neuroimmunomodulation. R. Ader called this new discipline psychoneuroimmunomodulation when the major emphasis was on its behavioral aspects. Neuroimmunomodulation (NIM) is devoted to the study of the interactions at different morphologic and functional levels among the immune, nervous, and endocrine systems. In fact, this science is the modern manifestation of an old science: in the words of B.D.



Jankovic (1987), "Neuroimmunomodulation is a modern reflection in neurosciences and immunosciences of the ideas and experience of philosophers and ingenious observers of ancient Egypt, Greece, China, India, and other civilizations that the mind is involved in the defense against diseases." Twelve years ago NIM was regarded by many conventional scientists almost as a form of witchcraft. Today it may be the fastest growing area of biomedical science research in the world. Important clinical applications will not be far behind. NIM research has also progressed in the field of oncology research. Topics such as treatment of hormone-dependent cancer with analogues of hypothalamic hormones, the role of opioids and T cells in cancer, stress-cancer-immune connections, the anticancer role of melatonin and cytokines, immunotherapy of cancer, and the role of psychotherapy in cancer patients represent some lines of research that have been or are being investigated by scientists. Some areas remain to be thoroughly investigated such as the influence of physical exercise (sports), music (classical or modern), and/or relaxation techniques (e.g. yoga) on the development of human cancer. This paper reviews the role of NIM in oncology and provides some perspectives for further research and development of clinical applications.

Cui, J., et al. (2012). "Systems biology in the frontier of cancer research: a report of the Second International Workshop of Cancer Systems Biology." *Chin J Cancer* **31**(9): 409-412.

The report summarizes the Second International Workshop of Cancer Systems Biology held on July 5-6, 2012 in Changchun, China. The goal of the workshop was to bring together cancer researchers with different backgrounds to share their views about cancer and their experiences in fighting against cancer, and to gain new and systems-level understanding about cancer formation, progression, diagnosis, and treatment through exchanging ideas.

da Luz Moreira, A., et al. (2009). "The evolution of prophylactic colorectal surgery for familial adenomatous polyposis." *Dis Colon Rectum* **52**(8): 1481-1486.

**INTRODUCTION:** Over the past 50 years, prophylactic colorectal surgery for patients with familial adenomatous polyposis has evolved as new technologies and ideas have emerged. The aim of this study was to review all the index surgeries for familial adenomatous polyposis performed at our institution to assess the changes in surgical techniques. **METHODS:** All index abdominal surgeries for polyposis from 1950 to 2007 were identified through the Polyposis Registry Database. We assigned the patients to prepouch (before 1983), pouch (after 1983), and laparoscopic (after 1991)

eras, and analyzed the changes in prophylactic surgery. **RESULTS:** Four hundred twenty-four patients were included; 51% were male. Median age at surgery was 26 (range, 9-66) years. In the prepouch era, 97% (66 of 68) of all surgeries and 100% of restorative surgeries were ileorectal anastomosis. After 1983, 70% (54 of 77) of patients with a severe phenotype had an ileal pouch-anal anastomosis. After 1991, 110 operations (43%) were laparoscopic (88 ileorectal and 22 ileal pouch-anal anastomosis). **CONCLUSION:** Colon surgery for familial adenomatous polyposis has evolved as advances in surgical technique have created more options to reduce the risk of cancer. Current strategy uses polyposis severity and distribution to decide on the surgical option, and laparoscopy to minimize morbidity.

Dahan, J. F. and C. F. Auerbach (2006). "A qualitative study of the trauma and posttraumatic growth of multiple myeloma patients treated with peripheral blood stem cell transplant." *Palliat Support Care* **4**(4): 365-387.

**OBJECTIVE:** The study was conducted to understand the emotional impact of multiple myeloma, as well as the impact of its principle treatment, peripheral blood stem cell transplant (PBSCT). The absence of psycho-oncology research literature on this population prompted the need for a hypothesis-generating investigation. Thus, a qualitative design was used to construct a theoretical model of the trauma relating to diagnosis and treatment of myeloma. The study also incorporates the important period of reflection and growth following treatment. **METHODS:** The sample consisted of 3 women and 3 men treated for myeloma at a New York City-based cancer treatment center. Data from individual interviews were audiotaped and transcribed. After extensive review, the data were categorized into groups of repeating ideas, themes and broad theoretical constructs. **RESULTS:** A five-construct model emerged from the data analysis that integrated a model of trauma and growth presented in earlier work (Auerbach et al., 2006). These constructs roughly correspond with stages of illness, but do not necessarily imply a linear process, as suggested by stage models. The first construct is diagnosis. Patients receive the news that they have multiple myeloma. Initial reactions are discussed and a treatment plan takes form. In the second construct, treatment, patients highlight the physical and emotional hurdles confronted throughout treatment. The third construct, network of safety, presents social factors that play a role in comforting patients throughout illness. Patients recognize the importance of a strong support system during their experiences. In the fourth construct, recuperation, physical energy is regained after an arduous recovery period. This contributes to higher spirits and a motivation to reengage with life. The fifth construct is

reflection and new existence. Patients strive to balance a new reality that relapse and death are inevitable, along with their need to live a meaningful life. Many do not yet appreciate how their disease has impacted them, but describe how their interpersonal lives and perceptions have changed, both positively and negatively. SIGNIFICANCE OF RESULTS: Limitations of the study, future directions for research and clinical implications are discussed.

Dalton, J. A., et al. (1998). "An examination of nursing attitudes and pain management practices." *Cancer Pract* **6**(2): 115-124.

**PURPOSE:** The purpose of this evaluation is to examine the relationship among nurses' pain management attitudes and pain management practices and to begin to explore the theoretical underpinnings that may influence this relationship. **DESCRIPTION OF STUDY:** A convenience sample of 29 female registered nurses working in hospice or home health settings participated in an educational program 1 day per week for 6 weeks. All participants were asked to complete the Cancer Pain Knowledge Inventory and Survey of Expectations and Pain Assessment Questionnaire 5 weeks before, immediately before, immediately after, 6 months after, and 12 months after the program. Seventeen participants completed all questionnaires at the 6-month follow-up; 16 participants completed all questionnaires at the 1-year follow-up. Personal beliefs about pain were evaluated in relation to the dimensions and treatment of pain. Intentions and expectations to perform specific activities were evaluated in relation to in-depth assessments, equianalgesic conversions, demonstration of new ideas, and communication. **RESULTS:** Nurses' attitudes, beliefs, intentions, and expectations about pain and pain management influenced nurses' patient care and educational activities. Nurses who believed that patients should be pain free and nurses who focused on both the dimensions and treatment of pain implemented more pain management activities. In general, nurses who had high intentions and expectations performed more pain management activities. **CLINICAL IMPLICATIONS:** Although nurses reported change in attitude, and high expectancy for change, feelings of increased credibility, and increased motivation as advocates for new approaches to practice, nurses sometimes found it difficult to implement new practices because of constraints in time and collaborative efforts. To implement new knowledge and achieve individualized goals for change, nurses must be allowed adequate time to analyze the relationships between their beliefs about pain and the ways that they solve patients' pain problems. In addition, more support for multidisciplinary collaboration is needed.

Dan, X. L. and T. B. Ng (2013). "Lectins in human cancer: both a devil and an angel?" *Curr Protein Pept Sci* **14**(6): 481-491.

Lectins are a group of proteins which could recognize different sugar structures and specifically initiate reversible binding with them. Lectins are universally expressed in different organisms and undertake important biological roles. Understanding of their inherent roles and mechanisms that they employ has inspired researches with new ideas and applications. For example, along with the revelation of their anti-insect function, plant lectins exhibit great potential in agriculture. In human beings, lectins shoulder great missions in cell communication, differentiation and vesicle trafficking etc., aberrant expression of lectins is always associated with diseases. Mannan-binding lectin deficiency leads to immune disorder and liver sinusoidal endothelial cell lectin is involved in colorectal carcinoma liver metastasis. In this review, we present two contradictory roles of lectins in human cancer: the promotive roles of homologous lectins and suppressive roles of heterologous lectins in cancer development. Hopefully, this review will facilitate a better understanding of tumorigenesis and provide references for cancer treatment.

D'Andrea, V., et al. (2014). "Cancer stem cells in surgery." *G Chir* **35**(11-12): 257-259.

The Cancer Stem Cells (CSC) hypothesis is based on three fundamental ideas: 1) the similarities in the mechanisms that regulate self-renewal of normal stem cells and cancer cells; 2) the possibility that tumour cells might arise from normal stem cells; 3) the notion that tumours might contain 'cancer stem cells' - rare cells with indefinite proliferative potential that drive the formation and growth of tumours. The roles for cancer stem cells have been demonstrated for some cancers, such as cancers of the hematopoietic system, breast, brain, prostate, pancreas and liver. The attractive idea about cancer stem cell hypothesis is that it could partially explain the concept of minimal residual disease. After surgical macroscopically zero residual (R0) resections, even the persistence of one single cell nestling in one of the so called "CSCs niches" could give rise to distant relapse. Furthermore the metastatic cells can remain in a "dormant status" and give rise to disease after long period of apparent disease free. These cells in many cases have acquired resistance traits to chemo and radiotherapy making adjuvant treatment vain. Clarifying the role of the cancer stem cells and their implications in the oncogenesis will play an important role in the management of cancer patient by identifying new prospective for drugs and specific markers to prevent and monitoring relapse and metastasis. The identification of the niche where the CSCs reside in a dormant status might represent a valid instrument to

follow-up patients also after having obtained a R0 surgical resection. What we believe is that if new diagnostic instruments were developed specifically to identify the localization and status of activity of the CSCs during tumor dormancy, this would lead to impressive improvement in the early detection and management of relapse and metastasis.

Day, R. S. (2015). "What Tumor Dynamics Modeling Can Teach us About Exploiting the Stem-Cell View for Better Cancer Treatment." *Cancer Inform* **14**(Suppl 2): 25-36.

The cancer stem cell hypothesis is that in human solid cancers, only a small proportion of the cells, the cancer stem cells (CSCs), are self-renewing; the vast majority of the cancer cells are unable to sustain tumor growth indefinitely on their own. In recent years, discoveries have led to the concentration, if not isolation, of putative CSCs. The evidence has mounted that CSCs do exist and are important. This knowledge may promote better understanding of treatment resistance, create opportunities to test agents against CSCs, and open up promise for a fresh approach to cancer treatment. The first clinical trials of new anti-CSC agents are completed, and many others follow. Excitement is mounting that this knowledge will lead to major improvements, even breakthroughs, in treating cancer. However, exploitation of this phenomenon may be more successful if informed by insights into the population dynamics of tumor development. We revive some ideas in tumor dynamics modeling to extract some guidance in designing anti-CSC treatment regimens and the clinical trials that test them.

de Kok, M., et al. (2008). "Implementation of an ultra-short-stay program after breast cancer surgery in four hospitals: perceived barriers and facilitators." *World J Surg* **32**(12): 2541-2548.

**BACKGROUND:** The objective of this study was to identify barriers and facilitators that professionals see when implementing a program incorporating ultra-short hospital admission in the treatment of breast cancer. Such an intervention is an essential step when designing a strategy for implementation of a care program that is different from established daily routines. **METHODS:** In a prospective quasi-experimental study qualitative data were collected from four hospitals in the Netherlands between January 2005 and July 2006. Potential barriers and facilitators for successful implementation were extracted from detailed notes of all contacts between the researchers and each participating hospital. Subsequently, these items were categorized according to themes. **RESULTS:** Over 40 items were identified. Most barriers concerned organizational and program-related aspects, whereas the most common facilitators addressed organizational issues. Six of the 29

study recommendations were perceived as impeding or facilitating. Thirty of the 40 barriers were mentioned in one hospital only. Several key factors were found that determine the success of implementation of an ultrashort-stay program. Provision of care in the home setting should be assured. Policy makers and insurance companies should acknowledge that multidisciplinary care teams and teams integrating primary and secondary care fulfill important roles in delivering continuity of care. Specific strategies should be set out to convince everybody in the organization about the new ideas, particularly the minority of people who do not agree with the plans. **CONCLUSIONS:** A set of barriers and facilitators for implementation of the program was described that may be used by any professional preparing to perform breast cancer surgery in an ultrashort-stay facility. The systematic approach that led to this set may be used by any healthcare professional concerned with implementation and consolidation of innovative programs in healthcare in order to enhance the effectiveness of the chosen strategy.

Delbar, V. (1999). "From the desert: transcultural aspects of cancer nursing care in Israel." *Cancer Nurs* **22**(1): 45-51.

Quality of life perceptions, the meaning of cancer perception, and the meaning of illness are culture bound. Culture includes learned and shared ways of interpreting the world and interacting in society, and thereby provides all individuals with ideas about what is good or bad, desirable or undesirable, valued or devalued in life. Israel is an immigration country, and its citizens came from all over the world. It is also a meeting zone between Middle Eastern traditional culture and Western modern medicine. Cancer patients and a substantial proportion of doctors, nurses, and other health care professionals are from different ethnic backgrounds. In hospitals, clinics, and other places where health professionals live, work, or relax, there is a network of cultural factors that plays an important role in the well-being of patients. Cultural effects can considerably complicate the assessment of how an individual is likely to react to various aspects of the hospital environment, medical condition, treatment, staff, fellow patients, and so on. Ideal management includes the foresight to forestall problems that may arise and to create favorable psychosomatic effects that help patients to respond positively to treatment. To illustrate the cultural component in nursing care, four cancer patients from totally different cultural backgrounds are described: a bedouin, an Israeli-born Jew whose parents immigrated from Tunisia, and two immigrant patients, one from the United States and the other from Ethiopia. All four patients were treated by chemotherapy, radiation, or both in an oncology day-care unit at the Soroka Medical Center in Beer-Sheva.

Also, a special education program for immigrant nurses is presented, as well as a new immigrant nurse from the former Soviet Union.

Downward, J. (2015). "RAS Synthetic Lethal Screens Revisited: Still Seeking the Elusive Prize?" *Clin Cancer Res* **21**(8): 1802-1809.

The RAS genes are critical oncogenic drivers activated by point mutation in some 20% of human malignancies. However, no pharmacologic approaches to targeting RAS proteins directly have yet succeeded, leading to suggestions that these proteins may be "undruggable." This has led to two alternative indirect approaches to targeting RAS function in cancer. One has been to target RAS signaling pathways downstream at tractable enzymes such as kinases, particularly in combination. The other, which is the focus of this review, has been to seek targets that are essential in cells bearing an activated RAS oncogene, but not those without. This synthetic lethal approach, while rooted in ideas from invertebrate genetics, has been inspired most strongly by the successful use of PARP inhibitors, such as olaparib, in the clinic to treat BRCA defective cancers. Several large-scale screens have been carried out using RNA interference-mediated expression silencing to find genes that are uniquely essential to RAS-mutant but not wild-type cells. These screens have been notable for the low degree of overlap between their results, with the possible exception of proteasome components, and have yet to lead to successful new clinical approaches to the treatment of RAS-mutant cancers. Possible reasons for these disappointing results are discussed here, along with a reevaluation of the approaches taken. On the basis of experience to date, RAS synthetic lethality has so far fallen some way short of its original promise and remains unproven as an approach to finding effective new ways of tackling RAS-mutant cancers. *Clin Cancer Res*; **21**(8); 1802-9. (c)2015 AACR. See all articles in this CCR Focus section, "Targeting RAS-Driven Cancers."

Dubey, K. K., et al. (2017). "Biotherapeutic potential and mechanisms of action of colchicine." *Crit Rev Biotechnol* **37**(8): 1038-1047.

Cancer is a clinical situation caused by uncontrolled cell division and is responsible for a large number of deaths worldwide. Colchicine is a classical antimetabolic, tubulin-binding agent (TBA) which is being explored for its antitumor activities, although its tubulin-binding ability leads to some toxicity toward normal cells proliferation. Colchicine derivatives are considered as potent antitumor compounds with less toxicity compared to colchicine. Derivatives with substituted functional groups at A-ring (methoxy), B-ring (acetamide) or C-ring (methoxy) have been synthesized via chemical and microbial routes and show modified

bioactivities and altered tropolonic functionality. Earlier reports, in combination with our group's research findings, suggest that microbial biotransformation is an efficient choice for the production of bioactive colchicine derivatives. This route has gained significant interest in the mass production of regio-specific, cost-effective, safe and eco-friendly derivatives. The present review paper critically analyzes and discusses the development and application of colchicine derivatives as a potent antitumor molecule and their production through a microbial transformation process. The information provided in this review might assist in the stimulation of new ideas regarding the development of alternative therapeutic agent(s) for cancer treatment.

Dy, G. K. and A. A. Adjei (2008). "Systemic cancer therapy: evolution over the last 60 years." *Cancer* **113**(7 Suppl): 1857-1887.

The 1940s marked the beginning of an era of important discoveries that contributed to modern concepts underlying the current practice of cancer chemotherapy, such as the log kill hypothesis reported by Skipper, the Norton-Simon hypothesis, and the Goldie-Coldman hypothesis. The early success of nitrogen mustards and antifolates in the treatment of hematologic malignancies paved the way for drug discovery platforms, which resulted in the generation of more drugs that nonetheless predominantly are genotoxic. The turn of the new millennium marked a new phase in the evolution of cancer chemotherapy. Scientific progress in the preceding 60 years elucidated the important ideas behind tumor microenvironment and 'targeted' therapy that had their inception in the late 19th century. Breakthroughs in molecular biology have paved the way for the development of novel agents that modulate the dysregulated molecular pathways implicated in carcinogenesis. The key approaches and evidence pertinent to the clinical development of these novel agents are presented in this review.

Dziegielewska, B., et al. (2014). "T-type calcium channels blockers as new tools in cancer therapies." *Pflugers Arch* **466**(4): 801-810.

T-type calcium channels are involved in a multitude of cellular processes, both physiological and pathological, including cancer. T-type channels are also often aberrantly expressed in different human cancers and participate in the regulation of cell cycle progression, proliferation, migration, and survival. Here, we review the recent literature and discuss the controversies, supporting the role of T-type Ca(2+) channels in cancer cells and the proposed use of channels blockers as anticancer agents. A growing number of reports show that pharmacological inhibition or RNAi-mediated downregulation of T-type channels leads to inhibition of cancer cell proliferation and

increased cancer cell death. In addition to a single agent activity, experimental results demonstrate that T-type channel blockers enhance the anticancer effects of conventional radio- and chemotherapy. At present, the detailed biological mechanism(s) underlying the anticancer activity of these channel blockers is not fully understood. Recent findings and ideas summarized here identify T-type Ca(2+) channels as a molecular target for anticancer therapy and offer new directions for the design of novel therapeutic strategies employing channels blockers. Physiological relevance: T-type calcium channels are often aberrantly expressed or deregulated in cancer cells, supporting their proliferation, survival, and resistance to treatment; therefore, T-type Ca(2+) channels could be attractive molecular targets for anticancer therapy.

Faena, I., et al. (2014). "Cytoreductive prostatectomy: evidence in support of a new surgical paradigm (Review)." *Int J Oncol* **45**(6): 2193-2198.

Prostate cancer (PCa) remains the second ranked cause of cancer deaths in the United States. The current standard of care for metastatic prostate cancer (mPCa) includes systemic therapies with no option for surgery. In contrast, in other malignancies such as breast and kidney cancer, cyto-reduction plays an integral role in the treatment of metastatic disease. In this framework, there are emerging data that suggest a potential oncologic benefit to cyto-reduction in mPCa. The majority of the data are retrospective in nature suggesting that patients with mPCa who had prior radical prostatectomy (RP) had a better survival, as well as improved response to systemic therapy. Similarly, patients who presented with metastatic disease and received definitive local therapy (RP or radiation) had greater survival than patients who received no treatment. In order to confer maximum potential benefit, operating in the setting of mPCa must be technically feasible with acceptable morbidity. It has been demonstrated in many studies that operating on locally advanced disease (T3a/b) does have similar morbidity as lower stage cancer. This may be applicable in the metastatic setting, because although PCa may have metastasized, it may remain locally advanced. On the molecular level there are a number of explanations concerning the potential benefit of cyto-reduction. However, these ideas remain speculative with no concrete evidence to date.

Falana, K., et al. (2015). "Short Course in the Microbiome." *J Circ Biomark* **4**: 8.

Over the past decade, it has become evident that the microbiome is an important environmental factor that affects many physiological processes, such as cell proliferation and differentiation, behaviour, immune function and metabolism. More importantly, it may contribute to a wide variety of diseases, including

cancer, inflammatory diseases, metabolic diseases and responses to pathogens. We expect that international, integrative and interdisciplinary translational research teams, along with the emergence of FDA-approved platforms, will set the framework for microbiome-based therapeutics and diagnostics. We recognize that the microbiome ecosystem offers new promise for personalized/precision medicine and targeted treatment for a variety of diseases. The short course was held as a four-session webinar series in April 2015, taught by pioneers and experts in the microbiome ecosystem, covering a broad range of topics from the healthy microbiome to the effects of an altered microbiome from neonates to adults and the long term effects as it is related to disease, from asthma to cancer. We have learned to appreciate how beneficial our microbes are in breaking down our food, fighting off infections and nurturing our immune system, and this information provides us with ideas as to how we can manipulate our microbiome to prevent certain diseases. However, given the variety of applications, there are scientific challenges, though there are very promising areas in reference to the clinical benefits of understanding more about our microbiome, whether in our gut or on our skin: the outlook is bright. A summary of the short course is presented as a meeting dispatch.

Farrow, B., et al. (2008). "The role of the tumor microenvironment in the progression of pancreatic cancer." *J Surg Res* **149**(2): 319-328.

Pancreatic cancer is the most lethal abdominal malignancy due to its aggressive growth and rapid development of distant metastases, thus making treatment extremely difficult. Additionally, pancreatic adenocarcinoma is locally invasive, surrounded by a dense desmoplastic reaction which can involve adjacent vital structures, limiting the number of patients who are candidates for surgical resection at the time of diagnosis. Recently the tumor microenvironment in other adenocarcinomas has been determined to be an important mediator of cancer cell behavior; however, few studies have elucidated the tumor-stroma interactions in pancreatic cancer. This review summarizes the role of pancreatic stellate cells, perineural invasion, angiogenesis, and inflammatory cells in fostering pancreatic cancer cell growth and invasion. The importance of extracellular matrix proteins, growth factors, and cytokines is also presented. Finally we suggest ideas for new avenues of research into the pancreatic tumor microenvironment which may permit the development of novel, more effective treatments for pancreatic cancer.

Fehniger, T. A., et al. (2002). "Interleukin-2 and interleukin-15: immunotherapy for cancer." *Cytokine Growth Factor Rev* **13**(2): 169-183.

Interleukin (IL)-2 and IL-15 are two cytokine growth factors that regulate lymphocyte function and homeostasis. Early clinical interest in the use of IL-2 in the immunotherapy of renal cell carcinoma and malignant melanoma demonstrated the first efficacy for cytokine monotherapy in the treatment of neoplastic disease. Advances in our understanding of the cellular and molecular biology of IL-2 and its receptor complex have provided rationale to better utilize IL-2 to expand and activate immune effectors in patients with cancer. Exciting new developments in monoclonal antibodies recognizing tumor targets and tumor vaccines have provided new avenues to combine with IL-2 therapy in cancer patients. IL-15, initially thought to mediate similar biological effects as IL-2, has been shown to have unique properties in basic and pre-clinical studies that may be of benefit in the immunotherapy of cancer. This review first summarizes the differences between IL-2 and IL-15 and highlights that better understanding of normal physiology creates new ideas for the immunotherapy of cancer. The application of high, intermediate, and low/ultra low dose IL-2 therapy in clinical trials of cancer patients is discussed, along with new avenues for its use in neoplastic diseases. The growing basic and pre-clinical evidence demonstrating that IL-15 may be useful in immunotherapy approaches to cancer is also presented.

Fejerskov, O. (2004). "Changing paradigms in concepts on dental caries: consequences for oral health care." *Caries Res* **38**(3): 182-191.

Kuhn proposed in his *Structure of Scientific Revolutions* (1962) that the theoretical framework of a science (paradigm) determines how each generation of researchers construes a causal sequence. Paradigm change is infrequent and revolutionary; thereafter previous knowledge and ideas become partially redundant. This paper discusses two paradigms central to cariology. The first concerns the most successful caries-preventive agent: fluoride. When it was thought that fluoride had to be present during tooth mineralisation to 'improve' the biological apatite and the 'caries resistance' of the teeth, systemic fluoride administration was necessary for maximum benefit. Caries reduction therefore had to be balanced against increasing dental fluorosis. The 'caries resistance' concept was shown to be erroneous 25 years ago, but the new paradigm is not yet fully adopted in public health dentistry, so we still await real breakthroughs in more effective use of fluorides for caries prevention. The second paradigm is that caries is a transmittable, infectious disease: even one caused by specific microorganisms. This paradigm would require caries prevention by vaccination, but there is evidence that caries is not a classical infectious disease. Rather it results from an ecological shift in the tooth-surface

biofilm, leading to a mineral imbalance between plaque fluid and tooth and hence net loss of tooth mineral. Therefore, caries belongs to common 'complex' or 'multifactorial' diseases, such as cancer, cardiovascular diseases, diabetes, in which many genetic, environmental and behavioural risk factors interact. The paper emphasises how these paradigm changes raise new research questions which need to be addressed to make caries prevention and treatment more cost-effective.

Feng, T., et al. (2017). "Cross-talk mechanism between endothelial cells and hepatocellular carcinoma cells via growth factors and integrin pathway promotes tumor angiogenesis and cell migration." *Oncotarget* **8**(41): 69577-69593.

Tumor angiogenesis plays a central role in the development and metastasis of hepatocellular carcinoma. Cancer cells secrete angiogenic factors to recruit vascular endothelial cells and sustain tumor vascular networks, which facilitate the migration and invasion of cancer cells. Therefore, the cross-talk between vascular endothelial cells and cancer cells is vitally necessary, however, little is known about the cross-talk mechanism of these cells interaction. In the present study, the proliferation, migration, invasion and tube formation of vascular endothelial EA.hy926 cells and hepatocellular carcinoma HepG2 cells were studied by exchanging their culture medium. The time-dependent differences of integrins induced signaling pathway associated with cell migration were investigated. Our results showed that HepG2 cells markedly enhanced the proliferation and migration ability as well as the tube formation of EA.hy926 cells by releasing growth factors. Also, the EA.hy926 cells promoted the proliferation, migration and invasion ability of HepG2 cells. The further analysis demonstrated that the integrins-FAK-Rho GTPases signaling events in both of two cells was activated under conditioned medium, and the signaling molecules in two cell lines showed a different time-dependent expression within 1h. These findings reveal the cross-talk mechanism between the endothelial cells and hepatocellular carcinoma cells, which were expected to find out new ideas for the prevention and treatment of hepatocellular carcinoma.

Folkman, J. (1995). "The influence of angiogenesis research on management of patients with breast cancer." *Breast Cancer Res Treat* **36**(2): 109-118.

The diagnosis and treatment of patients with breast cancer is beginning to be influenced by new ideas and discoveries emerging from the field of angiogenesis research. This field, pursued in the laboratory for more than 20 years, has in the past 5 years generated clinical applications. Some of these applications have begun to

change current thinking about cancer patients and especially about those with breast cancer. I here discuss how an understanding of the process of angiogenesis may contribute to improved management of patients with breast cancer.

Gallego, O. and V. Puentes (2006). "What can nanotechnology do to fight cancer?" *Clin Transl Oncol* **8**(11): 788-795.

The marriage of physics, chemistry and biology at the nanometric scale, nanotechnology, is a powerful technology which is predicted to have a large impact on life sciences and particularly cancer treatment. In the following we will show some examples of applications which has already reached clinical treatments as new ideas which may positively influence the understanding, diagnosis and therapy of cancer.

Gao, X. S. (2010). "Considerations of treatment standardization from the procession of NCCN guideline of esophageal cancer." *Chin J Cancer* **29**(10): 860-864.

Esophageal carcinoma is one of the most common malignant tumors, especially in China which is the high incidence area. As a result of mild symptoms of early-stage esophageal cancer, the majority of patients cannot be diagnosed until they develop to advanced cancer, and the treatment outcome of surgery or chemoradiotherapy is still unsatisfactory at present. The guidelines of esophageal cancer issued by National Comprehensive Cancer Network (NCCN) are regarded as important reference tools by clinical oncologists, and provide uniform criteria for the diagnosis and treatment of esophageal carcinoma. However, the guidelines are not always suitable for Chinese patients because the data come from European and American population which have significant ethnic difference from Chinese. We retrospectively analyzed the changes of treatment strategy of esophageal cancer in NCCN guidelines and the advance of treatment for esophageal carcinoma in China, aiming to provide our oncologists with new research ideas. We also hope to set up clinical cancer cooperation organizations, and release our own cancer guidelines to serve Chinese patients and oncologists.

Geiger, A. M., et al. (2008). "Survivorship research based in integrated healthcare delivery systems: the Cancer Research Network." *Cancer* **112**(11 Suppl): 2617-2626.

**BACKGROUND:** Integrated healthcare delivery systems present unique opportunities for cancer survivorship research. The National Cancer Institute funds the Cancer Research Network (CRN) to leverage these capabilities for all types of cancer research, including survivorship. **METHODS:** The authors gathered information from a recent CRN funding application, Survivorship Interest Group materials, the

CRN website, and published articles. CRN studies were selected to illustrate diverse topics and a variety of data-collection approaches. **RESULTS:** The 14 systems that participate in the CRN provide care for approximately 10.8 million individuals of all ages and racial/ethnic backgrounds, for whom approximately 38,000 new cancer diagnoses were made in 2005. CRN systems have the ability to use existing data and collect new data on patients, providers, and organizations through well established research centers staffed by independent scientists. Of the 45 funded and 2 pending CRN grant applications as of November 30, 2007, 21 include aspects related to cancer survivorship. These studies have examined clinical trial participation, patterns of care, age and racial/ethnic disparities, diffusion of clinical trial findings, treatment outcomes, surveillance, and end-of-life and palliative care. Breast, colorectal, lung, ovarian, and prostate cancers have been the focus of these studies. Results of these studies have been published widely in leading journals. **CONCLUSIONS:** Completed and ongoing CRN survivorship studies provide a strong foundation for future studies. Scientists from all institutional affiliations are welcome to approach the CRN with ideas and are encouraged to allow ample time to establish collaborative relationships and design rigorous studies.

Geldof, A. A., et al. (1998). "Neurotrophic factors in prostate and prostatic cancer." *Prostate Cancer Prostatic Dis* **1**(5): 236-241.

Recent progress in growth factor research has led to a reexamination of the involvement of neurotrophic factors outside their classical domain of the nervous system. These last few years have seen a substantial accumulation of data concerning Nerve Growth Factor (NGF)'s prevalence within the prostate. NGF and its receptors were reported from the normal prostatic tissue, benign hyperplasia and prostatic cancer. Divergent ideas about the biological role of this factor, its specific distribution pattern within the tissue and its implication in the progression of carcinogenesis have been proposed. Especially the role of NGF in the metastatic process bears direct clinical relevance for research in this area. Many questions remain to be solved like the one on the prevalence of other neurotrophic factors. It is now increasingly becoming clear that neurotrophic factors do play a role in normal physiology and pathology of prostatic cells, opening up new prospects for diagnosis and treatment.

Ghaffari, S. (2011). "Cancer, stem cells and cancer stem cells: old ideas, new developments." *F1000 Med Rep* **3**: 23.

It has been suggested that, at least in some forms of cancer, a sub-population of slow-cycling, therapy-resistant cancer stem cells exists that has the

ability to reconstitute the tumor in its entirety. If true, this model implies that conventional therapies based on targeting highly cycling cells within the tumor will leave the slow-cycling stem cell population intact, giving them the opportunity to reinitiate the tumor at a later date. This review discusses the evidence for this model and the likely implications for cancer treatment.

Gilbert, C. A. and A. H. Ross (2009). "Cancer stem cells: cell culture, markers, and targets for new therapies." J Cell Biochem **108**(5): 1031-1038.

A cancer stem cell (CSC) is defined as an undifferentiated cell with the ability to self-renew, differentiate to multiple lineages and initiate tumors that mimic the parent tumor. In this review, we focus on glioblastomas, describing recent progress and problems in characterizing these cells. There have been advances in CSC culture, but tumor cell heterogeneity has made purification of CSCs difficult. Indeed, it may be that CSCs significantly vary from tumor to tumor. We also discuss the proposal that CSCs are resistant to radiotherapy and chemotherapy and play a major role in repopulating tumors following treatment. To overcome their resistance to conventional therapies, we may be able to use our extensive knowledge of the signaling pathways essential for stem cells during development. These pathways have potential as targets for new glioblastoma therapies. Hence, although there is an ongoing debate on the nature of CSCs, the theory continues to suggest new ideas for both the lab and the clinic.

Glukhova, M. A. and C. H. Streuli (2013). "How integrins control breast biology." Curr Opin Cell Biol **25**(5): 633-641.

This article explores new ideas about how the ECM-integrin axis controls normal and malignant breast biology. We discuss the role of integrins in mammary stem cells, and how cell-matrix interactions regulate ductal and alveolar development and function. We also examine the contribution of integrins to tissue disorganization and metastasis, and how an altered stromal and ECM tumour microenvironment affects the cancer cell niche both within primary tumours and at distant sites. Finally, we mention novel strategies for integrin-directed breast cancer treatment.

Guo, Q. K. and C. Z. Liang (2005). "[Potassium ion channels and prostatic diseases]." Zhonghua Nan Ke Xue **11**(6): 458-461.

Potassium ion channels are a complex of protein molded in the cell membrane lipids. Its expression is strong in normal prostatic epithelia and weak in different degrees in prostatic cancer epithelia, but not clearly known in chronic prostatitis epithelia. Drugs affecting potassium ion channels could provide a

new direction and some new ideas for the treatment of prostatic diseases.

Haber, J. S., et al. (2013). "Industry progress report on neuro-oncology: a biotech update." J Neurooncol **112**(2): 315-321.

With steadily rising revenue and large numbers of clinical trials utilizing novel treatment strategies, the field of neuro-oncology is at the core of the growing cancer therapy industry. In June 2012, the Weill Cornell Brain and Tumor Center hosted the first Brain Tumor Biotech Summit as a forum for fostering and encouraging collaboration between researchers and investors to accelerate novel treatments for brain cancer. This event brought together neuro-oncologists, neurosurgeons, academicians, entrepreneurs, non-profits, CEOs and investors in an attempt to bring innovative treatments and concepts to the fore. Specific subjects presented at the meeting included new surgical devices and delivery techniques, targeted therapeutics, immunotherapy, and stem cell biology. The mission of the summit was to provide opportunities for researchers in neuro-oncology to directly interact with leaders from the investment community with insight into the commercial aspects of our work. Our shared goal is to shorten the time for basic science ideas to be translated into the clinical setting. The following serves as a progress report on the biotech industry in neuro-oncology, as presented at the Brain Tumor Biotech Summit.

Harguindey, S., et al. (1995). "Hydrogen ion-dependent oncogenesis and parallel new avenues to cancer prevention and treatment using a H(+)-mediated unifying approach: pH-related and pH-unrelated mechanisms." Crit Rev Oncog **6**(1): 1-33.

A comprehensive examination of phenomena related to cancer is presented that is based on hydrogen ion dynamics, as viewed from the biological, biochemical, and biophysical perspective. A model is described that considers an array of cancer-associated events from oncogenesis to carcinogenesis from this perspective. The basic ideas are viewed from various aspects, ranging from the cellular level to the clinical situation. The novel types of therapeutic and prophylactic agents that result from applying these concepts are elucidated. Considerable insight into this modern approach is seen from some of the mechanisms that characterize the phenomenon of spontaneous regression of cancer.

He, J. and J. C. Yu (2014). "[Research progress on the effects of acupuncture-moxibustion serum]." Zhongguo Zhen Jiu **34**(10): 1042-1046.

The acupuncture-moxibustion serum has received wide attention as a new idea and method. Its



application on researches in vivo and the treatment of disease not only has an important theory value, but also provides new ideas for overcoming the limitations of researches in vivo and some disease's treatment. Literature regarding the basic research of acupuncture-moxibustion serum for last more than 10 years is reviewed, and the effects of acupuncture-moxibustion serum on respiratory system, digestive system, cardiovascular system, nervous system, immune system, anti-aging, bone metabolism and anti-cancer are summarized, hoping to provide references for clinical treatment and evidence-based medicine.

Holmberg, L. (1996). "Future prospects of population-based mammographic screening." *Semin Surg Oncol* **12**(1): 26-31.

Mammographic screening is one worthwhile way of reducing deaths from breast cancer among women diagnosed in ages 50-69. Our knowledge is less clear for women below 50 and above 70. Major research issues include whether by new approaches we can achieve a definitive mortality reduction in women under 50 and investigations of the efficacy of screening in the elderly. The optimal interval time has yet to be decided. When screening is taken to previously unscreened populations, effects on many parameters have to be followed, e.g., sensitivity, specificity, positive predictive value, gains, and costs. We do not as yet know what the implications of finding large numbers of women with in situ cancer are. Keeping high standards in population-based programs also means fighting potential drawbacks: minimizing the proportion of "unnecessary" biopsies and anxiety, avoiding over-treatment of cancers with excellent prognosis, preventing false reassurance or that women with suspicious findings are left without advice. Potential drawbacks of screening are best dealt with within a team of specialists on breast cancer diagnosis and treatment. Mammographic screening has become widely accepted as one important way of reducing breast cancer deaths, and this success has been dependent on the fact that its development has been science driven. To continue to develop, the tradition of critical evaluation and unsentimental bold testing of new ideas has to be carried on.

Holtlander, L., et al. (2016). "Developing and pilot-testing a Finding Balance Intervention for older adult bereaved family caregivers: A randomized feasibility trial." *Eur J Oncol Nurs* **21**: 66-74.

**PURPOSE:** This study aimed to test the feasibility of a psychosocially supportive writing intervention focused on finding balance for older adult bereaved family caregivers of advanced cancer patients. **METHOD:** The Finding Balance Intervention (FBI) was tested for feasibility, acceptability and potential

influence on increasing hope, coping and balance through a multi-method pilot study employing a randomized trial design with 19 older adults with an average age of 72 years. The intervention group received the FBI and a follow up visit from an RN-RA. The control group received the FBI at a second visit. The FBI, a theory-based intervention was developed from grounded theory qualitative data, applying Delphi methods to design a self-administered, psychosocially supportive, writing intervention for older adults who had lost a spouse after caregiving. **RESULTS:** Feasibility was assessed and specific modifications identified. The FBI was easy to use, acceptable and of benefit. The FBI offered validation of emotions and ways to discover new ideas to find balance, which may enable bereaved caregivers to move forward on a unique journey through grief. The treatment group showed a statistically significant increase in restoration-oriented coping and higher oscillation activity. **CONCLUSIONS:** The results suggest the FBI was easy to use, acceptable and of benefit. A full scale study, with specific modifications to the design, is needed to test the effectiveness of this innovative intervention.

Hu, C. and X. Jiang (2016). "Role of NRP-1 in VEGF-VEGFR2-Independent Tumorigenesis." *Target Oncol* **11**(4): 501-505.

Recent studies suggest that neuropilin-1 (NRP-1) promotes angiogenesis mainly via VEGF and its receptors. It promotes tumorigenesis via formation of the NRP-1/ VEGF (vascular endothelial growth factor)/VEGFR2 (vascular endothelial growth factor receptor 2) complex. In addition to VEGF and its receptors, NRP-1 also binds with other growth factors such as platelet-derived growth factor (PDGF) and platelet-derived growth factor receptor (PDGFR). PDGF plays important roles in cellular proliferation and, in particular, blood vessel formation. Moreover, recent studies show that NRP-1 promotes angiogenesis via the NRP-1-ABL pathway, but independent of VEGF-VEGFR2. RAD51 is a protein involved in the signaling pathways of NRP1-ABL and PDGF(R), the expression of which is positively associated with cell radioresistance and chemoresistance. NRP-1 activates the signaling pathways of ABL and PDGF(R) to upregulate RAD51, which induces resistance to radiotherapy and chemotherapy in cancer cells. Furthermore, NRP-1 activates the tumor microenvironment by binding with fibronectin and activating ABL, thereby promoting tumor growth. Inhibition of NRP-1 may overcome the limitations of individually inhibiting the VEGF-VEGFR2 pathway in cancer therapy and provide new ideas for cancer treatment. Therefore, we review the role of NRP-1 in VEGF-VEGFR2-independent tumorigenesis.

Hu, Y., et al. (2013). "Chinese herbal medicine-derived compounds for cancer therapy: a focus on hepatocellular carcinoma." *J Ethnopharmacol* **149**(3): 601-612.

#### ETHNOPHARMACOLOGICAL

**RELEVANCE:** Hepatocellular carcinoma (HCC) as the major histological subtype of primary liver cancer remains one of the most common malignancies worldwide. Due to the complicated molecular pathogenesis of HCC, the option for effective systemic treatment is quite limited. There exists a critical need to explore and evaluate possible alternative strategies for effective control of HCC. With a long history of clinical use, Chinese herbal medicine (CHM) is emerging as a noticeable choice for its multi-level, multi-target and coordinated intervention effects against HCC. With the aids of phytochemistry and molecular biological approaches, in the past decades many CHM-derived compounds have been carefully studied through both preclinical and clinical researches and have shown great potential in novel anti-HCC natural product development. The present review aimed at providing the most recent developments on anti-HCC compounds derived from CHM, especially their underlying pharmacological mechanisms. **MATERIALS AND METHODS:** A systematic search of anti-HCC compounds from CHM was carried out focusing on literatures published both in English (PubMed, Scopus, Web of Science and Medline) and in Chinese academic databases (Wanfang and CNKI database). **RESULTS:** In this review, we tried to give a timely and comprehensive update about the anti-HCC effects and targets of several representative CHM-derived compounds, namely curcumin, resveratrol, silibinin, berberine, quercetin, tanshinone II-A and celastrol. Their mechanisms of anti-HCC behaviors, potential side effects or toxicity and future research directions were discussed. **CONCLUSION:** Herbal compounds derived from CHM are of much significance in devising new drugs and providing unique ideas for the war against HCC. We propose that these breakthrough findings may have important implications for targeted-HCC therapy and modernization of CHM.

Huang, J., et al. (2016). "[Strategies for diagnosis and treatment of bladder cancer in precise times]." *Zhonghua Wai Ke Za Zhi* **54**(10): 734-737.

Bladder cancer is one of the most common malignant tumors of the urinary system in China, but it is still difficult to be accurate in the diagnosis and treatment. The rapid development of high-throughput sequencing technology and data analysis of biological information pushes the medicine to enter into the precise times. In the review, the recent progress of molecular subtype, assessment of immune and metastatic status, efficacy prediction of chemotherapy, immunotherapy and targeted therapy are summarized. It provides new

ideas and methods for accurate diagnosis and treatment of bladder cancer.

Huang, S. Q., et al. (2018). "The dysregulation of tRNAs and tRNA derivatives in cancer." *J Exp Clin Cancer Res* **37**(1): 101.

Transfer RNAs (tRNAs), traditionally considered to participate in protein translation, were interspersed in the entire genome. Recent studies suggested that dysregulation was observed in not only tRNAs, but also tRNA derivatives generated by the specific cleavage of pre- and mature tRNAs in the progression of cancer. Accumulating evidence had identified that certain tRNAs and tRNA derivatives were involved in proliferation, metastasis and invasiveness of cancer cell, as well as tumor growth and angiogenesis in several malignant human tumors. This paper reviews the importance of the dysregulation of tRNAs and tRNA derivatives during the development of cancer, such as breast cancer, lung cancer, and melanoma, aiming at a better understanding of the tumorigenesis and providing new ideas for the treatment of these cancers.

Hull, L. C., et al. (2014). "Highlights of recent developments and trends in cancer nanotechnology research--view from NCI Alliance for Nanotechnology in Cancer." *Biotechnol Adv* **32**(4): 666-678.

Although the incidence of cancer and cancer related deaths in the United States has decreased over the past two decades due to improvements in early detection and treatment, cancer still is responsible for a quarter of the deaths in this country. There is much room for improvement on the standard treatments currently available and the National Cancer Institute (NCI) has recognized the potential for nanotechnology and nanomaterials in this area. The NCI Alliance for Nanotechnology in Cancer was formed in 2004 to support multidisciplinary researchers in the application of nanotechnology to cancer diagnosis and treatment. The researchers in the Alliance have been productive in generating innovative solutions to some of the central issues of cancer treatment including how to detect tumors earlier, how to target cancer cells specifically, and how to improve the therapeutic index of existing chemotherapies and radiotherapy treatments. Highly creative ideas are being pursued where novelty in nanomaterial development enables new modalities of detection or therapy. This review highlights some of the innovative materials approaches being pursued by researchers funded by the NCI Alliance. Their discoveries to improve the functionality of nanoparticles for medical applications includes the generation of new platforms, improvements in the manufacturing of nanoparticles and determining the underlying reasons for the movement of nanoparticles in the blood.

Huston, J. S. and A. J. George (2001). "Engineered antibodies take center stage." *Hum Antibodies* **10**(3-4): 127-142.

The start of the post-genomic era provides a useful juncture for reflection on the state of antibody engineering, which will be a critical technology for relating function and pathology to genomic sequence in biology and medicine. The phenomenal progress in deciphering the human genome has given significant impetus to the application of engineered antibodies in proteomics. Thus, advances in phage display antibody libraries can now help to define novel gene function and the measurement of abnormal protein expression in pathological states. Furthermore, intrabody and antibody engineering provide vehicles for the development of molecular medicines of the future. In addition to these new directions, antibody engineering has begun to show concrete success in its long-term efforts to develop targeted immunotherapies for cancer and other diseases. The cornerstones of clinical development are the detailed academic clinical trials that continue to push the boundaries of engineered antibodies into the real world. The field displays a healthy impatience for practical results, as research accelerates with concerted efforts to transfer preclinical insights into clinical trials. Growing private and governmental expenditures will lead to the rapid expansion of life-saving immunotherapeutic agents. The present review developed from our effort to report on the 11th Annual International Conference on Antibody Engineering (3-6 December 2000). This annual meeting is a forum for discussions on the latest advances in antibody engineering groups from around the world, and now includes the broader agenda of engineering in molecular immunology. In bringing scientists together to exchange ideas at this open forum, new collaborations and the threads of new discoveries are woven. For example, Professors Gerhard Wagner (Harvard Medical School), Dennis Burton (Scripps Research Institute), and Peter Hudson (CSIRO, Melbourne, Australia) gave exciting insights on structural immunobiology that had implications across many disciplines. The growth in antibody engineering was highlighted by the attendance of some 600 participants at the meeting, doubling that of the 1999 meeting. Dramatic clinical acceptance of monoclonal antibodies during the past two years has fostered this growth, with sales in 2000 of 1.8 billion dollars and projections for 2001 of 3 billion dollars. However, economic measures cannot begin to convey the medical revolution that is being effected by these first humanized and chimerized monoclonal antibodies. At this juncture, the 10 monoclonal antibody therapeutics in clinical use are of murine origin, of which 3 are entirely murine (OKT3, Mylotarg, 90Y-labeled Bexxar), 4 have been chimerized (human constant domains replacing murine) (ReoPro, Rituxan

and its <sup>131</sup>I-labeled analogue (Zevalin), Simulect, Remicade) and 3 were chimerized and humanized (human residues being substituted for at least some mouse-specific framework residues in VH and VL) (Zenapax, Herceptin, Synagis). Fully humanized anti-CD52 (CAMPATH-1H) has also been approved by the FDA for the treatment of B-cell chronic lymphocytic leukemia and should become available in late 2001. Humanization was initially developed by Dr. Greg Winter at the MRC Laboratory of Molecular Biology (Cambridge, UK), who presented the meeting's keynote address, "Antibodies as a Paradigm for Molecular Evolution". His pioneering work in antibody phage display libraries has been reformulated into a daring approach to develop truly novel proteins with genetically paired structural elements. He described studies in combinatorial protein engineering with enormous implications for both industrial and therapeutic applications of macromolecules.

Jackman, A. L., et al. (1996). "Tomudex (ZD1694): from concept to care, a programme in rational drug discovery." *Invest New Drugs* **14**(3): 305-316.

Folate-based anticancer drugs with specificity for thymidylate synthase (TS) have come of age. Ideas nurtured in the early 1970s led to the first-generation of antifolates with TS and dihydrofolate reductase (DHFR) inhibitory activities. Compounds with increased selectivity for TS followed with the highly specific inhibitor, CB3717 being synthesised in 1979 at the Institute of Cancer Research (ICR). CB3717 had significant clinical activity but its development had to be abandoned because its low aqueous solubility led to occasional nephrotoxicity. Collaborative laboratory studies between the ICR and ICI Pharmaceuticals (later to become Zeneca Pharmaceuticals) led to the discovery of ZD1694 (Tomudex), the first antifolate to be licensed for the treatment of cancer (UK 1995) in nearly 40 years and the first new drug for colorectal cancer in about 35 years. Tomudex belongs to a class of compounds that use the reduced-folate carrier (RFC) for uptake into cells and which are excellent substrates for folylpolyglutamate synthetase (FPGS). This paper reviews the underlying philosophies, and the milestones reached during the development of Tomudex.

Jimenez, J. (2012). "The CEO of Novartis on growing after a patent cliff." *Harv Bus Rev* **90**(12): 39-42, 135.

When Joseph Jimenez joined Novartis, in 2007, the company was facing a big challenge: Its blockbuster drug Diovan, which accounted for more than 20% of the pharmaceutical division's revenue, would lose its U.S. patent in 2012. His senior executives had some ideas for offsetting the loss-about 100 of them. From that list they chose three on which to focus: (1) The division invested significantly in testing Afinitor (a treatment for renal cell

carcinoma that was nearly ready for market) in breast cancer. (2) It set up Novartis China Commercial University to screen, hire, and train several hundred salespeople for rapid expansion in high-growth markets. (3) It began to transition to an outcomes-based approach to selling medicine by offering to screen patients for responsiveness to new drugs before they're prescribed. Five years later, Jimenez writes, those efforts are beginning to pay off: Revenue is expected to remain stable even as Diovan gives way to generics.

Johnston, P. G., et al. (1999). "The NCI All Ireland Cancer Conference." *Oncologist* 4(4): 275-277.

The National Cancer Institute (NCI) has recently decided to embark on an international partnership with the developing cancer programs on the Island of Ireland (Northern Ireland and the Republic of Ireland) in an attempt to further improve the quality and range of cancer services available for patients. This Transatlantic Partnership called the All Ireland-NCI Cancer Consortium offers exciting opportunities in cancer treatment, education and research as the cancer-caring communities from both the Republic of Ireland and Northern Ireland prepare to join with the U.S. NCI in this major endeavor. The inaugural event of the partnership will be the NCI All Ireland Cancer Conference to be held in Belfast, October 3-6, 1999. (See [www.allirelandcancer.com](http://www.allirelandcancer.com), for information on the conference.) Cancer is a significant cause of mortality and morbidity on the Island of Ireland. There are approximately 28,000 new cases and approximately 11,000 deaths from cancer each year. Therefore, Northern Ireland and the Republic of Ireland have among the highest cancer incidence and mortality rates in the Western World. In recent years there has been a major restructuring of cancer services in both parts of the Island. This is the result of several government reports such as the Campbell Report in Northern Ireland and the National Strategy Document for Cancer in the Republic of Ireland. The National Strategy Document proposes that cancer treatment services should be centered around primary care services, regional services, supra-regional centers and a national coordinating structure whereby the supra-regional centers deliver specialist surgery, medical and radiation oncology, rehabilitation and specialist palliative care. Three supra-regional cancer centers are being established in the cities of Dublin, Cork and Galway and a National Cancer Forum, which has served as a multidisciplinary advisory board to the Government, has pushed the development and implementation of this plan. This has already resulted in a major expansion in the number of medical oncologists practicing in Ireland but further development is required to facilitate multidisciplinary care, to establish programs of education and training and to harness the scientific talent

available to engage in the international effort against cancer. In Northern Ireland the Chief Medical Officer commissioned a report entitled "Cancer Services-Investing for the Future" whose key recommendations were that Northern Ireland should have one cancer center in Belfast and four smaller cancer units. This report also recommended the implementation of a multidisciplinary approach to cancer diagnosis, treatment and palliative care. As in the Republic, all the recommendations of the Report have been accepted and the planning and implementation of this plan are now well under way. Therefore, development of services for cancer patients is a top priority for both governments on the Island and, given the process of cancer service development, it is timely to bring international expertise such as the NCI on board as partners in this effort. The decision by the NCI to develop an agreement for cancer research and service development in Ireland is a major boost for those involved in cancer care and research and will, no doubt, help speed the process of redevelopment. There have already been several visits from senior NCI personnel to Ireland including Dr. Klausner, the Director of the NCI, to determine the potential impact of this agreement and to identify the most productive areas of interaction between the NCI and the Irish Cancer Community. As a result of these visits, the NCI has decided to focus on several areas of strategic importance whose objectives will be to enhance clinical services, improve patient care, promote North South collaboration and cement strategic Ireland-U.S. collaboration in cancer research and development. The agreement will build on existing informal links in U.S.-Irish scientific, medical education and training and also promote clinical trials and cancer epidemiology programs. Major components of the NCI Ireland Agreement will include some of the following: **EDUCATION AND EXCHANGE OF SCHOLARS:** Education will form one of the major platforms of this agreement through the support of educational programs for medical, nursing and scientific staff. These will include the exchange of scholars, including Ph.D., M.D. and nursing students. Particular emphasis will be given to the exchange of medical and nursing trainees focused on clinical research. This will have an immediate clinical impact and will naturally extend the support that has already been given to the training of medical and scientific trainees from the Island of Ireland. Further exchanges would include Ph.D. students, laboratory-based M.D.s in training, clinical visiting professors and investigators from the U.S. wishing to extend their studies in Ireland. **CLINICAL TRIALS:** Another major area for partnership will be the enhancement of a clinical trials infrastructure and clinical trial development. Modernization of cancer care requires that delivery of care should be in the context of evidence-based medicine. This requires a vigorous and contemporary

clinical trials infrastructure which would center around the clinical trials infrastructure already established at the Northern Ireland Cancer Centre and the Irish Clinical Oncology Research Group (ICORG) in the Republic of Ireland. The NCI has already commissioned the development of a new Clinical Trials Information System (CTIS) which seeks as its goal to set international standards in the clinical trials process, and it has already committed significant resources to its implementation. The outcome of this element of partnership will be that clinical trials performed in Irish institutions will immediately be compatible for collation, analysis and presentation with studies performed in the U.S. Moreover, this system will allow participating centers to immediately conform to international standards. This proposal therefore permits participating institutions in Northern Ireland and the Republic of Ireland to quickly achieve data management standards of the highest quality.

**TELECONFERENCING:** Teleconferencing capabilities are already established in both the NCI and in Ireland and indeed limited teleconferencing linkages have already been established between the partners. Further investment in this infrastructure will be vital to the success of major elements of this partnership. It will facilitate clinical trial development, education programs, patient services development and exchange of clinical and scientific ideas. Communication between sites will be essential to the success of this partnership.

**TUMOR REGISTRIES:** Another area for major collaboration and partnership will be in the use of the Cancer Tumor Registries in both Northern Ireland and the Republic of Ireland. The monitoring of improvements in cancer care can only be undertaken with a reliable tumor registry that tracks population-based cancer incidence and mortality. These data are now available in both Northern Ireland and the Republic of Ireland, and both Governments recognize their importance. The NCI proposes to assist both Tumor Registries by developing a common database that can assist in consultation, informatic tools and quality control. Consolidation of the Registries, North and South, will improve the overall quality of data collection and provide information on a genetically stable population. This therefore will act as a major tool for epidemiological investigations and programs focused on screening and prevention.

**DEVELOPMENTS IN CANCER CLINICAL SERVICES:** The NCI Ireland partnership also proposes to assist the further development of clinical service programs on the Island of Ireland. These will include the improvement and standardization of Radiation Oncology practice and the development of a consolidated Radiation Oncology program for research. There are a limited number of radiation facilities on the Island of Ireland and there are significant needs in terms of linking practice elements and the implementation of

uniform standards of practice. Assistance in standardizing and driving the development of clinical services will also extend to elements of medical and surgical oncology practice as well as palliative care. The development of palliative care services is already at an advanced stage on the Island of Ireland and is one that the NCI will carefully evaluate in terms of its own developing programs.

**THE NCI ALL IRELAND CANCER CONFERENCE:** An important event to highlight the commencement of this special relationship will be the NCI All Ireland Cancer Conference to be held in Belfast October 3-6, 1999. This Conference will address clinical, laboratory, epidemiological and political issues that are pertinent to the care of cancer patients. It will highlight important work by Irish, American and European scientists with further input from well-known international academic and biotechnology investigators from across the world. These international experts will not only be asked to speak on their areas of expertise but also to comment on clinical and scientific programs that may help improve North and South interaction and Transatlantic collaboration. Finally, it is hoped that the Conference will be a marker of a very special interaction on the Island of Ireland focused on the overall development of cancer services for patients. It will also signal the start of an important partnership between the NCI and those involved in cancer care and research in Ireland. This tripartite cooperative agreement is a most exciting venture and it will hopefully be an example of how an effort focused on a human problem common to all societies can generate a spirit of cooperation and help to eliminate strife.

Johnstone, T. C., et al. (2016). "The Next Generation of Platinum Drugs: Targeted Pt(II) Agents, Nanoparticle Delivery, and Pt(IV) Prodrugs." *Chem Rev* **116**(5): 3436-3486.

The platinum drugs, cisplatin, carboplatin, and oxaliplatin, prevail in the treatment of cancer, but new platinum agents have been very slow to enter the clinic. Recently, however, there has been a surge of activity, based on a great deal of mechanistic information, aimed at developing nonclassical platinum complexes that operate via mechanisms of action distinct from those of the approved drugs. The use of nanodelivery devices has also grown, and many different strategies have been explored to incorporate platinum warheads into nanomedicine constructs. In this Review, we discuss these efforts to create the next generation of platinum anticancer drugs. The introduction provides the reader with a brief overview of the use, development, and mechanism of action of the approved platinum drugs to provide the context in which more recent research has flourished. We then describe approaches that explore nonclassical platinum(II) complexes with trans

geometry or with a monofunctional coordination mode, polynuclear platinum(II) compounds, platinum(IV) prodrugs, dual-threat agents, and photoactivatable platinum(IV) complexes. Nanoparticles designed to deliver platinum(IV) complexes will also be discussed, including carbon nanotubes, carbon nanoparticles, gold nanoparticles, quantum dots, upconversion nanoparticles, and polymeric micelles. Additional nanoformulations, including supramolecular self-assembled structures, proteins, peptides, metal-organic frameworks, and coordination polymers, will then be described. Finally, the significant clinical progress made by nanoparticle formulations of platinum(II) agents will be reviewed. We anticipate that such a synthesis of disparate research efforts will not only help to generate new drug development ideas and strategies, but also will reflect our optimism that the next generation of approved platinum cancer drugs is about to arrive.

Kalso, E. (2005). "Improving opioid effectiveness: from ideas to evidence." *Eur J Pain* 9(2): 131-135.

Opioid effectiveness can be improved by individualizing dosing, route of administration and the drug. Particularly in the treatment of chronic non-cancer pain, careful patient selection is essential. The current review concentrates on new ideas about improving opioid effectiveness by increasing efficacy or reducing adverse effects by combining other drugs that modulate opioid receptor mediated effects. These pharmacological "opioid adjuvants" include e.g. alpha(2)-adrenergic agonists, non-steroidal anti-inflammatory analgesics, NMDA-receptor antagonists, CCK-antagonists, gabapentinoids and NK-1 receptor antagonists. The theoretical background and the clinical evidence of these combinations will be discussed.

Kantelhardt, E. J. and C. Thomssen (2008). "German Recommendations for Diagnosis and Treatment of Breast Cancer 2008. What is New from the Breast Commission of the German Gynaecological Oncology Working Group (AGO)?" *Breast Care (Basel)* 3(2): 93-99.

Some form of standardised treatment for patients with breast cancer is probably well established in German health institutions throughout the country. Keeping standards up to date, however, is a rather complex activity involving time and financial resources. Turnover of scientific knowledge is fast and numerous. Most health care professionals will not be able to ensure such kind of evidence-based diagnostics and treatment standards of care alone. The breast commission of the German Gynaecological Oncology Working Group (Arbeitsgemeinschaft Gynakologische Onkologie, AGO) has again published their yearly update on recommendations for the diagnosis and therapy of breast cancer. Literature was screened for new findings up to

the beginning of 2008. Changes were incorporated in nearly all of the 25 chapters. Notably, duration and schedules of adjuvant endocrine therapy, updated adjuvant chemotherapy regimens, findings in plastic surgery, radiotherapy for node positive disease, evaluation of new prognostic and predictive factors, classification of lobular neoplasia, treatment of Paget's disease, inflammatory breast cancer, and sarcoma, as well as lapatinib and bevacizumab are discussed, only to mention a few. Using this easy accessible tool, high quality care can be given to the patient, standards can be communicated and justified to the health care system and new ideas will arise for clinical and pre-clinical development.

Kestler, S. A. and G. LoBiondo-Wood (2012). "Review of symptom experiences in children and adolescents with cancer." *Cancer Nurs* 35(2): E31-49.

**BACKGROUND:** Inadequate symptom relief in children and adolescents with cancer leads to unnecessary suffering. This review assesses research on children and adolescents with cancer that had been published from 2002 to 2010. **OBJECTIVES:** The review identifies the symptom experiences of children and adolescents undergoing treatment and describes the progress that has been made since Docherty's 2003 systematic review of nurse researcher published studies from 1990 to 2002, which identified gaps in research on the symptoms of pediatric oncology patients. **METHOD:** A computerized search of medical and nursing literature produced 50 published studies and 2 dissertations that addressed the symptom experiences of children and adolescents receiving treatment for cancer. **RESULTS:** Pain from cancer-related procedures and fatigue were the most frequently identified symptoms, followed closely by nausea and vomiting. More preschool-aged subjects and nonwhite subjects need to be assessed, distinctions between age groups and gender should be explored, and instrumentation for the prereading group must be developed. **CONCLUSIONS:** Research on symptoms experienced by children and adolescents has gained momentum within the last 10 years, and some of the gaps identified by Docherty have been addressed. Multicenter trials would increase sample sizes and decrease enrollment time. **IMPLICATIONS FOR PRACTICE:** By synthesizing research completed from 2002 to 2010 on symptoms of children who had cancer, new ideas can be generated and shared with clinical nursing staff to improve patient care. Gaps to further direct research are also identified.

Khuda-Bukhsh, A. R. (2006). "Laboratory research in homeopathy: pro." *Integr Cancer Ther* 5(4): 320-332.

Homeopathy is a holistic method of treatment that uses ultralow doses of highly diluted natural substances originating from plants, minerals, or animals

and is based on the principle of "like cures like." Despite being occasionally challenged for its scientific validity and mechanism of action, homeopathy continues to enjoy the confidence of millions of patients around the world who opt for this mode of treatment. Contrary to skeptics' views, research on homeopathy using modern tools mostly tends to support its efficacy and advocates new ideas toward understanding its mechanism of action. As part of a Point-Counterpoint feature, this review and its companion piece in this issue by Moffett et al (*Integr Cancer Ther.* 2006;5:333-342) are composed of a thesis section, a response section in reaction to the companion thesis, and a rebuttal section to address issues raised in the companion response.

Kim, H. H. and S. H. Ahn (2011). "The current status and future perspectives of laparoscopic surgery for gastric cancer." *J Korean Surg Soc* **81**(3): 151-162.

Gastric cancer is most common cancer in Korea. Surgery is still the main axis of treatment. Due to early detection of gastric cancer, the innovation of surgical instruments and technological advances, gastric cancer treatment is now shifting to a new era. One of the most astonishing changes is that minimally invasive surgery (MIS) is becoming more dominant treatment for early gastric cancer. These MIS are represented by endoscopic resection, laparoscopic surgery, robotic surgery, single-port surgery and natural orifice transluminal endoscopic surgery. Among them, laparoscopic gastrectomy is most actively performed in the field of surgery. Laparoscopy-assisted distal gastrectomy (LADG) for early gastric cancer (EGC) has already gained popularity in terms of the short-term outcomes including patient's quality of life. We only have to wait for the long-term oncologic results of Korean Laparoscopic Gastrointestinal Surgery Study Group. Upcoming top issues following oncologic safety of LADG are function-preserving surgery for EGC, application of laparoscopy to advanced gastric cancer and sentinel lymph node navigation surgery. In the aspect of technique, laparoscopic surgery at present could reproduce almost the whole open procedures. However, the other fields mentioned above need more evidences and experiences. All these new ideas and attempts provide technical advances, which will minimize surgical insults and maximize the surgical outcomes and the quality of life of patients.

Krishnagopal, A., et al. (2017). "Stent-mediated gene and drug delivery for cardiovascular disease and cancer: A brief insight." *J Gene Med* **19**(5).

This review concisely recapitulates the different existing modes of stent-mediated gene/drug delivery, their considerable advancement in clinical trials and a rationale for other merging new technologies such as nanotechnology and microRNA-based

therapeutics, in addition to addressing the limitations in each of these perpetual stent platforms. Over the past decade, stent-mediated gene/drug delivery has materialized as a hopeful alternative for cardiovascular disease and cancer in contrast to routine conventional treatment modalities. Regardless of the phenomenal recent developments achieved by coronary interventions and cancer therapies that employ gene and drug-eluting stents, practical hurdles still remain a challenge. The present review highlights the limitations that each of the existing stent-based gene/drug delivery system encompasses and therefore provides a vision for the future with respect to discovering an ideal stent therapeutic platform that would circumvent all the practical hurdles witnessed with the existing technology. Further study of the improvisation of next-generation drug-eluting stents has helped to overcome the issue of restenosis to some extent. However, current stent formulations fall short of the anticipated clinically meaningful outcomes and there is an explicit need for more randomized trials aiming to further evaluate stent platforms in favour of enhanced safety and clinical value. Gene-eluting stents may hold promise in contributing new ideas for stent-based prevention of in-stent restenosis through genetic interventions by capitalizing on a wide variety of molecular targets. Therefore, the central consideration directs us toward finding an ideal stent therapeutic platform that would tackle all of the gaps in the existing technology.

Kuhl, C. K. (2015). "The Changing World of Breast Cancer: A Radiologist's Perspective." *Invest Radiol* **50**(9): 615-628.

Compared with other fields of medicine, there is hardly an area that has seen such fast development as the world of breast cancer. Indeed, the way we treat breast cancer has changed fundamentally over the past decades. Breast imaging has always been an integral part of this change, and it undergoes constant adjustment to new ways of thinking. This relates not only to the technical tools we use for diagnosing breast cancer but also to the way diagnostic information is used to guide treatment. There is a constant change of concepts for and attitudes toward breast cancer, and a constant flux of new ideas, new treatment approaches, and new insights into the molecular and biological behavior of this disease. Clinical breast radiologists and even more so, clinician scientists, interested in breast imaging need to keep abreast with this rapidly changing world. Diagnostic or treatment approaches that are considered useful today may be abandoned tomorrow. Approaches that seem irrelevant or far too extravagant today may prove clinically useful and adequate next year. Radiologists must constantly question what they do, and align their clinical aims and research objectives with the changing needs of contemporary breast oncology.

Moreover, knowledge about the past helps better understand present debates and controversies. Accordingly, in this article, we provide an overview on the evolution of breast imaging and breast cancer treatment, describe current areas of research, and offer an outlook regarding the years to come.

Kuhl, C. K. (2016). "The Changing World of Breast Cancer: A Radiologist's Perspective." *Plast Surg Nurs* **36**(1): 31-49.

Compared with other fields of medicine, there is hardly an area that has seen such fast development as the world of breast cancer. Indeed, the way we treat breast cancer has changed fundamentally over the past decades. Breast imaging has always been an integral part of this change, and it undergoes constant adjustment to new ways of thinking. This relates not only to the technical tools we use for diagnosing breast cancer but also to the way diagnostic information is used to guide treatment. There is a constant change of concepts for and attitudes toward breast cancer, and a constant flux of new ideas, new treatment approaches, and new insights into the molecular and biological behavior of this disease. Clinical breast radiologists and even more so, clinician scientists, interested in breast imaging need to keep abreast with this rapidly changing world. Diagnostic or treatment approaches that are considered useful today may be abandoned tomorrow. Approaches that seem irrelevant or far too extravagant today may prove clinically useful and adequate next year. Radiologists must constantly question what they do, and align their clinical aims and research objectives with the changing needs of contemporary breast oncology. Moreover, knowledge about the past helps better understand present debates and controversies. Accordingly, in this article, we provide an overview on the evolution of breast imaging and breast cancer treatment, describe current areas of research, and offer an outlook regarding the years to come.

Kurata, M., et al. (2018). "CRISPR/Cas9 library screening for drug target discovery." *J Hum Genet* **63**(2): 179-186.

CRISPR/Cas9-based tools have rapidly developed in recent years. These include CRISPR-based gene activation (CRISPRa) or inhibition (CRISPRi), for which there are libraries. CRISPR libraries for loss of function have been widely used to identify new biological mechanisms, such as drug resistance and cell survival signals. CRISPRa is highly useful in screening for gain of functions, and CRISPRi is a more powerful tool than RNA interference (RNAi) libraries in screening for loss of functions. Positive selection using a CRISPR library can detect survival cells with specific conditions, such as drug treatment, and it can easily clarify drug resistance mechanisms. Negative selection

is capable of detecting dead or slow-growing cells efficiently, and it can identify survival-essential genes, which can be promising candidates for molecularly targeted drugs. In addition, negative selection can be applied for synthetic lethality interactions, where the perturbation of both genes simultaneously results in the loss of viability, but that of either gene alone does not affect viability. This mechanism is highly important to identifying the optimal combination of molecularly targeted drugs. Survival-co-essential genes in cancer cells can be identified using new methods, such as the paired guide RNA system and in combination with single-cell RNA sequencing techniques. These efficient methods can clarify interesting biological mechanisms and suggest candidates for molecularly targeted drugs. This review identifies what types of screenings were performed and suggests ideas for the next CRISPR screenings to develop new drugs.

Levine, H. (2014). "Physical Biology : challenges for our second decade." *Phys Biol* **11**(3): 030201.

It is quite an honor to be asked to become the third editor-in-chief of *Physical Biology*. I am following in the footsteps of Tim Newman, who served with energy and enthusiasm. Hopefully, the entire community fully appreciates his contributions to moving the field forward. Thank you, Tim! With the honor, however, goes a clear responsibility. Our journal has survived its birth pangs and emerged as a serious venue for publishing quality research papers using physical science to address the workings of living matter. With the support of scientists in this field and with the ongoing commitment of the IOP, we have successfully reached adolescence. Yet, there is clearly much room to grow and there are clear challenges in defining and maintaining our special niche in the publishing landscape. In this still-developing state, the journal very much mimics the state of the field of physical biology itself. Few scientists continue to question the relevance of physical science for the investigation of the living world. But, will our new perspective and the methods that come with it really lead to radically new principles of how life works? Or, will breakthroughs continue to come from experimental biology (perhaps aided by the traditional physicist-as-tool-builder paradigm), leaving us to put quantitative touches on established fundamentals? In thinking about these questions for the field and for the journal, I have tried to understand what is really unique about our joint endeavors. I have become convinced that living matter represents a new challenge to our physical-science based conceptual framework. Not only is it far from equilibrium, as has been generally recognized, but it violates our simple notions of the separability of constituents, their interactions and the resulting large-scale behavior. Unlike, say, atomic physicists who can



do productive research while safely ignoring the latest developments in QCD (let alone particle physics at higher energies), we do not yet understand when the details of proteins and nucleic acids structure and function can be assumed constant when considering the cell. This problem is even more serious as we try to set higher sights and think of cells as constituents of tissue, organ and organism. Trying to understand higher-order biological systems is a bit like trying to play a board game where the pieces and rules are constantly changing, somehow in concert with what is happening at the scale of the game. Others will undoubtedly have their own view of what is really difficult and different about living systems. One of the roles of Physical Biology should therefore be to provide a needed forum to address some of these really difficult questions. Of course, most papers will operate with the safety-setting on, and will use established ideas in physics, either experimental or theoretical, to further our quantitative appreciation of living systems. These papers are without doubt an absolutely necessary part of the field, and we hope that our journal can serve as a home for the best of these. But, my real hope is that we can attract papers that really try to break new ground, that suggest ways in which the living world is not just an extremely messy example of the same phenomena that can be studied in non-biological contexts. Amazingly, this hope is actually shared by many leading biologists. In one of the most influential papers on cancer research in the past decades. Hanahan and Weinberg argue that 'one day, we imagine that cancer biology and treatment-at present, a patchwork quilt of cell biology, genetics, histopathology, biochemistry, immunology, and pharmacology-will become a science with a conceptual structure and logical coherence that rivals that of chemistry or physics.' We should take up the challenge, not just for cancer, and Physical Biology should help. Figuring out exactly how best to do this is now my responsibility, and I look forward to hearing from you and working with all of you, in order to make it happen.

Li, F. and N. Zhang (2015). "Ceramide: Therapeutic Potential in Combination Therapy for Cancer Treatment." *Curr Drug Metab* **17**(1): 37-51.

Combination therapy has become an important strategy for treating cancer in recent years. Ceramide, which is a powerful tumor suppressor, regulating the processes of cell proliferation, differentiation, senescence and apoptosis, has attracted tremendous attention in combination therapy for cancer treatment. It has been demonstrated that combination of chemotherapeutic drugs and ceramide led to a reversion of multidrug resistance (MDR), synergistic tumor inhibition while simultaneously reducing systemic toxicity in cancer treatment. In this review, we aim to reveal the interactions between some anticancer drugs

and ceramide, and summarize the research progress in combination therapies based on ceramide. Synthesis, metabolism and anticancer mechanisms of ceramide were described. Furthermore, the advantages of combination of chemotherapeutic drugs and exogenous ceramide, cerami-degenerating agents or modulators of ceramide metabolism were highlighted. Future perspective and problems to solve before the extension of ceramide's applications were also discussed. It is hoped that this review will provide new ideas for combination therapies in cancer treatment.

Lindee, M. S. (2002). "Genetic disease in the 1960s: a structural revolution." *Am J Med Genet* **115**(2): 75-82.

From about 1955 to about 1975, an explosion of new institutions, disciplines, databases, interventions, practices, techniques, and ideas turned technically driven human genetics from a medical backwater to an exotic and appealing medical research frontier. In the early 1960s, health care professionals were attracted to the new insights of cytogenetics, including the chromosomal explanation of Down syndrome and of other congenital defects and abnormalities of sexual development. The discovery of a connection between myeloid leukemia and chromosomal abnormalities in leukemic cells made human cytogenetics suddenly relevant to cancer research and diagnosis. Successful dietary treatment of phenylketonuria brought genetic disease into the domain of public health and provoked legislative programs with sweeping long-term consequences. Meanwhile, those promoting the importance of genetic disease to medical education began to elaborate the idea that disease was literally becoming more genetic, as a consequence of techno-historical change. In this article, I present an overview of these remarkable events and a framework for understanding how and why they occurred. I emphasize the important roles of family members, religious isolates, legislators, pediatricians, and others who were not trained in genetic science, but who became advocates, at many levels, of genetic medicine. And I suggest that the idea, so important to the Human Genome Project, that "all disease is genetic disease" was structurally realized and institutionalized long before technologies for mapping the genome were available.

Liu, C. C., et al. (2016). "Application of bee venom and its main constituent melittin for cancer treatment." *Cancer Chemother Pharmacol* **78**(6): 1113-1130.

Bee venom and its main constituent melittin (MEL) have been extensively studied in the treatment of tumors. However, the non-specific cytotoxicity and hemolytic activity have hampered the clinical application. Currently, a number of research groups have reported a series of optimization strategies, including gene therapy, recombinant immunotoxin

incorporating MEL or MEL nanoparticles, targeting tumor cells to attenuate the cytotoxicity and improve its antitumor efficiency and therapeutic capabilities, which have shown very promising in overcoming some of these obstacles. In this review, we summarize the current knowledge regarding anticancer effects of bee venom and its main compound MEL on different kinds of tumor cells as well as elucidate their possible anticancer mechanisms. It could be concluded that MEL exerts multiple effects on cellular functions of cancerous cells such as proliferation, apoptosis, metastasis, angiogenesis as well as cell cycle, and the anticancer processes involve diverse signal molecules and regulatory pathways. We also highlight the recent research progress for efficient delivery of MEL peptide, thus providing new ideas and hopeful strategies for the in vivo application of MEL.

Liu, F., et al. (2016). "Biomarkers for EMT and MET in breast cancer: An update." *Oncol Lett* **12**(6): 4869-4876.

Metastasis and recurrence are the leading cause of mortality due to breast cancer, but the underlying mechanisms are still poorly understood. Understanding the breast cancer metastasis mechanism is important for early diagnosis and treatment of breast cancer. The seeding and growth of breast cancer cells at sites distinct from the primary tumor is a complex and multistage process. Recently, it has been reported that the epithelial-mesenchymal transition (EMT) and the mesenchymal-epithelial transition (MET) are the main mechanisms for breast cancer metastasis. During EMT, carcinoma cells shed their differentiated epithelial characteristics, including cell-cell adhesion, polarity and lack of motility, and acquire mesenchymal traits, including motility and invasiveness. This review has summarized the studies of known EMT biomarkers in the context of breast cancer progression. These biomarkers include EMT-related genes, proteins, microRNAs and kinases. In general, the findings of these studies suggest that EMT markers are associated with the invasion and metastasis of breast cancer. Further studies on the link between EMT markers and breast cancer will contribute to identify biomarkers for predicting early breast cancer metastasis as well as to provide new ideas for the treatment of breast cancer.

Loh, W. Y., et al. (2015). "A regression tree approach to identifying subgroups with differential treatment effects." *Stat Med* **34**(11): 1818-1833.

In the fight against hard-to-treat diseases such as cancer, it is often difficult to discover new treatments that benefit all subjects. For regulatory agency approval, it is more practical to identify subgroups of subjects for whom the treatment has an enhanced effect. Regression trees are natural for this task because they partition the data space. We briefly review existing regression tree

algorithms. Then, we introduce three new ones that are practically free of selection bias and are applicable to data from randomized trials with two or more treatments, censored response variables, and missing values in the predictor variables. The algorithms extend the generalized unbiased interaction detection and estimation (GUIDE) approach by using three key ideas: (i) treatment as a linear predictor, (ii) chi-squared tests to detect residual patterns and lack of fit, and (iii) proportional hazards modeling via Poisson regression. Importance scores with thresholds for identifying influential variables are obtained as by-products. A bootstrap technique is used to construct confidence intervals for the treatment effects in each node. The methods are compared using real and simulated data.

Lu, H. and S. D. Xiao (2014). "New ideas for future studies of *Helicobacter pylori*." *J Dig Dis* **15**(1): 1-4.

Gastric cancer (GC) is one of the inflammation-associated cancers. *Helicobacter pylori* is now thought to be responsible for more than 95% of all GCs, and its development is associated with at least four mechanisms that lead to genetic instability of the gastric mucosa. The risk of developing GC can be predicted by assessing the extent and severity of corpus atrophy and the degree of risk can be estimated by using non-invasive methods such as the pepsinogen test, or endoscopic or histological cancer risk scoring systems such as the operative link for gastritis assessment. The eradication of *H. pylori* will stop the progression of gastritis, prevent atrophy and thus decrease the risk of cancer. *H. pylori* eradication should follow the dictum "use what works best locally". There are several new developments in the diagnosis and treatment of *H. pylori* infection including serological antibody, fluorescent in situ hybridization and antibiotic resistance tests. It is still necessary to develop a preventive or therapeutic vaccine to prevent GC.

Ma, D. L., et al. (2016). "Influence of continuous intervention on growth and metastasis of human cervical cancer cells and expression of RNAmiR-574-5p." *J Biol Regul Homeost Agents* **30**(1): 91-102.

This study was carried out to acquire solid evidence that some common treatments could affect micro ribonucleic acids (miRNAs) by revealing the regulatory effect of genes, so as to provide a reference for further exploration of the prevention and treatment of cervical cancer. Nude mouse tumorigenicity assay was used to study the effect of inhibiting miR-574-5p on development and tumorigenic ability of Henrietta Lacks (HeLa) tumor. Cell wound scratch assay, flow cytometry and real-time quantitative polymerase chain reaction (RT-qPCR) were adopted to study the effects of anoxia and temperature, etc., on expression of miR-574-5p and QKI in HeLa as well as on the clone and

migration ability of cells, to provide prevention and treatment of cervical cancer with new ideas and evidence. The results demonstrated that cervical cancer tissues had a significantly increased miR-574-5p expression compared with para-carcinoma tissues; conversely, Gomafu, overall QKI (pan-QKI) and QKI-5 messenger ribonucleic acid (mRNA) and protein expression all decreased. Part of the common nursing methods had a certain influence on miR-574-5p expression, HeLa reproduction and metastasis, and even cell cycle. For example, ultraviolet (UV) irradiation was effective in decreasing miR-574-5p expression of HeLa and inhibiting cell migration; severe hypoxia significantly decreased the survival rate of HeLa, leading to the increase of programmed death percentage and cell ratio in G2/M phase as well as the decrease of cell ratio in G1 phase. Incubation at different temperatures also affected miR-574-5p expression and cell proliferation. Thus, it can be known that miR-574-5p, Gomafu and QKI expression in cervical cancer tissues and para-carcinoma tissues are significantly up-regulated or down-regulated. Some treatments, such as UV irradiation, hypoxia, incubation temperatures, etc., can affect miR-574-5p expression and HeLa proliferation as well as metastases in different degrees. These findings provide a reference and basis for further study.

Maher, E. J. (2008). "An integrated support and information centre in a large U.K. Cancer Centre established in 1993 and replicated in more than 60 units across the United Kingdom and Australia." *Curr Oncol* **15 Suppl 2**(Suppl 2): s108 es164-107.

Established in 1993 after a 2-year consultation between professionals and cancer patients, the Lynda Jackson Macmillan Centre (LJMC) has been a catalyst for change in the United Kingdom. The Centre began with a small core staff in a purpose-built building next to a cancer centre, networking with outreach workers in 12 surrounding hospitals, with a mission to improve information, communication, and support for cancer patients. Since 1996, the LJMC model has been adopted and developed by the charity Macmillan Cancer Support and has been spread to more than 60 units across the United Kingdom and Australia. Introducing complementary therapies (CAMS) to a cancer centre was a particular early challenge. Establishing a shared understanding of the role of complementary therapies and developing nationally accredited written information about them, credible recruitment and governance procedures for therapy practitioners, agreed outcome measures, and peer-reviewed evaluation and research have all been important in engaging cancer physicians and managers; however, charitable funding is still required to support free access to most complementary therapies. An integrated supportive care

service for cancer patients begins with a shift in the culture of cancer treatment organizations, moving from a professional-centred to a patient-centred agenda. Real reach and impact requires "new" ideas and services to be integrated into the routine practice of the cancer care delivery organizations. A key lesson learned over the last 15 years is that an integrated support centre must continually adapt to be viable. Sustaining meaningful user guidance is a particular challenge. Support for self-management and the testing and development of CAM services are growing parts of the portfolio.

Manzoor, S., et al. (2015). "Hepatitis B virus therapy: What's the future holding for us?" *World J Gastroenterol* **21**(44): 12558-12575.

Hepatitis B is one of the leading causes of liver cancer worldwide and unfortunately the number of people affected with hepatitis B virus (HBV) infection is still on the rise. Although the HBV has been known to cause fatal illness since decades but the population effected by this lethal virus have still only a few options for its management. The major treatment strategies include interferons and nucleos(t)ide analogues. These agents have so far produced unsatisfactory results in terms of complete virus eradication. Interferons cannot be used for long term therapy because of their potential side effects. Prolong treatment with nucleos(t)ide analogues has also been reported to cause serious side effects besides the increasing resistance by the virus. The need for new innovative solutions for treatment of HBV has been realized by global research institutes and pharmaceutical industry. Present review focuses in detail on the new ideas that are being transformed into therapeutic tools for use as future therapies in HBV infection. Modern drug designing and screening methods have made the drug discovery process shorter and more reliable. HBV therapeutics will take a new turn in coming years owing to these intelligent drug designing and screening methods. Future therapy of HBV is aiming to include the use of vaccines (both prophylactic and therapeutic), immunomodulators such as antibodies, non-nucleoside antivirals such as RNAi and inhibitors of viral life cycle.

Mezni, F., et al. (2016). "Evaluation of Pistacia lentiscus seed oil and phenolic compounds for in vitro antiproliferative effects against BHK21 cells." *Pharm Biol* **54**(5): 747-751.

CONTEXT: Within the global context of increasing cancer diseases, natural products are important in devising new drugs and providing unique ideas in cancer therapy. In Tunisian folk medicine, Pistacia lentiscus L. (Anacardiaceae) fixed oil is used for cancer treatment. OBJECTIVE: This investigation studied, for the first time, the antiproliferative effect of Pistacia lentiscus fixed oil and its phenolic extract on

BHK21 cancer cells. **MATERIALS AND METHODS:** Oil was extracted from fruits harvested in northwest Tunisia and the phenolic fraction was obtained by mixing with methanol. The anti-proliferative activity of the two tested substances on BHK 21 cells were investigated in vitro using trypan blue assays. Cells were treated with different concentrations of *P. lentiscus* oil (0.009, 0.018, 0.036, and 0.09 g/mL) and the phenolic extract (0.007, 0.014, 0.03, and 0.07 g/mL) for 24, 48, and 72 h. **RESULTS:** The inhibitory effect of *Pistacia lentiscus* fixed oil increases with the increase in dose. The IC<sub>50</sub> value was estimated at 0.029 g/mL. The percentage of cell viability was 42.46 +/- 3.4% at a dose of 0.09 g/mL and was significantly lower than that of the untreated control (96.24 +/- 2.5%, p<0.01). The phenolic extract demonstrated a dose- and time-dependent inhibitory effect on BHK21 cell growth. After 48 h of incubation, the IC<sub>50</sub> value was estimated at 0.15 g/mL. **DISCUSSION AND CONCLUSION:** The results demonstrated the potential of *Pistacia lentiscus* fixed oil in treating cancer, as it is used in traditional medicine.

Micheli, A., et al. (2009). "International collaborations in cancer control and the Third International Cancer Control Congress." *Tumori* **95**(5): 579-596.

Over the past few decades, there has been growing support for the idea that cancer needs an interdisciplinary approach. Therefore, the international cancer community has developed several strategies as outlined in the WHO non-communicable diseases Action Plan (which includes cancer control) as the World Health Assembly and the UICC World Cancer Declaration, which both include primary prevention, early diagnosis, treatment, and palliative care. This paper highlights experiences/ideas in cancer control for international collaborations between low, middle, and high income countries, including collaborations between the European Union (EU) and African Union (AU) Member States, the Latin-American and Caribbean countries, and the Eastern Mediterranean countries. These proposals are presented within the context of the global vision on cancer control set forth by WHO in partnership with the International Union Against Cancer (UICC), in addition to issues that should be considered for collaborations at the global level: cancer survival (similar to the project CONCORD), cancer control for youth and adaptation of Clinical Practice Guidelines. Since cancer control is given lower priority on the health agenda of low and middle income countries and is less represented in global health efforts in those countries, EU and AU cancer stakeholders are working to put cancer control on the agenda of the EU-AU treaty for collaborations, and are proposing to consider palliative care, population-based cancer registration, and training and education focusing on

primary prevention as core tools. A Community of Practice, such as the Third International Cancer Control Congress (ICCC-3), is an ideal place to share new proposals, learn from other experiences, and formulate new ideas. The aim of the ICC-3 is to foster new international collaborations to promote cancer control actions in low and middle income countries. The development of supranational collaborations has been hindered by the fact that cancer control is not part of the objectives of the Millennium Development Goals (MDGs). As a consequence, less resources of development aids are allocated to control NCDs including cancer.

Miyahira, A. K., et al. (2016). "Multidisciplinary intervention of early, lethal metastatic prostate cancer: Report from the 2015 Coffey-Holden Prostate Cancer Academy Meeting." *Prostate* **76**(2): 125-139.

**BACKGROUND:** The 2015 Coffey-Holden Prostate Cancer Academy Meeting, themed: "Multidisciplinary Intervention of Early, Lethal Metastatic Prostate Cancer," was held in La Jolla, California from June 25 to 28, 2015. **METHODS:** The Prostate Cancer Foundation (PCF) sponsors an annual, invitation-only, action-tank-structured meeting on a critical topic concerning lethal prostate cancer. The 2015 meeting was attended by 71 basic, translational, and clinical investigators who discussed the current state of the field, major unmet needs, and ideas for addressing earlier diagnosis and treatment of men with lethal prostate cancer for the purpose of extending lives and making progress toward a cure. **RESULTS:** The questions addressed at the meeting included: cellular and molecular mechanisms of tumorigenesis, evaluating, and targeting the microenvironment in the primary tumor, advancing biomarkers for clinical integration, new molecular imaging technologies, clinical trials, and clinical trial design in localized high-risk and oligometastatic settings, targeting the primary tumor in advanced disease, and instituting multi-modal care of high risk and oligometastatic patients. **DISCUSSION:** This article highlights the current status, greatest unmet needs, and anticipated field changes that were discussed at the meeting toward the goal of optimizing earlier interventions to potentiate cures in high-risk and oligometastatic prostate cancer patients.

Miyahira, A. K., et al. (2014). "Global developments in prostate cancer research and clinical practice." *Asian J Androl* **16**(4): 503-504.

The prostate cancer foundation (PCF) is committed to the facilitation of global knowledge exchange as a mechanism for more rapidly discovering and developing new medicines and treatments for prostate cancer (PCa) patients worldwide. For the past 3 years, PCF has partnered with the Chinese Prostate

Cancer Consortium and Shanghai Changhai Hospital to host a conference in China that brings together basic, translational, and clinical researchers from China and abroad to form new partnerships and exchange findings, insights, perspectives, and ideas toward improving the treatment of PCa. The seventh forum of prostate disease held in Shanghai, China, on July 26-28, 2013, focused on current and emerging developments and approaches in PCa diagnosis, prognosis, and treatment, and the discovery and targeting of disease mechanisms that drive metastasis and lethal subtypes of castrate-resistant PCa (CRPC). This special edition of the Asian Journal of Andrology highlights some of the most pressing topics that were presented and discussed at the forum.

Morrissey, C., et al. (2016). "The biology and clinical implications of prostate cancer dormancy and metastasis." *J Mol Med (Berl)* **94**(3): 259-265.

Disseminated tumor cells (DTCs) are detected early in the disease process in prostate cancer (PCa) patients and can persist after radical prostatectomy. DTCs can remain dormant in patients with no evidence of disease for a prolonged period of time only to recur 10 or more years later. Recent advances in single-cell genomics and transcriptomics have provided much needed insight into DTC biology and cancer dormancy in patients. With the development of new in vitro and preclinical models, researchers recapitulate the clinical events in patients and therefore allow further elucidation of the molecular mechanisms underlying cancer dormancy and escape. In this review, we explore novel ideas on the detection, heterogeneous transcriptomic profiles, molecular and cellular mechanisms of dormancy, and potential mechanisms underlying dormancy escape by DTCs. As such, there is hope that identifying and targeting novel dormancy-associated pathways in patients with residual disease will have significant clinical implications for the treatment of PCa patients in the future.

Mould, R. F. (2007). "Priority for radium therapy of benign conditions and cancer." *Curr Oncol* **14**(3): 118-122.

In medicine, assigning priorities for original ideas and for first implementation of a new type of treatment or technology-radium afterloading, for example-is often difficult. This situation is certainly true for radium therapy, with conflicting claims coming from France, Germany, and the United States about who first implemented it. Moreover, if possible, a distinction must be made between the person who had the idea for a therapy and the person who actually implemented it. These people are not always one and the same. Difficulties in assigning priority also sometimes arise from the lack of a published claim in a medical journal, and extant photographic evidence is typically almost

impossible to find some 100 years after the event. The present article tries to solve the problems of priority regarding those who were really responsible for the ideas and implementation of radium therapy, including the technique of afterloading.

Mueller, M. M. (2006). "Inflammation in epithelial skin tumours: old stories and new ideas." *Eur J Cancer* **42**(6): 735-744.

The essential contribution of inflammation to tumour development and progression has gained increasing acceptance. For epithelial skin cancer, the observation that tumours arise in sites of chronic irritation and inflammation dates back to 1828 and has stimulated a whole field of research. Chemically-induced mouse skin tumours requiring inflammatory agents such as 12-O-tetradecanoylphorbol 13-acetate (TPA) for tumour-promotion have greatly contributed to our understanding of multi-stage carcinogenesis and have given important insights into the functional interaction between inflammatory micro-environment and epithelial tumour, especially when used in combination with transgenic animals. Data from these and additional new model systems clearly emphasise that the tumour-promoting micro-environment is indispensable for tumour formation and progression. It strongly resembles the wound and is largely orchestrated by inflammatory cells allowing tumour cells to co-opt signalling molecules of the innate immune system to promote their growth, invasion and metastasis. Consequently, anti-inflammatory drugs are of great clinical interest in prevention and treatment of epithelial skin cancers.

Needham, D. and M. W. Dewhirst (2001). "The development and testing of a new temperature-sensitive drug delivery system for the treatment of solid tumors." *Adv Drug Deliv Rev* **53**(3): 285-305.

Our laboratories have been working together in close collaboration for over 10 years concerning the design and performance of lipid-based drug delivery systems. Over the past 3 years we have conceived of, developed, and tested pre-clinically, a new liposome-based temperature-sensitive drug delivery system for the treatment of solid tumors. This work is reported in a series of four publications: "J. Liposome Res. 9 (1999) 491; Cancer Res. Adv. Brief 60(5) (2000) 1197; Cancer Res. 6(9) (2000) 748; and Cancer Res. 60 (2000) 6950". Following a brief introduction concerning the motivations behind the work, this article will review these studies, including some of our earlier work that led to these ideas, and will present the rational design of the new liposome formulation from a materials engineering perspective.

Oh, M. C. and D. A. Lim (2009). "Novel treatment strategies for malignant gliomas using neural stem cells." *Neurotherapeutics* **6**(3): 458-464.

Recent studies in stem cell biology have refined our understanding of the origin and progression of cancer. Identification and characterization of endogenous neural stem cells (NSCs), especially those in the adult human brain, have inspired new ideas for selectively targeting and destroying malignant gliomas. Gliomas consist of a heterogeneous population of cells, and some of these cells have characteristics of cancer stem cells. These brain tumor stem cells (BTSCs) share certain characteristics with normal NSCs. It is still unclear, however, whether malignant gliomas in human patients originate from these aberrant BTSCs. Nonetheless, the cellular and molecular similarities between BTSCs and normal NSCs suggest a common research landscape underlying both normal and cancer stem cell biology, wherein findings of one field are relevant to the other. Furthermore, the natural tropism of NSCs to gliomas has generated the idea that modified NSCs can deliver modified genes to selectively destroy malignant brain tumor cells, and even BTSCs, while leaving healthy surrounding neurons intact. These studies and others on the basic biology of both BTSCs and NSCs will be crucial to expanding our treatment strategies for malignant gliomas.

Oldham, R. A. A. and J. A. Medin (2017). "Practical considerations for chimeric antigen receptor design and delivery." *Expert Opin Biol Ther* **17**(8): 961-978.

The development of chimeric antigen receptor (CAR)-modified immune cells has become a highly active field of research since the introduction of this approach in 1989. New ideas are constantly being proposed and tested, resulting in CARs that are more effective and specialized. Areas covered: Many aspects of CAR design and administration can be varied in order to achieve the best possible outcomes; optimization of this therapeutic schema is an active area of research. Here, the authors summarize the work that has been carried out thus far to assess different adaptations for each portion of the CAR itself. They also discuss the various methods used for CAR transgene transfer into effector cells. Expert opinion: While the field has made significant advancements in terms of expansion and testing of the variations available for CAR therapy, it remains difficult to ascertain which options are truly superior and under what conditions. Continued research in this area, as well as in aspects such as improving the safety profile and the anti-tumor potency of CARs, will be required to bring this therapy from early-phase clinical trials to standard of care as an effective treatment for a broad range of tumor types.

Pan, Y., et al. (2013). "[Whole-genome sequencing: a new approach for understanding of pathogenesis and individualized treatment of cancer]." *Zhejiang Da Xue Xue Bao Yi Xue Ban* **42**(1): 103-108.

With the development of sequencing technology, the cost of whole-genome sequencing was significantly declined. Meanwhile, with the application of combined whole-genome sequencing with epigenetic analysis on methylation and histone acetylation, the comprehensive and systematic analysis of numerous samples became a reality and we are able to re-understand the genesis and development of cancer. New ideas are emerging in comparative genomics research methods, from comparison of genomes among different individuals to horizontal self-comparison of different tissues and vertical self-comparison of genomes recently. Individualized diagnosis and treatment of cancer has shown a bright future.

Patel, J. D., et al. (2016). "Relationship between efficacy outcomes and weight gain during treatment of advanced, non-squamous, non-small-cell lung cancer patients." *Ann Oncol* **27**(8): 1612-1619.

**BACKGROUND:** Unintentional weight loss occurs among advanced non-small-cell lung cancer (NSCLC) patients and is associated with worse survival. Small studies have suggested that weight gain during treatment is associated with superior survival. **PATIENTS AND METHODS:** A retrospective analysis analyzed data from three international phase III studies comprising 2301 advanced, non-squamous NSCLC patients who received a platinum-based, first-line doublet, with or without bevacizumab and maintenance therapy. Body weight was recorded before and after treatment by each study's schedule. The relationship between weight gain and overall survival (OS) and progression-free survival (PFS) was assessed using log-rank test and adjusted Cox modeling. Logistic regression assessed the association between baseline covariates and post-baseline weight gain. **RESULTS:** Four hundred and twenty-one (18.3%) patients had >5% weight gain after baseline. More than half of the weight gain cohort exhibited initial weight gain by 3 weeks. The median OS was 16.7 months versus 10.7 months for the >5% versus ≤5% weight gain subgroup (n = 1880) (P < 0.001). PFS was 6.9 versus 4.8 months, respectively (P < 0.001). Differences in overall tumor response rate (50.8% versus 25.4%, respectively) and disease control rate (tumor response or stable disease) (91.5% versus 63.6%, respectively) were also significant (P < 0.001). The Cox modeling revealed the >5% subgroup had longer survival [hazard ratio (HR) = 0.54, 95% confidence interval (CI) 0.47-0.62; P < 0.001] than the ≤5% subgroup after adjusting for baseline factors. Similar significant results were found for PFS (HR = 0.59, 95% CI 0.52-0.67; P < 0.001). Unadjusted logistic

regression indicated a significant association between weight gain (>5% versus ≤5%) and age, and BMI. CONCLUSIONS: Weight gain during treatment may be an early indicator of clinical benefit. If confirmed in prospective studies, monitoring weight change may provide important information regarding survival outcomes in NSCLC and may provide ideas for new therapeutic strategies.

Patel, S., et al. (2008). "Definitive chemoradiotherapy for non-small cell lung cancer with N2 disease." Thorac Surg Clin **18**(4): 393-401.

The treatment of NSCLC continues to evolve over time. Newer therapies and techniques help achieve success in this difficult disease. Since the 1970s, one can observe trends in median survival and notice that they have improved from 9 to 10 months to now 15 to 24 months with concurrent chemoradiation. Unfortunately, despite the advances made, most patients still die from their disease. Chemoradiation without induction or consolidation therapy continues to remain the standard of care in this country for unresectable locally advanced NSCLC. Evaluation of epidermal growth factor receptor tyrosine kinase inhibitors and other biologics continue to be investigated but are not considered standard of care yet. Technologies continue to expand including the use of four-dimensional CT scans and PET scans to more accurately plan patients. Future application of molecular profiling to predict patients most likely to benefit from tailored chemotherapeutic approaches is awaited following validation in early- and advanced-stage disease. With continued diligence to testing new ideas in NSCLC, it is hoped that outcomes will continue to improve the lives of patients with this devastating disease.

Peng, Q., et al. (2013). "[Effect of carcinoma-associated fibroblasts on cancer occurrence and development]." Sheng Wu Yi Xue Gong Cheng Xue Za Zhi **30**(1): 200-203.

Tumor microenvironment has been confirmed to play an important role in the occurrence, invasion and metastasis of many kinds of tumors. Carcinoma-associated fibroblasts (CAFs) are the primary type of host cells in the tumor microenvironment. CAFs have an assignable role in tumor development. CAFs create a suitable "soil" for tumor origination, secrete a large amount of growth factors promoting tumor growth and angiogenic factors promoting tumor angiogenesis. In addition, CAFs attract a large number of inflammatory cytokines, and secrete a great quantity of soluble products promoting tumor cell invasion and metastasis. Therefore, CAFs may become new targets for targeted cancer therapy, and provide new ideas for the clinical cancer comprehensive treatment.

Piantadosi, S., et al. (1993). "Guidelines for analysis and reporting of clinical trials in oncology." Jpn J Cancer Res **84**(9): 929-937.

When analyzing and reporting the results of clinical trials, investigators should follow a simple approach. The purpose of a trial is to estimate an effect or treatment difference, which if present would have clinical utility when treating new patients. Procedures or methods that do not facilitate precisely and impartially estimating and reporting the treatment effect are likely to mislead investigators. Most often in clinical trials, investigators are interested in estimates of risk ratios (specifically odds or hazard ratios) between the treatment groups or levels of a prognostic factor. These simple ideas suggest that the most useful results from clinical trials will be estimated risk ratios and their confidence limits. Especially in cancer, where disease progression, recurrence, and death are common events following treatment, estimates of risk difference are very relevant. Hypothesis tests and associated P-values, although often (or exclusively) reported, are of lesser utility because they do not fully summarize the data. These recommendations may be seen by some investigators to be contrary to accepted practice. It is true that they are somewhat contrary to common practice but their general acceptance is evident in many journals and presentations by clinical trial methodologists. Despite some disagreement among statisticians regarding the need for adjustment of analyses for imbalanced prognostic factors, it is helpful to see if treatment effects change after accounting for imbalances. When this occurs, it may be of clinical interest. Although we discourage analyses that exclude any patients who meet the eligibility criteria, some circumstances will require that this be done (e.g., when a patient refuses to participate after randomization). Investigators should report, and emphasize as primary, those analyses that include all eligible patients. It is our hope and belief that analysis and reporting of trial results along the guidelines suggested here will result in impartial and useful information for journal readers.

Pienta, K. J., et al. (2014). "Beyond the androgen receptor: new approaches to treating metastatic prostate cancer. Report of the 2013 Prouts Neck Prostate Cancer Meeting." Prostate **74**(3): 314-320.

INTRODUCTION: The Prouts Neck Meetings on Prostate Cancer began in 1985 through the efforts of the Organ Systems Branch of the National Cancer Institute to stimulate new research and focused around specific questions in prostate tumorigenesis and therapy. METHODS: These meetings were think tanks, composed of around 75 individuals, and divided equally between young investigators and senior investigators. Over the years, many new concepts related to prostate cancer resulted from these meetings and the prostate

cancer community has sorely missed them since the last one in 2007. **RESULTS:** We report here the first of a new series of meetings. The 2013 meeting focused on defining how the field of treatment for metastatic prostate cancer needs to evolve to impact survival and was entitled: "Beyond AR: New Approaches to Treating Metastatic Prostate Cancer." As castrate resistant prostate cancers escape second generation anti-androgen agents, three phenotypes/genotypes of CRPC appear to be increasing in prevalence and remain resistant to treatment: NeuroEndocrine Prostate Cancer, Persistent AR-Dependent Prostate Cancer, and Androgen Receptor Pathway Independent Prostate Cancer. **DISCUSSION:** It is clear that new treatment paradigms need to be developed for this diverse group of diseases. The Prouts Neck 2013 Meeting on Prostate Cancer helped to frame the current state of the field and jumpstart ideas for new avenues of treatment.

Poller, D. N., et al. (1994). "Ideas in pathology. Ductal carcinoma in situ of the breast: a proposal for a new simplified histological classification association between cellular proliferation and c-erbB-2 protein expression." *Mod Pathol* **7**(2): 257-262.

The diagnosis of ductal carcinoma in situ of the breast (DCIS) has become common with the advent of breast screening programs. **METHODS:** Proliferation indices (S-phase fraction) were studied in 76 cases of pure DCIS. Tumors were classified according to conventional criteria and also according to a novel simplified classification based on cellular necrosis and morphology. This new classification defines three distinct tumor groups: pure comedo in 19 (25.0%) cases, DCIS with necrosis (non-pure comedo) in 21 (27.6%) patients, and DCIS without necrosis in 36 (47.4%) of cases, the latter group comprising largely classical cribriform or micropapillary architectural subtypes. **RESULTS:** Flow cytometric DNA analysis showed a significantly higher S-phase fraction in comedo DCIS than in the subgroup of DCIS tumors without necrosis ( $P < 0.01$  [anova]). A preliminary analysis of disease recurrence and disease-free survival in a large series of 391 cases of pure DCIS showed that of 181 cases of pure comedo DCIS there were 19 local recurrences at the 7-year stage (82% 7-year disease-free survival), with 5 local recurrences in 51 cases of DCIS with necrosis (non-pure comedo) (85% 7-year disease-free survival) and only 6 local recurrences in the 159 cases of the DCIS-without-necrosis subgroup (94% 7-year disease-free survival). The chi 2 value for the frequency of disease recurrence of all cases of DCIS with necrosis (i.e., combining the groups of comedo DCIS and DCIS with necrosis (non-pure comedo)) as compared to DCIS without histological evidence of necrosis was 5705 ( $df = 2$ ;  $P = 0.0001$ ), and the chi 2 for disease-free survival of types of DCIS with necrosis as compared to cases

without necrosis was 178 ( $df = 2$ ;  $P = 0.0001$ ). This analysis indicates that the histological presence of necrosis appears to be a relatively powerful predictor of increased disease recurrence and poorer disease-free survival after treatment for DCIS. **CONCLUSIONS:** Necrosis in DCIS in the absence of pure classical comedo morphology is a feature of more biologically aggressive in situ breast cancer with an intermediate proliferative fraction as compared with the high proliferative fraction of pure comedo DCIS and the low proliferative fraction of DCIS without necrosis. There was no significant difference in DNA ploidy (diploid or aneuploid) between the subgroups as assessed by chi 2 analysis. Further larger studies are required to establish if DCIS with necrosis (non-pure comedo) also shows a greater tendency to local recurrence after breast conservation treatment than do subtypes of DCIS without necrosis. DCIS with necrosis (non-pure comedo) should be adopted as a distinct histological subgroup of DCIS in future clinical studies of in situ mammary carcinoma.

Pui, C. H. and W. E. Evans (2013). "A 50-year journey to cure childhood acute lymphoblastic leukemia." *Semin Hematol* **50**(3): 185-196.

The 50th anniversary of Seminars in Hematology coincides with the 50th anniversary of St. Jude Children's Research Hospital, and both milestones are inexorably linked to studies contributing to the cure of childhood acute lymphoblastic leukemia (ALL). We thought it fitting, therefore, to mark these events by traveling back in time to point out some of the achievements, institutions, study groups, and individuals that have made cure of childhood ALL a reality. In many instances, progress was driven by new ideas, while in others it was driven by new experimental tools that allowed more precise assessment of the biology of leukemic blasts and their utility in selecting therapy. We also discuss a number of contemporary advances that point the way to exciting future directions. Whatever pathways are taken, a clear challenge will be to use emerging genome-based or immunologic-based treatment options in ways that will enhance, rather than duplicate or compromise, recent gains in outcome with classic cytotoxic chemotherapy. The theme of this journey serves as a reminder of the chief ingredient of any research directed to a catastrophic disease such as ALL. It is the audacity of a small group of investigators who confronted a childhood cancer with the goal of cure, not palliation, as their mindset.

Rees, S. and A. Young (2016). "The Experiences and Perceptions of Women Diagnosed with Breast Cancer during Pregnancy." *Asia Pac J Oncol Nurs* **3**(3): 252-258.



**OBJECTIVE:** Although much has been documented about the experience of breast cancer, the accounts of young women have been relatively neglected, despite that around 20% of the breast cancer diagnoses occur in women under the age of 50. In particular, the voices of young women diagnosed during pregnancy are missing from research. Breast cancer is the most common cancer associated with pregnancy, and it is diagnosed in about 1 in 3000 pregnancies. **METHODS:** This study presents data from three women drawn from a larger study of women who had been diagnosed under the age of 45 and had completed their treatment for breast cancer. Semi-structured qualitative interviews were undertaken, with a methodology informed by social constructionist grounded theory and feminism. **RESULTS:** The findings here report the ways that having breast cancer during pregnancy disrupted taken-for-granted assumptions about their pregnancies, new motherhood, and their future life course, and how this occurred within the context of gendered ideas about femininity and motherhood. **CONCLUSIONS:** Breast cancer during pregnancy has a far-reaching impact on young women's lives, and women affected may need practical support in caring for young children, and counselling may be appropriate. Further research is needed in this important area.

Retsky, M., et al. (2005). "Recent translational research: computational studies of breast cancer." Breast Cancer Res 7(1): 37-40.

The combination of mathematics--queen of sciences--and the general utility of computers has been used to make important inroads into insight-providing breast cancer research and clinical aids. These developments are in two broad areas. First, they provide useful prognostic guidelines for individual patients based on historic evidence. Second, by suggesting numeric tumor growth laws that are correlated to clinical parameters, they permit development of biologically relevant theories and comparison with patient data to help us understand complex biologic processes. These latter studies have produced many new ideas that are testable in clinical trials. In this review we discuss these developments from a clinical perspective, and ask whether and how they translate into useful tools for patient treatment.

Ruitenber, E. J. (1991). "Contributions of basic immunology to human health." Neth J Med 39(3-4): 316-321.

Considerable progress has been achieved in immunology and the development of novel immunological intervention strategies. In this review some new concepts in immunology, and particularly the role played by T cells, are discussed: new ideas on the pathogenesis and possible treatment of autoimmune

diseases, on the pathogenesis and immunological treatment of HIV infections, new approaches to transplantation, novel concepts in tumour immunology and cancer immunotherapy and the development of new (molecular) vaccines against infectious diseases. It is anticipated that these new concepts will lead to novel immunological drugs.

Saji, S., et al. (2011). "[The 9th international conference of the asian clinical oncology society in Japan after a twenty year interval--what is the standpoint of Japan in Asia ?]." Gan To Kagaku Ryoho 38(6): 885-891.

The 9th International Conference of the Asia Clinical Oncology Society(ACOS)was held at Gifu Grand Hotel, Gifu Japan on August 25, 26, and 27 2010. The Society was established in Osaka, Japan, in October 1991. Meeting have been held every two years, starting in Osaka, and then to Bangkok, Kunming, Bali, Taipei, Seoul, Beijing, Manila, and now to Gifu. There was a twenty year interval in Japan between meetings in Osaka and Gifu. The main theme of the 9th ACOS was titled "Talk to the Worldwide from Asia," and the sub-theme was titled "Multidisciplinary Treatment for Asian Cancer Patients "For this 9th ACOS, we gathered 42 councilors from Asian countries to serve on the ACOS committee and 365 doctors from Japan to serve on a local organizing committee. For congress program, we scheduled 161 special sessions for the president's lectures, key note lectures, special lectures, educational lectures, symposium, workshop, luncheon seminars, etc. We received about 500 abstracts for oral or poster presentations; among them, 140 abstracts came from Asian countries. As for speakers, 475 were from Japan, 85 from Korea, 34 from Taiwan, 27 from China, over 10 from India, Indonesia, Viet Nam, USA, and other countries. Finally a total of 704 speakers were gathered from 20 countries(from the outside Asia; UK, France, Germany, and Australia). The total number of registered investigators was 1, 136, and the total number of participants, including our congress staffs, volunteers, neighborhood doctors, Gifu citizens, patients, etc., was over 1, 500. In this 9th ACOS we discussed some new ideas, such as Asian cancer statistics, mission, vision and core values of ACOS, new anti-cancer drugs developed from Japan(TS-1 and Xeloda), Inter group clinical trials among Asian countries, less invasive surgery using endoscopic assisted operation, Asian traditional medicine, open workshops with citizens, etc. Moreover, we published a commemorative book entitled" Recent Advances of Cancer in Asian Countries.

Salaga, M., et al. (2016). "RGS proteins as targets in the treatment of intestinal inflammation and visceral pain: New insights and future perspectives." Bioessays 38(4): 344-354.

Regulators of G protein signaling (RGS) proteins provide timely termination of G protein-coupled receptor (GPCR) responses. Serving as a central control point in GPCR signaling cascades, RGS proteins are promising targets for drug development. In this review, we discuss the involvement of RGS proteins in the pathophysiology of the gastrointestinal inflammation and their potential to become a target for anti-inflammatory drugs. Specifically, we evaluate the emerging evidence for modulation of selected receptor families: opioid, cannabinoid and serotonin by RGS proteins. We discuss how the regulation of RGS protein level and activity may modulate immunological pathways involved in the development of intestinal inflammation. Finally, we propose that RGS proteins may serve as a prognostic factor for survival rate in colorectal cancer. The ideas introduced in this review set a novel conceptual framework for the utilization of RGS proteins in the treatment of gastrointestinal inflammation, a growing major concern worldwide.

Sangild, P. T., et al. (2018). "Animal models of chemotherapy-induced mucositis: translational relevance and challenges." *Am J Physiol Gastrointest Liver Physiol* **314**(2): G231-G246.

Chemotherapy for cancer patients induces damaging tissue reactions along the epithelium of the gastrointestinal tract (GIT). This chemotherapy-induced mucositis (CIM) is a serious side effect of cytotoxic drugs, and several animal models of CIM have been developed, mainly in rodents and piglets, to help understand the progression of CIM and how to prevent it. Animal models allow highly controlled experimental conditions, detailed organ (e.g., GIT) insights, standardized, clinically relevant treatment regimens, and discovery of new biomarkers. Still, surprisingly few results from animal models have been translated into clinical CIM management and treatments. The results obtained from specific animal models can be difficult to translate to the diverse range of CIM manifestations in patients, which vary according to the antineoplastic drugs, dose, underlying (cancer) disease, and patient characteristics (e.g., age, genetics, and body constitution). Another factor that hinders the direct use of results from animals is inadequate collaboration between basic science and clinical science in relation to CIM. Here, we briefly describe CIM pathophysiology, particularly the basic knowledge that has been obtained from CIM animal models. These model studies have indicated potential new preventive and ameliorating interventions, including supplementation with natural bioactive diets (e.g., milk fractions, colostrum, and plant extracts), nutrients (e.g., polyunsaturated fatty acids, short-chain fatty acids, and glutamine), and growth factor peptides (e.g., transforming growth factor and glucagon-like peptide-2), as well as manipulations of the

gut microbiota (e.g., prebiotics, probiotics, and antibiotics). Rodent CIM models allow well-controlled, in-depth studies of animals with or without tumors while pig models more easily make clinically relevant treatment regimens possible. In synergy, animal models of CIM provide the basic physiological understanding and the new ideas for treatment that are required to make competent decisions in clinical practice.

Sastre-Serra, J., et al. (2012). "The effects of 17beta-estradiol on mitochondrial biogenesis and function in breast cancer cell lines are dependent on the ERalpha/ERbeta ratio." *Cell Physiol Biochem* **29**(1-2): 261-268.

**BACKGROUND/AIMS:** 17beta-estradiol (E2) is a risk factor for the development of breast cancer, and cause tumorigenesis in epithelial breast cells. Moreover, E2 has distinct effects on different tissues that are attributed to the presence of two estrogen receptor isoforms, ERalpha and ERbeta. **METHODS:** The effect of E2 on mitochondrial biogenesis and function was investigated in two breast cancer cell lines with different estrogen receptor ratios, MCF-7 (high ERalpha/ERbeta ratio) and T47D (low ERalpha/ERbeta ratio) cell lines treated with physiological concentrations of E2 (1 nM). **RESULTS:** Mitochondria of the MCF-7 cell line showed an increase in proliferation but a decrease in functionality, while the T47D cell line, with low ERalpha/ERbeta ratio, maintained functionality with fewer mitochondria. **CONCLUSION:** Our results suggest that ERs endowment and its subtypes relation have an effect on treatment response and could contribute new ideas about mitochondria and ERs in breast cancer, as well as new indicators to the disease progression.

Schonfeld-Warden, N. and C. H. Warden (1997). "Pediatric obesity. An overview of etiology and treatment." *Pediatr Clin North Am* **44**(2): 339-361.

Pediatric obesity is a chronic and growing problem for which new ideas about the biologic basis of obesity offer hope for effective solutions. Prevalence of pediatric and adult obesity is increasing despite a bewildering array of treatment programs and severe psychosocial and economic costs. The definition of obesity as an increase in fat mass, not just an increase in body weight, has profound influence on the understanding and treatment of obesity. In principle, body weight is determined by a balance between energy expenditure and energy intake, but this observation does not by itself explain obesity. There is surprisingly little evidence that the obese overeat and only some evidence that the obese are more sedentary. Understanding of the biologic basis of obesity has grown rapidly in the last few years, especially with the identification of a novel endocrine pathway involving the adipose tissue secreted

hormone leptin and the leptin receptor that is expressed in the hypothalamus. Plasma leptin levels are strongly correlated with body fat mass and are regulated by feeding and fasting, insulin, glucocorticoids, and other factors, consistent with the hypothesis that leptin is involved in body weight regulation and may even be a satiety factor (Fig. 2, Table 1). Leptin injections have been shown to reduce body weight of primates, although human clinical trials will not be reported until summer 1997. So many peptides influencing feeding have been described that one or more may have therapeutic potential (Fig. 2, Table 1). Although the complexity of pathways regulating body weight homeostasis slowed the pace of understanding underlying mechanisms, these complexities now offer many possibilities for novel therapeutic interventions (Fig. 2). Obesity is a major risk factor for insulin resistance and diabetes, hypertension, cancer, gallbladder disease, and atherosclerosis. In particular, adults who were obese as children have increased mortality independent of adult weight. Thus, prevention programs for children and adolescents will have long-term benefits. Treatment programs focus on modification of energy intake and expenditure through decreased calorie intake and exercise programs. Behavior-modification programs have been developed to increase effectiveness of these intake and exercise programs. These programs can produce short-term weight loss. Long-term losses are more modest but achieved more successfully in children than in adults. Several drug therapies for obesity treatment recently have been approved for adults that produce sustained 5% to 10% weight losses but experience with their use in children is limited. Identification of the biochemical pathways causing obesity by genetic approaches could provide the theoretic foundation for novel, safe, and effective obesity treatments. The cloning of leptin in 1994 has already led to testing the efficacy of leptin in clinical trials that are now underway. Although novel treatments of obesity are being developed as a result of the new biology of obesity, prevention of obesity remains an important goal.

Schwab, E. D. and K. J. Pienta (1996). "Cancer as a complex adaptive system." *Med Hypotheses* **47**(3): 235-241.

The second leading cause of death in the USA is cancer. Institutions worldwide are devoting significant resources to the treatment of cancer, and the elucidation of the disease pathway. While great progress has been made in understanding and treating carcinogenesis, many aspects of the disease remain intractable. Throughout the history of science many other disciplines--astronomy, particle physics, etc.--have been advanced when the fundamental ideas governing the discipline were redefined. These redefinitions are often termed 'paradigm shifts'. The new

sciences of chaos theory and complexity have led to paradigm shifts in many unrelated disciplines such as economics, meteorology and seismology. Our current understanding of carcinogenesis has resulted from a conventional view of the disease process. In this perception, the mutation of a gene, or several genes, leads to cancer. Applying the formalism of chaos theory and complexity to carcinogenesis, however, leads to a different perception of the disease. If we look closer, cancer can be viewed as a complex adaptive system. Redefining our perception of cancer may lead to a deeper understanding of the disease, and possibly result in novel methods of therapeutic intervention.

Schweiger, M. R., et al. (2013). "Genomics and epigenomics: new promises of personalized medicine for cancer patients." *Brief Funct Genomics* **12**(5): 411-421.

Recent years have brought about a marked extension of our understanding of the somatic basis of cancer. Parallel to the large-scale investigation of diverse tumor genomes the knowledge arose that cancer pathologies are most often not restricted to single genomic events. In contrast, a large number of different alterations in the genomes and epigenomes come together and promote the malignant transformation. The combination of mutations, structural variations and epigenetic alterations differs between each tumor, making individual diagnosis and treatment strategies necessary. This view is summarized in the new discipline of personalized medicine. To satisfy the ideas of this approach each tumor needs to be fully characterized and individual diagnostic and therapeutic strategies designed. Here, we will discuss the power of high-throughput sequencing technologies for genomic and epigenomic analyses. We will provide insight into the current status and how these technologies can be transferred to routine clinical usage.

Seymour, M. T., et al. (1997). "Attitudes and practice in the management of metastatic colorectal cancer in Britain. Colorectal Cancer Working Party of the UK Medical Research Council." *Clin Oncol (R Coll Radiol)* **9**(4): 248-251.

Evidence-based medicine is widely held to be the essential basis of modern therapeutics. The principle of adopting into clinical practice those treatments proved to be of value in randomized trials, or in the systematic review of several trials, in encouraging a welcome proliferation of clinical research and meta-analysis. However, many things affect clinical practice; quantifiable therapeutic benefit is only one of them. Furthermore, in many situations, clear evidence of the best treatment is not available. When discussing ideas for a new trial in advanced colorectal cancer that was launched in 1996, the MRC Colorectal Cancer Working

Party carried out a survey of the attitudes and practice of surgeons and oncologists who were treating this condition. This revealed substantial diversity of practice amongst experts in the treatment of this common disease, and prompted us to review the factors that affect clinical practice and to discuss the implications.

Shah, N., et al. (2014). "Single incision laparoscopic surgery - trans anal endoscopic microsurgery: A technological innovation." *J Minim Access Surg* **10**(2): 99-101.

Trans anal endoscopic microsurgery (TEM) first burst upon the scene several decades ago and then underwent a period of immersion. We have herein reported our experience in two cases who underwent TEM using laparoscopic techniques. The advent of single incision laparoscopic surgery (SILS) has made great inroads into various fields of general and gastrointestinal (GI) surgery. We decided to make use of the same technique in TEM for two patients who had large sessile villous adenomas of the rectum. We used this port and fixed it transanally to the edge of the anus. Carbon dioxide used for insufflation in laparoscopic surgery was used through one of the ports, and a telescope was inserted to the larger port. We made sure that the entire polyp was cut out completely until the circular muscle of the internal sphincter was clearly exposed. Next, the cut edges of the rectum were undermined between the mucosa and the circular muscles in order to bring the cut edges closer together. We were able to perform this SILS TEM in two cases. In both the cases, well differentiated villous adenoma (colonoscopically, biopsy proven before surgery) was confirmed after excision. The question has been raised whether TEM is the new laparoscopy for anorectal surgery. Increasingly, several reports are showing promise for treatment for early stage cancers and large rectal adenomas using TEM. Adoption of our technique using the SILS port that has not been previously described in medical literature, seems to be a promising tool for the future. TEM first burst upon the scene several decades ago and then under went a period of immersion. In recent years, with the onset of laparoscopic surgery, the thoughts and the ideas of using a laparoscopic surgical technique have invaded the area of colorectal cancer as well. We have herein reported our experience in two cases who underwent TEM using laparoscopic techniques.

Sharma, P., et al. (2016). "Biomarkers for prostate cancer: present challenges and future opportunities." *Future Sci OA* **2**(1): FSO72.

Prostate cancer (PCa) has variable biological potential with multiple treatment options. A more personalized approach, therefore, is needed to better define men at higher risk of developing PCa,

discriminate indolent from aggressive disease and improve risk stratification after treatment by predicting the likelihood of progression. This may improve clinical decision-making regarding management, improve selection for active surveillance protocols and minimize morbidity from treatment. Discovery of new biomarkers associated with prostate carcinogenesis present an opportunity to provide patients with novel genetic signatures to better understand their risk of developing PCa and help forecast their clinical course. In this review, we examine the current literature evaluating biomarkers in PCa. We also address current limitations and present several ideas for future studies.

Shi, Z., et al. (2018). "In silico identification of potent small molecule inhibitors targeting epidermal growth factor receptor 1." *J Cancer Res Ther* **14**(1): 18-23.

**BACKGROUND:** The receptor tyrosine kinase of the epidermal growth factor receptor (EGFR, ErbB) family played an important role in multisignaling pathways, which controlled numerous biological activities including proliferation, differentiation, apoptosis, etc. EGFR abnormalities have been associated with a variety of human tumors, which was a well-characterized target for cancer treatment. It was known to all that drug repositioning has been considered as a useful tool to accelerate the process of drug development. **MATERIALS AND METHODS:** Herein, a total of 1408 small molecule drugs approved by the Food and Drug Administration (FDA) were employed to identify potential EGFR inhibitors by a series of bioinformatics approaches, including virtual screening and molecular dynamics (MD) simulations. **RESULTS:** According to the docking score, five small molecules were chosen for further MD simulations. Following the 5 ns MD simulations, ZINC03830276 (Benzonate) were finally recognized as "new use" of FDA-approved EGFR-targeting drug. **CONCLUSIONS:** Our findings suggested that the small molecule ZINC03830276 (Benzonate) could be a promising EGFR inhibitor candidate and may also provide new ideas for designing more potent EGFR inhibitors for the future study.

Singh, A. K., et al. (2017). "Indole-fused azepines and analogues as anticancer lead molecules: Privileged findings and future directions." *Eur J Med Chem* **142**: 244-265.

The search for new lead compounds of simple structure, displaying highest quality anti-tumor potency with new mechanisms of action and least adverse effects is the major intention of cancer drug discovery now a days. For the time being, indole-fused azepines emerged as a simple class of compounds prolifically designed with strong pharmacological significances in particular of cancer protecting ability. In the recent years from the efforts of our research group, indole-fused

heteroazepines, a simple structural class achieved by fusion of indole with oxygen, sulphur and nitrogen containing heteroazepine rings, have known for its superior outcomes in cancer treatment. Surprisingly, the chemistry and biology of these unique families with an amazing role in cancer drug discovery has remained broadly unexplored. This short review is consequently an endeavor to highlight the preliminary ideas over this structural class and to draw the medical attention towards future development of indole-fused azepines and analogues for their promising function in cancer drug discovery.

Skripcak, T., et al. (2014). "Creating a data exchange strategy for radiotherapy research: towards federated databases and anonymised public datasets." *Radiother Oncol* **113**(3): 303-309.

Disconnected cancer research data management and lack of information exchange about planned and ongoing research are complicating the utilisation of internationally collected medical information for improving cancer patient care. Rapidly collecting/pooling data can accelerate translational research in radiation therapy and oncology. The exchange of study data is one of the fundamental principles behind data aggregation and data mining. The possibilities of reproducing the original study results, performing further analyses on existing research data to generate new hypotheses or developing computational models to support medical decisions (e.g. risk/benefit analysis of treatment options) represent just a fraction of the potential benefits of medical data-pooling. Distributed machine learning and knowledge exchange from federated databases can be considered as one beyond other attractive approaches for knowledge generation within "Big Data". Data interoperability between research institutions should be the major concern behind a wider collaboration. Information captured in electronic patient records (EPRs) and study case report forms (eCRFs), linked together with medical imaging and treatment planning data, are deemed to be fundamental elements for large multi-centre studies in the field of radiation therapy and oncology. To fully utilise the captured medical information, the study data have to be more than just an electronic version of a traditional (un-modifiable) paper CRF. Challenges that have to be addressed are data interoperability, utilisation of standards, data quality and privacy concerns, data ownership, rights to publish, data pooling architecture and storage. This paper discusses a framework for conceptual packages of ideas focused on a strategic development for international research data exchange in the field of radiation therapy and oncology.

Song, P., et al. (2017). "Hepatocellular carcinoma treated with anti-epidermal growth factor receptor

antibody nimotuzumab: A case report." *Medicine (Baltimore)* **96**(39): e8122.

**RATIONALE:** Molecular targeted therapy provides new ideas and hope for the treatment of hepatocellular cancer. Epidermal growth factor receptor (EGFR) is closely related to tumor cell proliferation, apoptosis, invasion, and metastasis. **PATIENT CONCERNS:** Several reports indicate that the EGFR is expressed frequently in hepatocellular carcinoma (HCC), thus targeting EGFR research has become a hot topic to explore the treatment of HCC patient. **DIAGNOSES:** Anti-EGFR might serve as a potential therapeutic agent, especially for patients with HCC who are unable to tolerate chemotherapy and surgery. **INTERVENTIONS:** Although phase II open-label study of cetuximab in unresectable HCC was negative, the clinical relevance of this report by Song et al which is based on a single patient is questionable. **OUTCOMES:** We for the first time report that nimotuzumab (an anti-EGFR mAb) resulted in a complete remission (CR) in an 87-year-old patient with HCC. The patient was in B stage according to Barcelona center staging criteria and his liver function was Child-Pugh B grade. **LESSONS:** Our case suggested that anti-EGFR mAbs might be potential therapeutic options for HCC.

Sonntag, H. G., et al. (1995). "[Hygienic aspects with regard to nursing of home care patients with AIDS, chronic diseases and mental handicaps]." *Zentralbl Hyg Umweltmed* **197**(1-3): 26-44.

A human handicap is defined as a broad, hard and long lasting restriction of the mental development and the social integration. Groups of handicapped persons can be divided into mentally, psychologically, physically, sensory (blind, deaf) handicapped as well as into multiple disabled and chronically sick persons and those in need of care (old). New groups with demands for aid are among others people suffering from AIDS, psychologically sick (old) and people getting old as well as mentally, physically und multiple handicapped persons, people suffering from cancer, severely ill and dying people. For all handicapped people should be demanded the possibility of living almost normal lives. For all persons directly concerned as well as their families such a normal life should include: the right of self-determination and autonomy, the demand for complex styles of living and nearby care/support, the providing of respective infrastructures such as barrier free living and access to public institutions, access to public transport and homes fitting for handicapped persons, the demand for out-patient treatment by a complex range of various possibilities of support and finally, the providing of alternative forms of living in contrast to the traditional way of life of handicapped people like families or homes. Three important living areas can be derived from these ideas, namely: living

conditions, education/professional and working field, social life/social environment. These important living areas require preventive measures, mainly advice and information centres, places to go early recognition and early promotion of handicapped people and those in risk of a handicap (especially children) as well as medical, professional and social rehabilitation or integration. Concerning the spectrum of support, aid and care in the homely area up to now already exists a variety of offers by out-patient services (information services, social units, mobile support services/organized neighbourhood assistance, individual care of severely sick persons, food services, laundry services, social psychiatric services for chronic mentally sick persons, cancer advice/care, hospital aid, care of persons suffering from AIDS, family relieving services for family members of mentally disabled persons, supervised living) partial treatment of indoor-patients such as daily care units, daily nursing or daily clinics others like nursing families, living communities, short-time care/accommodation, homes for sick people. Moving forces of these offers are mainly charitable organizations such as organisation of social welfare and churches. Besides, aid for handicapped people is also realized by state and local community authorities (Social Welfare and Public Health Department) and private initiatives. In spite of these offers there exist numerous problems und gaps. With regard to the problems one should mention predominantly the financing of measures, specific problems concerning the home care of persons (among others, asking for help too late, less preventive orientation of the services, low orientation of the services with regard to the needs of the handicapped persons and their families, few coordination or cooperation among the services, nursing crisis, few persons engaged in community services) as well as problems in the field of living and living environment (non existence of handicapped-fit or specially furnished homes, lacking infrastructure, public transport not sufficiently equipped for handicapped people, practices of physicians, pharmacies or shops not accessible for handicapped persons). Gaps in the offers are among others the long-time care, crisis intervention/emergencies particularly for singles as well as the nursing possibilities of partial treatment.

Spaide, R. F. (2006). "Rationale for combination therapies for choroidal neovascularization." *Am J Ophthalmol* **141**(1): 149-156.

**PURPOSE:** To provide a conceptual framework for the development and use of combination therapies for choroidal neovascularization secondary to age-related macular degeneration. **DESIGN:** Literature review, integration of data, and creation of hypothesis. **METHODS:** An assessment of angiogenesis, cancer therapy, and inflammation was performed as they may

pertain to choroidal neovascularization. A conceptual framework was created in which therapies for choroidal neovascularization could be evaluated alone or in combination. **RESULTS:** Angiogenesis occurs because cells produce angiogenic stimuli to encourage blood vessels to develop. This growth of vessels involves an orchestrated interaction among many mediators offering opportunity to modulate or inhibit the entire process. A two-component model for choroidal neovascularization is proposed. The vascular component of choroidal neovascularization is comprised of vascular endothelial cells, endothelial cell precursors, and pericytes. The extravascular component, which by histopathology appears to be both the source of angiogenic stimuli and often the largest component volumetrically, is comprised of inflammatory, glial and retinal pigment epithelial cells, and fibroblasts. Tissue damage can be caused by either component. Each component can be targeted through a variety of monotherapies. Combination therapies offer the possibility of attacking one component in more than one way or by attacking both components simultaneously. **CONCLUSIONS:** The two-component model of choroidal neovascularization can be used to evaluate the mechanism of action and possible interactions of these agents in a conceptual framework. Extension of these ideas can help guide development of new treatment agents and approaches.

Stopper, H., et al. (2014). "Antidepressant fluoxetine and its potential against colon tumors." *World J Gastrointest Oncol* **6**(1): 11-21.

Colon cancer is one of the most common tumors worldwide, with increasing incidence in developing countries. Patients treated with fluoxetine (FLX) have a reduced incidence of colon cancer, although there still remains great controversy about the nature of its effects. Here we explore the latest achievements related to FLX treatment and colon cancer. Moreover, we discuss new ideas about the mechanisms of the effects of FLX treatment in colon cancer. This leads to the hypothesis of FLX arresting colon tumor cells at the G1 cell-cycle phase through a control of the tumor-related energy generation machinery. We believe that the potential of FLX to act against tumor metabolism warrants further investigation.

Strimpakos, A. S., et al. (2011). "Updates on first-line treatment of metastatic pancreatic adenocarcinoma. Highlights from the "2011 ASCO Annual Meeting". Chicago, IL, USA; June 3-7, 2011." *JOP* **12**(4): 339-342.

Despite the extensive research, mounting knowledge in the cancer field and enormous investments, pancreatic cancer remains a rather incurable disease with aggressive natural course and

high mortality rate. The very slow progress is a result of the complex pathogenesis of this disease, which prevents us from targeting the culprit and making a step forward. Therefore, the field is still unexplored and this is a real challenge and opportunity for new ideas and novel approaches. In this paper, we will present the most interesting studies in the first line pancreatic cancer setting, presented at the American Society of Clinical Oncology (ASCO) 2011 Annual Meeting. While there are few studies testing the role of combining the cytotoxic S-1 and gemcitabine, the majority of the studies are examining the safety and impact of adding to the classic gemcitabine treatment novel molecular agents which target key pathways or overexpressed proteins.

Sun, F. D., et al. (2018). "Ibrutinib presents antitumor activity in skin cancer and induces autophagy." *Eur Rev Med Pharmacol Sci* **22**(2): 561-566.

**OBJECTIVE:** Skin cancer is one of the most common malignancies in dermatology. Patient compliance and prognosis of skin cancer are poor. Ibrutinib, a Bruton's Tyrosine Kinase (BTK) inhibitor, is a new anticancer drug used to treat many cancers. Therefore, we aimed to explore the role of ibrutinib in the treatment of skin cancer. **MATERIALS AND METHODS:** Cell Counting Kit-8 (CCK8) and plate cloning assay were used to detect cell proliferation. Apoptosis was determined by flow cytometry. Western blotting analysis was used to analyze the expression of key proteins that regulated autophagy. Proliferation and apoptosis of skin cancer cells and induction of autophagy induced by ibrutinib were evaluated. **RESULTS:** CCK8 plate cloning assays showed that ibrutinib can gradually inhibit the skin cancer cell proliferation as the treatment time and dose increased. Results of flow cytometry showed that apoptosis in skin cancer cells were induced after ibrutinib treatment. Western blot showed that autophagy in skin cancer cells was found induced by ibrutinib and also related to the time and concentration of ibrutinib treatment. Combination treatment of ibrutinib and 3MA for skin cancer cells can significantly increase apoptosis. **CONCLUSIONS:** Ibrutinib has anti-tumor activity in skin cancer and can induce autophagy. Binding to autophagy inhibitors can promote ibrutinib's anti-skin cancer activity. Our experimental results provided new ideas for developing skin cancer drugs.

Sun, Z., et al. (2014). "The roles of mesenchymal stem cells in tumor inflammatory microenvironment." *J Hematol Oncol* **7**: 14.

Tumor behavior is not entirely determined by tumor cells. Studies have demonstrated that a variety of non-tumor cells in the tumor microenvironment affect tumor behavior; thus, a new focus of cancer research has

been the development of novel cancer treatment ideas and therapeutic targets based on the effects of these cells. Mesenchymal stem cells (MSCs) are an important component of the tumor microenvironment; however, previous studies have produced controversial results regarding whether MSCs promote or inhibit tumor growth and progression. In particular, Naive MSCs and tumor-derived MSCs (T-MSCs) have different functions. Naive MSCs could exert bidirectional effects on tumors because these cells can both promote and inhibit tumor progression while T-MSCs promote tumor progression due to influences from the tumor itself and from the inflammatory tumor microenvironment. As an unhealed wound, tumor produces a continuous source of inflammatory mediators and causes aggregation of numerous inflammatory cells, which constitute an inflammatory microenvironment. Inflammatory factors can induce homing of circulating MSCs and MSCs in adjacent tissues into tumors, which are then being "educated" by the tumor microenvironment to support tumor growth. T-MSCs could recruit more immune cells into the tumor microenvironment, increase the proportion of cancer stem cells and promote tumor angiogenesis, further supporting tumor progression. However, as plasticity is a fundamental feature of MSCs, MSCs can also inhibit tumors by activating various MSC-based signaling pathways. Studies of the mechanisms by which interactions among tumors, MSCs, and the inflammatory microenvironment occur and methods to disrupt these interactions will likely reveal new targets for cancer therapy.

Tamm, I., et al. (2001). "Antisense therapy in oncology: new hope for an old idea?" *Lancet* **358**(9280): 489-497.

There is a potential role for antisense oligonucleotides in the treatment of disease. The principle of antisense technology is the sequence-specific binding of an antisense oligonucleotide to target mRNA, resulting in the prevention of gene translation. The specificity of hybridisation makes antisense treatment an attractive strategy to selectively modulate the expression of genes involved in the pathogenesis of diseases. One antisense drug has been approved for local treatment of cytomegalovirus-induced retinitis, and several antisense oligonucleotides are in clinical trials, including oligonucleotides that target the mRNA of BCL2, protein-kinase-C alpha, and RAF kinase. Antisense oligonucleotides are well tolerated and might have therapeutic activity. Here, we summarise treatment ideas in this field, summarise clinical trials that are being done, discuss the potential contribution of CpG motif-mediated effects, and look at promising molecular targets to treat human cancer with antisense oligonucleotides.

Tao, T., et al. (2015). "[2014 Annual Meeting of the American Urological Association: early screening and molecular markers of prostate cancer]." Zhonghua Nan Ke Xue **21**(6): 555-560.

The 109th Annual Meeting of the American Urological Association was held in Orlando, Florida, USA in May 2014, which received more than 1,000 abstracts on prostate cancer (PCa), covering new epidemiological data about PCa, new theories of early screening, novel molecular markers, new surgical methods, new ideas of diagnosis and treatment of castration-resistant PCa, and progress in basic researches. This paper focuses on the new theories of early screening and novel molecular markers of PCa, including the risk factors of PCa, a revolutionary understanding of the relationship between testosterone and PCa, and new application of PSA, new imaging techniques and molecular markers in the early diagnosis of PCa.

Teng, W. J., et al. (2016). "Construction of a protein-protein interaction network of Wilms' tumor and pathway prediction of molecular complexes." Genet Mol Res **15**(2).

Wilms' tumor (WT), or nephroblastoma, is the most common malignant renal cancer that affects the pediatric population. Great progress has been achieved in the treatment of WT, but it cannot be cured at present. Nonetheless, a protein-protein interaction network of WT should provide some new ideas and methods. The purpose of this study was to analyze the protein-protein interaction network of WT. We screened the confirmed disease-related genes using the Online Mendelian Inheritance in Man database, created a protein-protein interaction network based on biological function in the Cytoscape software, and detected molecular complexes and relevant pathways that may be included in the network. The results showed that the protein-protein interaction network of WT contains 654 nodes, 1544 edges, and 5 molecular complexes. Among them, complex 1 is predicted to be related to the Jak-STAT signaling pathway, regulation of hematopoiesis by cytokines, cytokine-cytokine receptor interaction, cytokine and inflammatory responses, and hematopoietic cell lineage pathways. Molecular complex 4 shows a correlation of WT with colorectal cancer and the ErbB signaling pathway. The proposed method can provide the bioinformatic foundation for further elucidation of the mechanisms of WT development.

Theeraladanon, C., et al. (2010). "Rational approach to the synthesis, evaluation, and (68)Ga labeling of a novel 4-anilinoquinoline epidermal growth factor receptor inhibitor as a new imaging agent that selectively targets

the epidermal growth factor receptor tyrosine kinase." Cancer Biother Radiopharm **25**(4): 479-485.

Certain small-molecule inhibitors that target epidermal growth factor receptor (EGFR), such as Gefitinib, Erlotinib, and Lapatinib, provide a new approach for cancer treatment. In accordance with the pharmacophore model for inhibitor competition at EGFR-binding site, this study proposes a rationalized design for a novel 4-anilinoquinoline EGFR tyrosine kinase inhibitor, [6,7-dimethoxyethoxy]-quinolin-4-yl-(3-ethynylphenyl)-amine (YCU07). This is the first study to apply ring-closing metathesis toward synthesis of the quinoline nucleus for this 4-anilinoquinoline EGFR inhibitor. YCU07 expressed significant inhibitory activity for EGFR tyrosine kinase in A431 cells, as confirmed by an ABTS microwell peroxidase substrate system read colorimetrically at 405 nm. Injection of (68)Ga-labeled glutamic acid polypeptide (GAP)-YCU07 conjugate in nude mice implanted with A431 was imaged by animal PET camera (LabPET8; Gamma Medica-Ideas) and computed tomography (eXplore Locus; GE Healthcare), to evaluate its biodistribution. (68)Ga-GAP-YCU accumulated in the receptor-positive tumors, with uptake values of 1.50% +/- 0.09% and 2.36% +/- 0.36% of injected activity per gram tissue at 30 and 90 minutes, respectively.

Tian, Y., et al. (2014). "[Progress of platelet derived growth factor family in non-small cell lung cancer]." Zhongguo Fei Ai Za Zhi **17**(1): 42-48.

Non-small cell lung cancer (NSCLC) is a malignant tumour with quite high cancer specific mortality, and it still lacks stable and reliable markers for NSCLC's prognosis. Platelet derived growth factor (PDGF) and PDGFR has been considered to be involved in the process of cell proliferation, migration, metastasis and epithelial mesenchymal transition of cancer cell through various intracellular signal pathways. Pathology analysis showed that PDGF pathway mainly stimulates the proliferation of NSCLC tumour stroma through paracrine pattern, and some research found that PDGF pathway directly promotes some NSCLC cell's proliferation. The expression of PDGF and PDGFR within NSCLC tissue correlates with status of lymphatic metastasis and patients' prognosis. In clinical treatment of NSCLC, the great effect of PDGF pathway in angiogenesis and promoting distribution of chemotherapy by inhibition of PDGF should not be neglected. As an important pro-angiogenesis pathway, functions of PDGF in radiotherapy is discovered by more and more fundamental research. This review focuses on the progress of PDGF pathway in NSCLC and aims to provide some new ideas for clinical and fundamental researchers.



Toi, M., et al. (2000). "[Antiangiogenesis therapy and hormone therapy--their resemblance and applications of prognostic and predictive factors]." Gan To Kagaku Ryoho **27**(8): 1212-1216.

Many new ideas to control tumor angiogenesis are now being tested in clinical trials. In considering strategies for clinical development of antiangiogenesis treatment, that of endocrine therapy might be particularly useful as a model. Endocrine therapy is a unique treatment used only for hormone-dependent tumors; however, its clinical fruits are exceptional in the entire history of cancer therapy. It is now clearly proven that long-term continuous treatment with antihormones brings a magnificent survival benefit for primary breast cancer patients. This benefit is tumor-phenotype oriented, where the hormone receptor is characterized as a potent predictive factor. Antiangiogenesis treatments seem to have several similarities with endocrine therapy, in that both treatments are cytostatic, stroma-targeting, time-dependent and less effective for large tumor burdens. A combination effect with chemotherapy is often observed with both treatments, at least in animal experiments. In a sense, anti-oncogene product therapy follows endocrine therapy in clinical development. Although antiangiogenesis treatments should be developed based on original concepts, the successful experience of endocrine therapy may provide many hints for the development of antiangiogenesis therapy.

Toi, M., et al. (2011). "Identifying gaps in the locoregional management of early breast cancer: highlights from the Kyoto Consensus Conference." Ann Surg Oncol **18**(10): 2885-2892.

A consensus conference was held to investigate issues related to the local management of early breast cancer. Here, we highlight the major topics discussed at the conference and propose ideas for future studies. Regarding axillary management, we examined three major issues. First, we discussed whether the use of axillary reverse mapping could clarify the lymphatic system of breast and whether the ipsilateral arm might help avoid lymphedema. Second, the use of an indocyanine green fluorescent navigation system was discussed for intraoperative lymphatic mapping. These new issues should be examined further in practice. Finally, some agreement was reached on the importance of "four-node diagnosis" to aid in the diagnostic accuracy of sentinel nodes. Regarding breast treatment, there was general agreement that the clinical value of surgical margins in predicting local failure was dependent on the tumor's intrinsic biology and subtypes. For patients treated with preoperative chemotherapy, less extensive excision may be feasible in those who respond to systemic therapy in an acceptable manner. Most trials of preoperative chemotherapy lack outcome data on local recurrence. Therefore, there is a need for

such data for overview analysis. We also agreed that radiation after mastectomy may be beneficial in node-positive cases where more than four nodes are involved. Throughout the discussions for both invasive and noninvasive disease, the investigation of nomograms was justified for major issues in the decision-making process, such as the presence or absence of microinvasion and the involvement of nonsentinel nodes in sentinel node-positive patients.

Trincaus, M. R. and A. K. Correa (2007). "[Life-death duality in the experience of metastasis patients]." Rev Esc Enferm USP **41**(1): 44-51.

The new millennium brings along a new reality to Brazil: population aging, and with it an increase in cases of chronic diseases, among them cancer. With the purpose of understanding how oncological patients under chemotherapeutic treatment due to the metastasis experience the possibility of dying, seven interviews with patients from an oncology clinic were carried out in a small town in the state of Parana. In order to analyze these interviews, ideas from Martin Heidegger's philosophical reference were used. From this analysis, death showed itself in different ways: implicitly; as a natural phenomenon, experienced in an impersonal way through someone else's death; as a phenomenon that permeates life. The it-happens-to-the-other condition made possible to unveil death through words, actions and looks, which at the same time shelter and denounce; and through the relation with the health professionals through caring forms almost always unauthentic.

Tripathy, D. (1998). "Breast cancer advocacy in clinical care." Breast Dis **10**(5-6): 3-14.

Although still in a continual state of evolution, breast cancer advocacy has come of age in the last few years. Advocacy is a very broad term that can be defined as the viewpoint of a breast cancer patient or survivor, or a viewpoint that is fully patient centered. In the area of clinical care and research, a cooperative atmosphere has developed that has required a close working relationship and understanding of cultures between advocates and those in the professional medical care and research communities. Interaction with patients and decision makers, which reflects individual values and preferences, requires a firm knowledge of medical outcomes; in this way, the advantages and disadvantages of a screening, diagnostic, or treatment plan can be analyzed. Moreover, a clear communication strategy needs to be in place to convey these concepts to patients and to elicit their individual choices and concerns. The development of optimal, shared decision making will require ongoing innovations in all these areas, and some are now being piloted and tested in the areas of screening, prevention, and treatment. The role of advocacy in research has likewise involved a sharp

learning curve from both sides. Multiple models of mutual education, exchange of ideas, and the conversion of this interaction into research strategies are now in place in many settings. The intent of such interaction is to move forward with discovery and clinical application in a way that forces a rethinking and innovation of approaches but emphasizes proper scientific methodology. Patient-focused themes of relevance to patients with breast cancer, timely translation to the clinic, and a broader scope of research and ideas are all being integrated into the scientific review process. An emphasis on advocacy issues, along with stepwise scientific progress, will be essential in the new era of rapid technology development, clinical testing, and adoption into the standard of patient care.

Tullis, J. A. (2010). "Bring about benefit, forestall harm: what communication studies say about spirituality and cancer care." *Asian Pac J Cancer Prev* **11 Suppl 1**: 67-73.

Technological advances in medicine allow health care providers to diagnose diseases earlier, diminish suffering, and prolong life. These advances, although widely revered for changing the face of cancer care, come at a cost for patients, families, and even health care providers. One widely cited consequence of better diagnostics and improved treatment regimens is the sense that there is always one more test or therapy available to extend life. Such an approach to cancer care can prove detrimental to patients' healing. In addition, these new tests and treatments further focus attention on the body as the site of healing and cure while downplaying other aspects of health. The absence of psychological, social, and spiritual care from a patient's cancer care plan compromises healing and makes palliative and end of life care more complicated. In this essay, I discuss the tensions that exist between contemporary cancer care and spirituality and use Communication Studies scholarship to navigate the challenges of integrating a patient's religious or spiritual beliefs into their cancer treatment and care. In addition to discussing the challenges of communicating about sensitive topics such as illness, spirituality, and dying, this article uses narrative examples from a comprehensive cancer center and a hospice (both in the United States) to understand how people with cancer and other terminal illnesses communicate their spirituality and how these conversations influence health care choices and provide comfort. By understanding how patients communicate about topics such as the meaning of life, quality of life, dying and death, providers are better equipped to offer care that is consistent with a patient's beliefs and life goals. This approach maintains that communication is more than a means of transferring information, but is constitutive. By understanding that communication creates our lives and shapes our worlds,

lay and professional caregivers can meet patients where they are spiritually, emotionally, and socially and offer effective care that is culturally situated. For many in Muslim societies, a cancer diagnosis is Divine fate. Understanding a cancer diagnosis as destiny offers comfort to some, yet cancer patients and their family members may experience isolation because of the stigmas associated with the disease. This double-bind can lead to spiritual or existential crises, which draws further attention to the need for effective spiritual care that ultimately fosters patient and family healing whether or not a cure is possible. Bringing together various approaches to communicating about diverse spiritual and religious ideas may allow for enhanced comprehensive cancer care.

Vignali, M., et al. (2002). "Endometriosis: novel etiopathogenetic concepts and clinical perspectives." *Fertil Steril* **78(4)**: 665-678.

**OBJECTIVE:** To discuss current ideas about therapy for endometriosis derived from new observations generated by using molecular biology techniques and in vivo animal models of disease. **METHOD(S):** The MEDLINE database was reviewed for English-language articles on new drugs that affect the endocrine or immunologic system, the possibility that endometriosis has multiple forms, and the association of endometriosis with cancer. Specific attention was given to in vivo studies in animals or humans. **CONCLUSION(S):** Among the novel potential candidate drugs, aromatase inhibitors and raloxifene should be considered for treatment of postmenopausal women with endometriosis. Notable observations have emerged from studies of immunomodulators and antiinflammatory agents in animal models of disease. These findings must be confirmed in women. The histogenesis of ovarian endometriomas is still unclear, thus limiting new experimental approaches to this form of disease. Given the low but established risk for malignant transformation of endometriosis, efforts should be directed toward identification of susceptibility loci for the disease and its potential transformation into cancer.

Vukovic, Z. (1998). "[Anniversaries of the Serbian Medical Society. 60 years since its founding. The dream is fulfilled--the home of the Serbian Medical Society is opened]." *Srp Arh Celok Lek* **126(5-6)**: 217-221.

The Serbian Medical Society was founded in Belgrade in 1872, 126 years ago. At that time, Serbia was liberated from the Ottoman domination, and was one of some thirty existing independent states gaining international recognition in 1878. In 1932 an old dream has been fulfilled--on the occasion of the 60th anniversary of the existence and activity of the Serbian Medical Society--the home of Serbian Medical Society

was opened. A 30-year-long period in which the building of the Home was one of the main preoccupations and a "guiding light" of Serbian doctors thus ended. Money from charitable funds was used, which caused certain benefactors to be praised as noted personalities. Medical practice in those days was in the state of choice. There were no means for adequate treatment of certain ailments, and therapy without realistic scientific base was given, often covered by fictitious reasons. This was especially true for tuberculosis and cancer. Under the pretext of the introduction of "new therapeutical approaches" into medical practice and treatment, diverse pharmaceutical formulas were introduced without knowledge of their real effect--injections of milk, drug containing animal embrional cells and special attention was paid to transplantation of the sexual glands. The injection of "camphor oil" (5 cc) was thus "recommended, harmless but useless". The treatment of tuberculosis, which domineered the pathology of population, was very chaotic. The greatest number of drugs for "successful cure" were to be found here. Most commotion was caused by the so-called Friedman's cure for tuberculosis which was rejected only after vigorous debates. Our drug "Joannin" on the basis of "the old tuberculine" was also represented in this confusion (and Koch himself was forced to recant it). This medicament was also hailed as "successful cure". The origin of serious scientific efforts, however, are to be found around newly formed journal "Medicinski pregled", which attracted new and progressive contributors. At this time, the newly formed Ministry of Public Health started a campaign for the introduction of a modern organization of the health care and the inclusion of all population in it. However, in a country devastated by war and stricken by poverty, anomalies in the functioning of the health care existed, as financial preconditions did not exist and health insurance was still in its infancy. This made the status of doctors difficult, causing long debates in the Serbian Medical Society and fierce criticism of the Ministry of Public Health. The responsible persons were accused of introducing and promoting communist ideas and revolution under the guise of health care for the population.

Wang, C. and J. Li (2015). "Pathogenic Microorganisms and Pancreatic Cancer." *Gastrointest Tumors* **2**(1): 41-47.

**BACKGROUND:** Pancreatic cancer is one of the most lethal cancers worldwide. No effective screening methods exist, and available treatment modalities do not effectively treat the disease. Established risk factors for pancreatic cancer, including smoking, chronic pancreatitis, obesity and type 2 diabetes mellitus, collectively account for less than half of all pancreatic cancer cases. Accumulating reports

have demonstrated that there is an association between pathogenic microorganisms and pancreatic cancer. **SUMMARY:** A substantial amount of preclinical and clinical evidence suggests that microbiota are likely to influence pancreatic carcinogenesis. This review summarizes the literature on studies examining infections that have been linked to pancreatic cancer. **KEY MESSAGE:** Helicobacter pylori infection may be a risk factor for pancreatic cancer; chronic hepatitis virus and oral microbiota may also play a role in pancreatic carcinogenesis. **PRACTICAL IMPLICATIONS:** Considering the worldwide burden of the disease, the association between microbiota and pancreatic cancer in this review may provide new ideas to prevent and treat pancreatic cancer more efficiently. Further studies in this direction are urgently needed.

Wang, C., et al. (2017). "MACC1 mediates chemotherapy sensitivity of 5-FU and cisplatin via regulating MCT1 expression in gastric cancer." *Biochem Biophys Res Commun* **485**(3): 665-671.

Chemotherapeutic insensitivity is a main obstacle for effective treatment of gastric cancer (GC), the underlying mechanism remains to be investigated. Metastasis-associated in colon cancer-1 (MACC1), a transcription factor highly expressed in GC, is found to be related to chemotherapy sensitivity. Monocarboxylate transporter 1 (MCT1), a plasma membrane protein co-transporting lactate and H(+), mediates drug sensitivity by regulating lactate metabolism. Targeting MCT1 has recently been regarded as a promising way to treat cancers and MCT1 inhibitor has entered the clinical trial for GC treatment. However, the correlation of these two genes and their combined effects on chemotherapy sensitivity has not been clarified. In this study, we found that MACC1 and MCT1 were both highly expressed in GC and exhibited a positive correlation in clinical samples. Further, we demonstrated that MACC1 could mediate sensitivity of 5-FU and cisplatin in GC cells, and MACC1 mediated MCT1 regulation was closely related to this sensitivity. A MCT1 inhibitor AZD3965 recovered the sensitivity of 5-FU and cisplatin in GC cells which overexpressed MACC1. These results suggested that MACC1 could influence the chemotherapy sensitivity by regulating MCT1 expression, providing new ideas and strategy for GC treatment.

Wang, L., et al. (2015). "Changes of serum vascular endothelial growth factor of patients with rectal cancer before and after neoadjuvant chemotherapy and tumor progress." *J Biol Regul Homeost Agents* **29**(1): 159-165.

In the rapid development of armamentarium, neoadjuvant chemotherapy has become an important part of a multi-instrument comprehensive treatment of malignant tumor, which presents promising application

prospects. This paper researches changes of Vascular Endothelial Growth Factor (VEGF) and Vascular Endothelial Growth Factor-2 (VEGF-2) in serum of patients with rectal cancer before and after neoadjuvant chemotherapy and discusses how tumor progression rules relate to curative effect and prognosis. Enzyme linked immunosorbent serologic assay (ELISA) was applied for the detection of VEGF expression and VEGF-2 expression of 45 patients with rectal cancer (treatment group) before and after neoadjuvant chemotherapy, which was compared to the expressions of 45 healthy people (control group). After 8 weeks of continuous neoadjuvant chemotherapy, the results did not present obvious differences of VEGF and VEGF-2 expression in patients with different curative effects between pre-chemotherapy and post-chemotherapy. However, VEGF and VEGF-2 expression of patients with CR+PR and NC significantly decreased. This proved the excellent curative effect of neoadjuvant chemotherapy, with which the expressions of VEGF and VEGF-2 of rectal cancer patients decreased. The above experiment provides new ideas for the application of neoadjuvant chemotherapy in treating rectal cancer.

Wang, X. Z., et al. (2015). "Correlation between p53 and epidermal growth factor receptor expression in breast cancer classification." *Genet Mol Res* **14**(2): 4282-4290.

This study aimed to explore new opportunities for developing targeted therapy for triple-negative breast cancer (TNBC) by analyzing the significance and association between p53 and epidermal growth factor receptor (EGFR) expression in different molecular subtypes of breast cancer. The clinical and pathological data of 264 patients with breast cancer receiving surgery in our hospital from January 2012 to August 2013 were retrospectively analyzed. According to the expression of estrogen receptor, progesterone receptor, human epidermal growth factor receptor 2 (HER2), Ki-67, CK5/6, p53, and EGFR detected by immunohistochemical methods, breast cancer was divided into four molecular subtypes. Then, the expression of p53 and EGFR as well as their correlation in the different subtypes were determined. Among the four subtypes, luminal B breast cancer was the most common type. TNBC and HER2-enriched breast cancer had larger tumor sizes with higher expression of Ki-67 as compared with the luminal types. TNBC had a lower lymph node metastasis rate but higher CK5/6 and EGFR expression than the other three types. The expression of p53 was higher in luminal B, HER2-enriched, and triple-negative breast cancers, and this was positively correlated with the expression of EGFR in TNBC but not in the other subtypes. p53 and EGFR expression was positively correlated in TNBC, which enables us to explore the molecular biological characteristics of

TNBC, so as to provide new ideas for the treatment of TNBC.

Wang, Y., et al. (2017). "CD90 positive cells exhibit aggressive radioresistance in esophageal squamous cell carcinoma." *J Thorac Dis* **9**(3): 610-620.

**BACKGROUND:** Cancer stem cells (CSCs) are widely abundant and considered to be an important factor in therapy resistance. They are also promising potential targets for conquering tumors. We explored the effects of radiation on stem cell-like tumor cells via the candidate marker CD90 to provide new ideas for the comprehensive treatment of esophageal squamous cell carcinoma (ESCC). **METHODS:** We constructed CD90 overexpression ESCC cells by lentiviral transfection and observed differences of toxicity, proliferation, and clone number, apoptosis, migration, invasion, and in vivo tumor formation after irradiation. **RESULTS:** We found that the population of CD90 positive cells showed CSC-like characteristics, including increased tumorigenicity and migration in ESCC cells. We discovered that these capacities were strengthened to varying degrees in remaining cells after irradiation. Further exploration revealed that the genes of ETS-1 and its downstream target MMPs changed significantly, which are correlated with the epithelial mesenchymal transition (EMT). These effects lead to enhanced tumor growth and resistance to radiation. **CONCLUSIONS:** We show that CD90 overexpressing ESCC cells exhibit CSC-like characteristics and radiation resistance. From a clinical perspective, ESCC patients with tumors that have high CD90 expression, which inhibits apoptosis, could exhibit more local invasion as well as distant metastasis, indicating a poorer prognosis. Research on the mechanism of CD90 may provide a new perspective to therapeutic strategies for patients with ESCC.

Weber, R. S. (2007). "Improving the quality of head and neck cancer care." *Arch Otolaryngol Head Neck Surg* **133**(12): 1188-1192.

The 2001 report by the Institute of Medicine (IOM) titled *Crossing the Quality Chasm: A New Health System for the 21st Century* highlighted the gap that exists between what we know to be effective, beneficial care and the care that is often delivered to an individual patient. (1) In the report, the IOM stated, "Between the health care we have and the care we could have lies not just a gap, but a chasm." (1)(p1) The report, signifying a national initiative to improve the quality of care in the United States, articulated the following 6 aims for a new health care system: (1) to increase the safety of health care by avoiding injuries to patients through care intended to help them; (2) to provide effective services based on scientific knowledge and to avoid services of no proven benefit; (3) to deliver individualized treatment respectful of and responsive to the patient's

preferences, needs, and values; (4) to deliver timely care by reducing wait times and harmful delays; (5) to increase efficiency by not wasting equipment, supplies, ideas, and energy; and (6) to deliver care that is equitable and does not vary by personal characteristics, patient sex, ethnicity, geography, and social economic status. The IOM also recognized a need to optimize quality cancer care in the United States.

Whelan, R. L. (2001). "Laparotomy, laparoscopy, cancer, and beyond." *Surg Endosc* **15**(2): 110-115.

The fate of laparoscopic methods for the treatment of cancer remains uncertain. Published middle-range oncologic results from nonrandomized studies demonstrate that laparoscopic methods are associated with an outcome comparable with results after open resection. The world awaits the 3- and 5-year oncologic results of the ongoing randomized and prospective trials. There is a possibility that laparoscopic methods may be associated with a survival benefit. Port tumors remain a concern. However, results at this writing suggest that these recurrences take place at a frequency similar to that of incisional recurrences following open cancer resection. Port tumors currently are viewed as local recurrences. Traumatization of the tumor at the time of resection is thought to be the most important surgery-related risk factor. The demonstration of a survival benefit in a randomized trial would likely have a tremendous impact on the surgical world. Avoidance of laparotomy-related immunosuppression and tumor stimulation, both of which have been well demonstrated in animal studies, theoretically, might account for differences in cancer outcome. The early postoperative period may be a critical time during which the fate of many cancer patients is determined. It is possible that this may be an ideal time frame for antitumor immunotherapy because the tumor burden is at its lowest, and because immunotherapy, unlike conventional chemotherapy, is unlikely to have a negative impact on wound and anastomotic healing. Perioperative nonspecific upregulation of immune function via pharmacologic means may improve long-term oncologic results. Similarly, preoperative tumor vaccines might provide patients with a specific means of combating any remaining tumor cells after curative resection. The results of several recently completed murine studies support both of these ideas. Finally, early postoperative administration of monoclonal antitumor antibodies might provide patients with specific means of combating any remaining tumor cells after curative resection. The introduction of advanced minimally invasive techniques nearly a decade ago has led to new methods of approaching malignant tumors that have the potential to have an impact on the oncologic outcome of cancer patients. This decade-long journey also has led to new insights regarding the impact of surgery on the

patient. It also has alerted us concerning the importance of the immediate postoperative period in the patient's ongoing struggle against the tumor. These insights hopefully will lead to better surgical methods and new perioperative adjuvant therapies that will increase the rate of survival and reduce the recurrence rates for cancer patients.

Wilentz, R. (2001). "The Latest in Pancreatic Cancer Research: Lustgarten Foundation Awardees Present Their Findings." *Int J Gastrointest Cancer* **29**(2): 123-126.

On June 13 and 14, 2001, the Lustgarten Foundation held its third annual Pancreatic Cancer Scientific Conference in Baltimore, Maryland. This conference was entitled "Pancreatic Cancer: From Genes to Treatment" and was held in conjunction with The Johns Hopkins University School of Medicine. As it had for the previous two years, the conference enabled pancreatic cancer scientists from around the world to meet and discuss new concepts in pancreatic cancer research. The conference also included a lecture series and poster presentations on current topics in pancreatic cancer research and treatment. These presentations gave researchers and health care professionals the opportunity to share their ideas, with the ultimate goal of finding a cure for pancreatic cancer.

Wilson, S. K. and J. W. Costerton (2012). "Biofilm and penile prosthesis infections in the era of coated implants: a review." *J Sex Med* **9**(1): 44-53.

**INTRODUCTION:** The numbers of inflatable penile prosthesis (IPP) implanted has increased yearly due to the large numbers of patients treated for prostate cancer, patients becoming refractory to the five phosphodiesterase inhibitors and Peyronie's disease. **AIM:** Prosthesis implantation can be associated with a variety of complications with device infection being the most dreaded one. **MAIN OUTCOME MEASURES:** An understanding of the pathogenesis of these infections is necessary to allow the surgeon to plan treatment. **METHODS:** Infection begins with colonization of planktonic bacteria in the implant space. Biofilm forms around the bacterial mass within 48 hours. Bacteria in biofilm have reduced growth rates, may change phenotypically, and develop resistance to drugs. Antibiotics and the body's macrophages will kill the planktonic bacteria released from the biofilm but never eliminate the infecting organisms. This review will delineate present thinking on infection prevention and biofilm's role in device infection. IPP infection before and after the coated implants will be characterized. Future ideas for prevention and treatment of infection will be explored. **RESULTS:** The coated implants have reduced the incidence of IPP infections. The bacteria

that cause the majority of infections in the era of the coated implant seem to have changed from predominantly nosocomial coagulase-negative Staphylococcus to more virulent organisms. Device infection requires new paradigms of prevention and treatment strategy because the infecting bacteria are different and the patients are sicker. **CONCLUSIONS:** The problem of infection is considerably decreased with coated IPP, yet those infections that do occur are systemic in nature and seem to be caused by more aggressive organisms. These infections are not usually amenable to salvage because the virulence of the bacteria. Future research to prevent these infections must be directed to magnifying the effective dosage of antibiotics to penetrate the biofilm or eliminating the bacteria's ability to secrete the slime.

Wright, R. W. and H. S. Schwartz (1994). "Pathologic acetabular fractures: new concepts in surgical management." *Semin Arthroplasty* **5**(2): 95-105.

Pathologic fracture of the pelvis and acetabulum secondary to metastases is a disabling condition for cancer patients. Management has for the most part remained nonoperative because the complexities of pelvic anatomy and reconstruction yield risks which have outweighed potential benefits. No advances in surgical reconstruction have been reported in one and a half decades. Previous reports and ideas addressing surgical reconstruction have focused on which type of total hip arthroplasty best suits the acetabular bone stock remaining following removal of the tumor. As improving medical management of metastatic cancer increases longevity, improved methods for surgical management of pathologic fractures are required. A new concept for surgically managing periacetabular fractures due to metastases is introduced whose premise is based on pelvic rather than hip pathology. Resection of tumor-infiltrated acetabular columns creates reconstructive challenges best met by the techniques and knowledge gained from trauma surgeons repairing acetabular fractures. The additional use of reinforced polymethylmethacrylate and subchondral bone cement augments fixation. These concepts have been incorporated into a new classification system and treatment strategy which is critically examined in 13 individuals. Tumor resection and pelvic-periacetabular reconstruction can satisfactorily be performed through extensile pelvic approaches without necessarily performing a hip arthroplasty. A more complete oncologic resection, superior reconstruction, and quicker rehabilitation for affected individuals can result in approximately one half of individuals.

Wu, H., et al. (2015). "Autophagic responses to hypoxia and anticancer therapy in head and neck cancer." *Pathol Res Pract* **211**(2): 101-108.

Autophagy is a major intracellular pathway involving in the degradation and recycling of cytosolic material, including organelles, proteins, and ribosomes. Autophagy is commonly active in tumor cells and could be induced by stress conditions such as hypoxia, nutrient depletion and anticancer therapy. Increasing evidence supports the role of autophagy in modulating cancer behavior in head and neck squamous cell carcinoma (HNSCC). Despite recent advances in surgery combined with chemotherapy and radiotherapy, the survival rate of patients with HNSCC has not been improved substantially. To adapt to the hostile microenvironment induced by stress condition including hypoxia and anticancer therapy, more biological changes such as autophagy are induced in tumor cells contributing to their malignant and aggressive behavior. In the present review, we summarized recent findings on the molecules involved in the autophagy induced by hypoxia and anticancer therapy and basic mechanisms of autophagy, and focused on elucidating the role of autophagy in tumor progression of HNSCC. Some novel studies on the relationships between mircoRNA and autophagy were also discussed in this review. A better understanding of this knowledge may provide new ideas and targets for effective prevention and treatment in HNSCC.

Xiang, Y., et al. (2016). "Myocardin inhibits estrogen receptor alpha-mediated proliferation of human breast cancer MCF-7 cells via regulating MicroRNA expression." *IUBMB Life* **68**(6): 477-487.

Myocardin is frequently repressed during human malignant transformation, and restoration of myocardin expression in sarcoma cells contributes to the inhibition of malignant growth. However, its role in breast carcinoma has barely been addressed. Here, we reported that myocardin could inhibit the proliferation of MCF-7 cells. Notably, we show that myocardin inhibited ERalpha-mediated proliferation of breast cancer MCF-7 via impairing ER-dependent transcriptional activation, mainly through the inhibition of the activity of ERalpha. Importantly, the molecular mechanism for the inhibition of the ERalpha-mediated proliferation is that myocardin inhibited the transcription and expression of ERalpha-induced PCNA, Ki-67, and E2F1 to impair ERalpha-mediated proliferation of breast cancer MCF-7. Interestingly, myocardin significantly enhanced the transcription and expression of miR-885 depending on the CARG box in miR-885 promoter, and miR-885 targeted the 3' untranslated regions (UTR) of E2F1 to silence the expression of E2F1. Thus, our data provided important and novel insights into how myocardin may deeply

influence ERalpha-mediated breast cancer proliferation. In conclusion, myocardin could be seen as a breast cancer tumor suppressor so that it will provide new ideas for the treatment of breast cancer. (c) 2016 IUBMB Life, 68(6):477-487, 2016.

Xie, F. W., et al. (2014). "Relationship between the expression of CES2, UGT1A1, and GUSB in colorectal cancer tissues and aberrant methylation." *Neoplasma* **61**(1): 99-109.

Irinotecan (CPT-11) is considered an important drug in the treatment of colorectal cancer, but its continuous administration reduces its sensitivity and influences the curative effect. The metabolism of CPT-11 is mainly controlled by carboxy-lesterase (CES), UDP-glucuronosyltransferase 1A (UGT1A), and beta-glucuronidase (GUSB). Studies to date have shown that methylation acts as an important mechanism for gene expression to suppress the metabolic enzymes of many chemotherapeutics. This study, which selected 99 colorectal cancer patients, 23 of whom had paracancerous tissues and eight of whom had large intestine adenomas, aimed to investigate the correlation between the protein expression of the CPT-11 metabolic enzyme genes CES2, UGT1A1, and GUSB and various clinical pathological parameters of colorectal cancer tissues, as well as the relationship between methylation regulation and the gene expression of CES2, UGT1A1, and GUSB. We used immunohistochemistry staining, methylation-specific PCR, and clinical status to reveal the possible regulatory targets of chemotherapeutic resistance in colorectal cancer and to provide new ideas and countermeasures to reverse anti-cancer drug resistance and chemosensitization. The results showed that the expression of CES2, UGT1A1, and GUSB varies in colorectal pathology tissues and that the expression of CES2 is somewhat related to tumor staging. This relationship is likely caused by the gene regulation of UGT1A1 and GUSB, and other regulation mechanisms may also be involved. The methylation of the CES2 gene is irrelevant to the morbidity associated with colorectal cancer. The GUSB gene showed no significant differences in methylation, and the hemimethylation was also positive, the regulating ability of which needs to be verified. The potential role of these genes in the colorectal cancer progression, which may be directly related to the methylation regulation of UGT1A1, requires further research. The promoter of the UGT1A1 gene in colorectal cancer cells is methylated, which is an important mechanism of UGT1A1 gene silencing and can be regarded as the target point of research for CPT-11 drug resistance and control mechanisms for the reversal of drug resistance.

Xu, W., et al. (2015). "Viruses, Other Pathogenic Microorganisms and Esophageal Cancer." *Gastrointestinal Tumors* **2**(1): 2-13.

**BACKGROUND:** Esophageal cancer (EC) is the eighth most prevalent malignant tumor and the sixth leading cause of cancer mortality throughout the world. Despite the technical developments in diagnosis and treatment, the 5-year survival rate is still low. The etiology of EC remains poorly understood; multiple risk factors may be involved and account for the great variation in EC incidence in different geographic regions. **SUMMARY:** Infection with carcinogenic pathogens has been proposed as a risk factor for EC. This review explores the recent studies on the association of human papillomavirus (HPV), Epstein-Barr virus (EBV), *Helicobacter pylori* and esophageal bacterial biota with EC. **KEY MESSAGE:** Among the above-mentioned pathogens, HPV most likely contributes to esophageal squamous cell carcinoma (ESCC) in high-risk populations. New techniques are being applied to studies on the role of infection in EC, which will inevitably bring novel ideas to the field in the near future. **PRACTICAL IMPLICATIONS:** Multiple meta-analyses support the finding of a higher HPV detection rate in regions associated with high risk for ESCC compared to low-risk areas. A potential role of HPV in the rise of esophageal adenocarcinoma (EAC) was proposed recently. However, further studies are required before a firm conclusion can be drawn. Less work has been done in studying the association between EBV and ESCC, and the results are quite controversial. *H. pylori* infection is found to be inversely related to EC, which is probably due to the reduced incidence of gastroesophageal reflux disease. Analysis of the esophageal bacterial biota revealed distinct clusters of bacteria in normal and diseased esophagi. A type II microbiome rich in Gram-negative bacteria potentially contributes to EAC by inducing chronic inflammation. Novel findings from such studies as these may benefit public health by justifying anti-infection measures to prevent EC.

Xu, W., et al. (2016). "From pathogenesis to clinical application: insights into exosomes as transfer vectors in cancer." *J Exp Clin Cancer Res* **35**(1): 156.

Exosomes are nanoscale extracellular membrane vesicles that are created by the fusion of an intracellular multivesicular body with the cell membrane. They are widely distributed in serum, urine, saliva and other biological fluids. As important transfer vectors for intercellular communication and genetic material, exosomes can stimulate target cells directly via receptor-mediated interactions or via the transfer of various bioactive molecules, such as cell membrane receptors, proteins, mRNAs and microRNAs, thus exerting their biological functions. This review focuses

on the biological characteristics of exosomes, as well as their role and underlying mechanisms of action in the evolution of tumor formation, metastasis, drug resistance and other malignant behaviors. Additionally, this review emphasizes the potential applications of exosomes in the treatment of tumors. Further research may provide new ideas and methods to establish effective, exosome-based strategies for the early diagnosis and treatment of tumors.

Yan, H., et al. (2015). "Effect of the WWOX gene on the regulation of the cell cycle and apoptosis in human ovarian cancer stem cells." *Mol Med Rep* **12**(2): 1783-1788.

In order to examine new ideas for gene therapy in ovarian cancer, the specific mechanism underlying the effects of the WW domain containing oxidoreductase (WWOX) gene on cell cycle regulation and apoptosis in human ovarian cancer stem cells was investigated. Ovarian cancer stem cells were transfected with a eukaryotic expression vector carrying the WWOX gene in vitro (recombinant plasmid) and cells transfected with the empty plasmid (empty plasmid) or untransfected cells were used as controls. Stably transfected cells were screened and amplified in culture and the WWOX protein was detected by western blot analysis in the three groups of cells. Western blot analysis was performed to detect the expression of cell cycle regulatory proteins cyclin E, cyclin-dependent kinase (CDK) 2, cyclin D1, CDK4 and apoptosis-related protein Wnt-5alpha and c-Jun N-terminal kinase (JNK), while polymerase chain reaction (PCR) was used to detect alterations in the mRNA expression levels of caspase-3. The results demonstrated that the WWOX protein was stably expressed in cells of the recombinant plasmid group, but was not detected in cells of the empty plasmid group and the control group. Cell proliferation at each time point decreased significantly in the recombinant plasmid group compared with the empty plasmid group and the control group. Flow cytometric analysis demonstrated that the proportion of cells in the G0/G1 phase in the recombinant plasmid group was significantly higher than that of cells in the empty plasmid group and the control group. The rate of apoptosis in the recombinant plasmid group was significantly higher than that of cells in the empty plasmid group and the control group. Western blot analysis demonstrated that the expression levels of cyclin E, CDK2, cyclin D1 and CDK4 in the recombinant plasmid group were significantly lower than those in the empty plasmid group and the control group; however, the expression levels of Wnt-5alpha and JNK were significantly higher than those in the empty plasmid group and the control group. PCR results demonstrated that the mRNA expression level of caspase-3 in the recombinant plasmid group was

significantly higher than that in the empty plasmid group and the control group. In conclusion, the present study demonstrated that the WWOX gene can be stably expressed in ovarian cancer stem cells and that it inhibits the proliferation of ovarian cancer stem cells. The WWOX gene can downregulate the expression levels of cell cycle proteins cyclin E-CDK2 and cyclin D1-CDK4, which affects the cell cycle of ovarian cancer stem cells. Furthermore, the WWOX gene can upregulate the mRNA expression levels of Wnt-5alpha, JNK and caspase-3, thus contributing to apoptosis of ovarian cancer stem cells. The present study demonstrated that the WWOX gene may be an important molecular target for the treatment of ovarian cancer in the future.

Yardley, S. J., et al. (2001). "Receiving a diagnosis of lung cancer: patients' interpretations, perceptions and perspectives." *Palliat Med* **15**(5): 379-386.

Lung cancer has a higher incidence than any other type of cancer and more than 80% of sufferers die within a year of diagnosis. An important aspect of caring for cancer patients is the breaking of bad news, something that most doctors admit to having difficulty with. Only a few publications on this issue adopt the patients' perspective. This study aimed to document patients' views on delivery of lung cancer diagnoses, their attitudes to methods used and ideas for improvement. Patients were selected from medical, surgical and general practitioner clinics to provide insight into patients' perceptions of care in different environments. Those who gave informed consent completed a taped semi-structured interview. Transcripts were analysed qualitatively using a phenomenological approach. Recruitment was stopped when saturation was reached: no new themes were being identified. A summary of results was sent to patients, whenever possible, for their comment. An independent researcher coded four transcripts to establish the degree of inter-rater reliability. Thirteen patients were recruited. There were five key areas: communication (including the use of words such as 'tumour' and 'growth'), family/community issues, reaction to diagnosis, views on treatment and prognosis (all of which were very variable), and suggested improvements (e.g. a clearer explanation of the experience of bronchoscopy in the patient information leaflet, PIL). Inter-rater reliability was good. The PIL is being revised. Factors including family situation and personal experience of illness vary greatly and yet they influence patients' reactions to receiving a diagnosis of lung cancer, their interpretation of this and their attitudes to the illness and treatment. These findings underline the need to continue to develop lung cancer services that can provide quality care tailored to each patient.



Yeung, R. S. (1994). "Management of recurrent cutaneous melanoma." *Curr Probl Cancer* **18**(3): 143-186.

Recurrent melanoma occurs in approximately one third of patients treated for cutaneous melanoma. Although the majority of recurrence occurs within the first few years of primary therapy, a significant number remains at risk beyond 10 years. With rising incidence of recurrent melanoma in Western countries, physicians will undoubtedly face the challenge of managing these patients with the limited therapeutic options currently available. Once melanoma has recurred, the overall prognosis is poor. Localized disease is best treated with complete resection, if indicated. Our existing armamentarium for systemic treatment falls short of altering the course of natural history of melanoma, but regional chemotherapy is an effective modality for in-transit disease and satellitosis. Translational research in molecular genetics and immunology will fuel new ideas for the design of rational strategies toward tumor eradication. Ongoing trials that use gene-modified melanoma cells have begun a new chapter in cancer therapeutics and lend us a closer examination of bench-top science at the bedside.

Yilmaz, B. and E. Ciftci (2013). "An FDTD-based computer simulation platform for shock wave propagation in electrohydraulic lithotripsy." *Comput Methods Programs Biomed* **110**(3): 389-398.

Extracorporeal Shock Wave Lithotripsy (ESWL) is based on disintegration of the kidney stone by delivering high-energy shock waves that are created outside the body and transmitted through the skin and body tissues. Nowadays high-energy shock waves are also used in orthopedic operations and investigated to be used in the treatment of myocardial infarction and cancer. Because of these new application areas novel lithotripter designs are needed for different kinds of treatment strategies. In this study our aim was to develop a versatile computer simulation environment which would give the device designers working on various medical applications that use shock wave principle a substantial amount of flexibility while testing the effects of new parameters such as reflector size, material properties of the medium, water temperature, and different clinical scenarios. For this purpose, we created a finite-difference time-domain (FDTD)-based computational model in which most of the physical system parameters were defined as an input and/or as a variable in the simulations. We constructed a realistic computational model of a commercial electrohydraulic lithotripter and optimized our simulation program using the results that were obtained by the manufacturer in an experimental setup. We, then, compared the simulation results with the results from an experimental setup in which oxygen level in water was varied. Finally, we

studied the effects of changing the input parameters like ellipsoid size and material, temperature change in the wave propagation media, and shock wave source point misalignment. The simulation results were consistent with the experimental results and expected effects of variation in physical parameters of the system. The results of this study encourage further investigation and provide adequate evidence that the numerical modeling of a shock wave therapy system is feasible and can provide a practical means to test novel ideas in new device design procedures.

Yu, H., et al. (2010). "Research progress in cancer stem cells and their drug resistance." *Chin J Cancer* **29**(3): 261-264.

Traditional theories suggest that tumor growth occurs when all tumor cells work together and result in proliferation, so treatment has been mainly directed against the majority of the cells in tumor tissue, which often relapse, metastasize, and lead to treatment failure. As cancer stem cells have been successfully isolated from different tumor tissues, in-depth study of their function in relation to traditional cancer treatment faces enormous challenges. At the same time, a new theoretical basis has been provided for the in-depth study of tumorigenesis and the evaluation of prognosis of cancer therapy. Also, new ideas have been introduced for cancer therapy. Therefore, radical treatment of cancer can be achieved through killing cancer stem cells. This article reviews the research progress on cancer stem cells and their drug resistance.

Zajicek, G. (2001). "Cancer and metaphysics." *Med Hypotheses* **57**(2): 243-248.

Metaphysics, is generally a pleasant, and harmless intellectual endeavor. Even if leading to wrong conclusions, nobody is hurt. Suppose that contrary to general belief, the Big Bang (1) never happened and the world is eternal. No harm is done. Some philosophers, like Kant, enjoyed life despite the fact that, nature, or the thing in itself, eluded their understanding (2). But suppose that the thing in itself is your patient, and you apply metaphysical reasoning for his treatment, metaphysics may occasionally be damaging. This is particularly pertinent to cancer, a disease that is haunted by false metaphysical statements. Since cancer is part of medicine, the present discourse deals with medical metaphysics. Medicine provides a simple way, or rule of thumb, for distinguishing between correct and wrong medical metaphysical statements. If they harm the patient, they are wrong, and if they aid him, they are correct. Statements that do not affect a patient's well being, e.g., 'Big Bang may be hazardous to your health', are of no apparent value and doubtful. Since treatment outcome is generally uncertain, the physician continually searches for new ideas that may aid his

patient, even if they are metaphysical. In diseases, like cancer, that elude his understanding, his adherence to metaphysics intensifies, and he is ready to consider even doubtful suggestions for treatment. Yet by relaxing the rules of thumb for evaluating metaphysical concepts, he gradually slips into the irrational domain.

Zeng, R., et al. (2016). "Multiple Roles of WNT5A in Breast Cancer." *Med Sci Monit* **22**: 5058-5067.

Breast cancer is one of the most common malignant tumors of women. Modern combinatorial therapeutic regimens can reduce patient tumor burdens to undetectable levels, yet in many cases these tumors will relapse. Understanding of breast cancer biology, developing more potent therapeutic approaches, and overcoming resistance are of great importance. WNT5A is a non-canonical signaling member of the WNT family. Its role in breast cancer still remains unclear. Most of the evidence shows that WNT5A is a suppressor in breast cancer and loss of its expression is associated with poor prognosis, while some evidence suggests the tumorigenicity of WNT5A. WNT signaling molecules are potent targets for treatment of cancer. Therefore, understanding the role of WNT5A in breast cancer may provide new ideas and methods for breast cancer treatment. We review the evidence concerning WNT5A and breast cancer involving the signaling pathways and the molecular-targeted therapy of WNT5A. Our results show that the role WNT5A plays depends on the availability of key receptors and intercellular interactions among different cell types.

Zhan, X., et al. (2010). "[Expression and clinical significance of SHP2 in the tumor tissues of smokers with lung cancer]." *Zhongguo Fei Ai Za Zhi* **13**(9): 877-881.

**BACKGROUND AND OBJECTIVE:** It has been proved that protein phosphorylation and dephosphorylation were important mechanisms in lung cancer development, and tobacco smoking is an important risk factor of lung cancer. The aim of this study is to investigate the expression and clinical significance of protein tyrosine phosphatase SHP2 in non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC); the relationship between tobacco smoking and the expression of SHP2 is also studied. **METHODS:** Immunohistochemistry (Invision) and fluorescence in situ hybridization (FISH) were used to detect the expression of SHP2 and the augment of SHP2 mRNA in the 53 lung cancer specimens. **RESULTS:** The weak positive rate of SHP2 was 80% (which was also the total positive rate) in normal bronchial epithelium. The weak, moderate and strong positive rates were 35.4%, 43.8% and 6.2% (total positive rate was 85.4%) in 48 NSCLC patients, 0%, 80% and 20% (total positive rate was 100%) in 5 SCLC patients,

40.7%, 37.4% and 3.7% (total positive rate was 81.5%) in the tumor tissues of 27 NSCLC patients who didn't smoke and 23.8%, 71.4% and 4.7% (total positive rate was 100%) in the tumor tissues of 21 NSCLC patients whose smoking indexes were  $\geq 400$ . Significant differences of SHP2 expression were observed between tumor tissues and normal bronchial epithelium, NSCLC and SCLC, and between different smoking indexes ( $P < 0.05$ ). **CONCLUSIONS:** The enhancement of SHP2 expression in the tumor tissues of NSCLC patients who smoke may be correlated with tobacco smoking; SHP2 may play certain role in the development of lung cancer; SHP2 prospectively provides new ideas for the drug research and development of lung cancer treatment.

Zhang, G., et al. (2018). "ATX-LPA axis facilitates estrogen-induced endometrial cancer cell proliferation via MAPK/ERK signaling pathway." *Mol Med Rep* **17**(3): 4245-4252.

Autotaxin (ATX) is a key enzyme that converts lysophosphatidylcholine to lysophosphatidic acid (LPA). ATX is a crucial factor that facilitates cancer progression; however, the effect of ATX on endometrial cancer has not been explored. The aim of the present study was to investigate the role of ATX in the progression of endometrial cancer. The immunohistochemical results revealed higher protein expression levels of ATX and LPA receptors (LPA 1, 2 and 3) in human endometrial cancer tissue than in non-carcinoma tissue. In addition, reverse transcription-quantitative polymerase chain reaction and western blotting analysis demonstrated that ATX and LPA receptor mRNA and protein expression was greater in Ishikawa cells, which are positive for estrogen receptor (ER), than in Hec-1A cells that exhibit low ER expression. Short interfering RNA knockdown of ATX in Ishikawa cells led to decreased cell proliferation and cell colony number, as determined by Cell Counting kit-8 and colony formation assays. Estrogen stimulated ATX mRNA expression. Inhibition of ATX decreased estrogen and LPA-induced cell proliferation. High LPA levels markedly elevated the phosphorylation levels of extracellular signal-regulated kinase (ERK). ATX downregulation moderately decreased estrogen- and LPA-induced phosphorylation of ERK. In addition, the ERK inhibitor, PD98059, reduced cell proliferation with estrogen, ATX and LPA treatment. The present study suggested that the ATX-LPA axis may facilitate estrogen-induced cell proliferation in endometrial cancer via the mitogen-activated protein kinase/ERK signaling pathway. The present study may provide ideas and an experimental basis for clinicians to identify new molecular targeted drugs for the treatment of endometrial cancer.

Zhang, K. and H. Wang (2015). "[Cancer Genome Atlas Pan-cancer Analysis Project]." *Zhongguo Fei Ai Za Zhi* **18**(4): 219-223.

Cancer can exhibit different forms depending on the site of origin, cell types, the different forms of genetic mutations which also affect cancer therapeutic effect. Although many genes have been demonstrated to change a direct result of the change in phenotype, however, many cancers lineage complex molecular mechanisms are still not fully elucidated. Therefore, The Cancer Genome Atlas (TCGA) Research Network analyzed a large human tumors, in order to find the molecular changes in DNA, RNA, protein and epigenetic level, The results contain a wealth of data provides us with an opportunity for common, personality and new ideas throughout the cancer lineages form a whole description. Pan-cancer genome program first compares the 12 kinds of cancer types. Analysis of different tumor molecular changes and their functions, will tell us how effective treatment method is applied to a similar phenotype of the tumor.

Zhang, T. Y., et al. (2015). "Effect of overexpression of hypoxia-inducible factor-1alpha induced by hyperoxia in vivo in LNCaP tumors on tumor growth rate." *Asian Pac J Trop Med* **8**(10): 813-820.

**OBJECTIVE:** To study effect of overexpression of hypoxia-inducible factor-1alpha induced by hyperoxia in vivo in LNCaP tumors on tumor growth rate. **METHODS:** The prostate cancer LNCaP cells were inoculated in the abdomen of mice. All the mice were randomly placed in the gas chamber with different oxygen content. The groups were divided as follows: twelve mice in hypoxia group, sixteen mice in normoxia group, ten mice in hyperoxia group. After 28 d of treatment, the mice were weighed, the blood samples were taken from the left ventricle, and the tumor was isolated and weighed. Tumor growth, angiogenesis and vascularization, HIF-1alpha expression and intracellular signal transduction molecules expression in each group of xenografts were detected and analyzed by using Western blotting and immunofluorescence and determination of hemoglobin. **RESULTS:** Comparison of the growth of xenografts in each group showed that, the xenografts growth of hypoxia group was more quickly than that of normoxia group. The difference was statistically significant ( $P = 0.004$ ). The difference in xenografts growth between hyperoxia group compared and normoxia group was not statistically significant ( $P > 0.05$ ). The expressions of HIF-1alpha, VEGF and VEGF-R of xenografts in hyperoxia group were significantly higher than those of normoxia group ( $P < 0.05$ ). The expression of HIF-1alpha of xenografts in hypoxia group and normoxia group were similar. The blood growth rate of xenografts in hypoxia group (170%) was significantly higher than that of normoxia

group (40%) ( $P < 0.05$ ). The expression of Nrf2 of xenografts in hyperoxia group was significantly higher than that of normoxia group ( $P < 0.05$ ). **CONCLUSIONS:** When hyperoxia induces the overexpression of HIF-1alpha in LNCaP tumor, it will not affect tumor growth. It provides a new ideas and theoretical basis for the clinical treatment of prostate cancer.

Zhang, Y., et al. (2018). "[Progress of Long Non-coding RNA in Non-small Cell Lung Cancer]." *Zhongguo Fei Ai Za Zhi* **21**(1): 43-49.

Lung cancer is one of the most important malignant tumors in the world. The morbidity and mortality rank the first in all kinds of cancer. Long non-coding RNA (lncRNA) is at least 200 nt long and has no protein coding capacity. It plays an important role in the epigenetic regulation, cell cycle regulation, the regulation of cell differentiation, and many other life activities. The studies indicate that dysregulation of lncRNAs in non-small cell lung cancer (NSCLC) tissue and blood circulation is associated with the occurrence and development of cancer. The lncRNAs play an significant role in proliferation, differentiation, migration and apoptosis of the tumor cells. Explore the potential mechanism between lncRNAs and NSCLC is beneficial for the early diagnosis, target therapy and improve prognosis. Therefore, the study aims to demonstrate the latest studies on the lncRNAs related to occurrence, diagnosis, therapy and prognosis of NSCLC. It can help to deeply understanding of lncRNA, and provide new ideas for the prevention of NSCLC.

Zhao, J. Y., et al. (2015). "Five miRNAs Considered as Molecular Targets for Predicting Esophageal Cancer." *Med Sci Monit* **21**: 3222-3230.

**BACKGROUND:** Esophageal cancer (EC) is one of the most aggressive malignant gastrointestinal tumors; however the traditional therapies for EC are not effective enough. Great improvements are needed to explore new and valid treatments for EC. We aimed to screen the differentially expressed miRNAs (DEMs) in esophageal cancer and explore the pathogenesis of esophageal cancer along with functions and pathways of the target genes. **MATERIAL AND METHODS:** miRNA high-throughput sequencing data were downloaded from The Cancer Genome Atlas (TCGA), then the DEMs underwent principal component analysis (PCA) based on their expression value. Following that, TargetScan software was used to predict the target genes, and enrichment analysis and pathway annotation of these target genes were done by DAVID and KEGG, respectively. Finally, survival analysis between the DEMs and patient survival time was done, and the miRNAs with prediction potential were identified. **RESULTS:** A total of 140 DEMs were obtained, 113

miRNAs were up-regulated including hsa-mir-153-2, hsa-mir-92a-1 and hsa-mir-182; while 27 miRNAs were down-regulated including hsa-mir comprising 29a, hsa-mir-100 and hsa-mir-139 and so on. Five miRNAs (hsa-mir-103-1, hsa-mir-18a, hsa-mir-324, hsa-mir-369 and hsa-mir-320b-2) with diagnostic and preventive potential were significantly correlated with survival time. CONCLUSIONS: The crucial molecular targets such as p53 may provide great clinical value in treatment, as well to provide new ideas for esophageal cancer therapy. The target genes of miRNA were found to play key roles in protein phosphorylation, and the functions of the target genes during protein phosphorylation should be further studied to explore novel treatment of EC.

Zheng, J., et al. (2016). "YB-1, a new biomarker of glioma progression, is associated with the prognosis of glioma patients." *Acta Biochim Biophys Sin (Shanghai)* 48(4): 318-325.

Y box protein 1 (YB-1) is a multifunctional cellular protein expressed in various cancers, and is a potential target in cancer therapy. Although there is evidence showing that YB-1 plays a role in human cancers, the clinical significance of YB-1 expression in glioma has not been established. In the present study, we investigated the YB-1 level in glioma tumors and analyzed the relationship between the YB-1 level and the grade of malignant glioma, with the aim of providing new ideas for the diagnosis and treatment of gliomas in clinical and basic research settings. A total of 108 patients, comprising 14, 31, 30, and 33 with gliomas of Grades I, II, III, and IV, respectively, were included in this study. The mRNA and protein levels of YB-1 were found to be significantly different between Grade IV and lower-grade tumors. The YB-1 levels in cerebrospinal fluid were significantly higher in Grades III and IV glioma patients than in Grades I and II patients. Immunofluorescence staining was used to detect the levels of YB-1 in the cytoplasm and the nucleus, and results indicated that the intracellular distribution was significantly associated with the pathological grade of glioma. A higher level of YB-1 was associated with shortened survival, suggesting that YB-1 plays a role in the progression of human glioma.

The above contents are the collected information from Internet and public resources to offer to the people for the convenient reading and information disseminating

and sharing.

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