Stem Cell and Life Extend Research Literatures

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Abstract: Stem cells are derived from embryonic and non-embryonic tissues. Most stem cell studies are for animal stem cells and plants have also stem cell. Stem cells were discovered in 1981 from early mouse embryos. Stem cells have the potential to develop into all different cell types in the living body. Stem cell is a body repair system. When a stem cell divides it can be still a stem cell or become adult cell, such as a brain cell. Stem cells are unspecialized cells and can renew themselves by cell division, and stem cells can also differentiate to adult cells with special functions. Stem cells replace the old cells and repair the damaged tissues. Embryonic stem cells can become all cell types of the body because they are pluripotent. Adult stem cells are thought to be limited to differentiating into different cell types of their tissue of origin. This article introduces recent research reports as references in the related studies.
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Introduction

The stem cell is the origin of an organism's life that has the potential to develop into many different types of cells in life bodies. In many tissues stem cells serve as a sort of internal repair system, dividing essentially without limit to replenish other cells as long as the person or animal is still alive. When a stem cell divides, each new cell has the potential either to remain a stem cell or become another type of cell with a more specialized function, such as a red blood cell or a brain cell. This article introduces recent research reports as references in the related studies.

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Acharya, M. M., et al. (2011). "Stem cell transplantation strategies for the restoration of cognitive dysfunction caused by cranial radiotherapy." J Vis Exp(56).

Radiotherapy often provides the only clinical recourse for those afflicted with primary or metastatic brain tumors. While beneficial, cranial irradiation can induce a progressive and debilitating decline in cognition that may, in part, be caused by the depletion of neural stem cells. Given the increased survival of patients diagnosed with brain cancer, quality of life in terms of cognitive health has become an increasing concern, especially in the absence of any satisfactory long-term treatments. To address this serious health concern we have used stem cell replacement as a strategy to combat radiation-induced cognitive decline. Our model utilizes athymic nude rats subjected to cranial irradiation. The ionizing radiation is delivered as either whole brain or as a highly focused beam to the hippocampus via linear accelerator (LINAC) based stereotaxic radiosurgery. Two days following irradiation, human neural stem cells (hNSCs) were stereotaxically transplanted into the hippocampus. Rats were then assessed for changes in cognition, grafted cell survival and for the expression of differentiation-specific markers 1 and 4-months after irradiation. Our cognitive testing paradigms have demonstrated that animals engrafted with hNSCs exhibit significant improvements in cognitive function. Unbiased stereology reveals significant survival (10-40%) of the engrafted cells at 1 and 4-months after transplantation, dependent on the amount and type of cells grafted. Engrafted cells migrate extensively, differentiate along glial and neuronal lineages, and express a range of immature and mature phenotypic markers. Our data demonstrate direct cognitive benefits derived from engrafted human stem cells, suggesting that this procedure may one day afford a promising strategy for the long-term functional restoration of cognition in individuals subjected to cranial radiotherapy. To promote the dissemination of the critical procedures necessary to replicate and extend our studies, we have provided written and visual documentation of several key steps in our experimental plan, with an emphasis on stereotaxic radiosurgey and transplantation.

Aversa, F., et al. (1998). "Mismatched T cell-depleted hematopoietic stem cell transplantation for children with high-risk acute leukemia." Bone Marrow Transplant **22 Suppl 5**: S29-32.

The aim of this study was to extend allogeneic hematopoietic stem cell transplantation to leukemia patients without a matched donor. To

prevent graft failure, large doses of T cell-depleted hematopoietic stem cells were transplanted following a highly myeloablative and immunosuppressive conditioning regimen. Fifteen children with high-risk acute leukemia received T cell-depleted hematopoietic stem cells from full-haplotype mismatched family members after a conditioning regimen that included single-dose TBI, thiotepa, ATG and fludarabine. To prevent GVHD, marrow cells were T-depleted by soybean agglutinin and E-rosetting, peripheral blood cells by E-rosetting followed by positive selection of the CD34+ cells. No post-transplant prophylaxis for GVHD was administered. In all patients full donor-type engraftment was achieved. None of the evaluable patients developed either acute or chronic GVHD. Regimen-related toxicity was minimal. Five patients are alive and event-free at a median follow-up of 18 months (range 13-28). All surviving patients have a good quality of life. Seven patients have relapsed. This study shows that GVHD and graft failure, which limited the use of full-haplotype mismatched bone marrow transplants, have been overcome. Since almost all children have a mismatched relative, advances in this area should make mismatched transplants a routine consideration for patients with high-risk leukemia without a matched related or unrelated donor.

Fennel, J. A. (2008). "Alternate nuclear transfer is no alternative for embryonic stem cell research." Bioethics **22**(2): 84-91.

Recent developments allow for the creation of human stem cells without the creation of human embryos, a process called alternate nuclear transfer ('ANT'). Pursuing this method of stem cell research makes sense for pro-lifers if arguments for the sanctity of the human embryo do not apply to ANT. However, the technology that makes ANT possible undermines the erstwhile technical barrier between human embryos and somatic cell DNA. These advances bring home the force of hypothetical arguments about the potential of the DNA in somatic cells, showing that there is not a morally relevant difference between the potential of an embryo and the potential of the DNA in a somatic cell. Therefore, the supposed distinction between entities that are potential human life and entities that are human life does not give any support to arguments for the sanctity of the human embryo because those arguments extend value to too many entities.

Giralt, S. (2002). "Update on non-myeloablative stem cell transplantation for hematologic malignancies." Int J Hematol **76 Suppl 1**: 368-375.

Allogeneic stem cell transplantation is an established treatment modality for a variety of hematologic malignancies. Unfortunately it carries a high risk of complications and toxicities related to the intensive preparative regimen which is traditionally used for pre-transplant myeloablation and the graft versus host disease, which may be life threatening. Thus allogeneic stem cell transplantation has been used only for younger patients with a good performance status, excluding many other potential candidates due to advanced age or comorbid conditions. Non ablative or reduced intensity preparative regimens for allogeneic stem cell transplantation (NST) have been proposed as a strategy that would allow exploiting the graft versus tumor effect of allogeneic transplantation without the toxicity of myeloablative therapy. After more than five years of cumulative clinical experience, it is now well established that NST is a feasible treatment option for patients with suboptimal performance status and is mostly effective in slow proliferating malignancies, which gives time for a graft versus malignancy effect to take place. Additionally achievement of stable donor cell engraftment with NSTs provides a platform for adoptive immune cell treatments and may allow to extend indications of stem cell transplantation in the future.

Giralt, S. (2002). "Update on non-myeloablative stem cell transplantation for hematologic malignancies." Int J Hematol **76 Suppl 1**: 176-183.

Allogeneic stem cell transplantation is an established treatment modality for a variety of hematologic malignancies. Unfortunately it carries a high risk of complications and toxicities related to the intensive preparative regimen which is traditionally used for pre-transplant myeloablation and the graft versus host disease, which may be life threatening. Thus allogeneic stem cell transplantation has been used only for younger patients with a good performance status, excluding many other potential candidates due to advanced age or comorbid conditions. Non ablative or reduced intensity preparative regimens for allogeneic stem cell transplantation (NST) have been proposed as a strategy that would allow exploiting the graft versus tumor effect of allogeneic transplantation without the toxicity of myeloablative therapy. After more than five years of cumulative clinical experience, it is now well established that NST is a feasible treatment option for patients with suboptimal performance status and is mostly effective in slow proliferating malignancies, which gives time for a graft versus malignancy effect to take place. Additionally achievement of stable donor cell engraftment with NSTs provides a platform for adoptive immune cell

treatments and may allow to extend indications of stem cell transplantation in the future.

Munz, M., et al. (2008). "Glycosylation is crucial for stability of tumour and cancer stem cell antigen EpCAM." Front Biosci **13**: 5195-5201.

Epithelial cell adhesion molecule EpCAM is strongly over-expressed in a variety of carcinomas where it is involved in signalling events resulting in increased expression of target genes such as c-Myc, cyclins and others, eventually conferring cells an oncogenic phenotype. However, EpCAM is also expressed in a series of healthy epithelia, albeit generally to a far lesser extend. We have uncovered differential glycosylation of EpCAM as a means to discriminate normal from malignant tissues. EpCAM was hyperglycosylated in carcinoma tissue as compared with autologous normal epithelia. All three N-glycosylation consensus sequences within EpCAM's extracellular domain were used in human and murine cells. We show that glycosylation at asparagine198 is crucial for protein stability. Mutants of EpCAM that substitute asparagine198 for alanine showed a decreased overall expression and half-life of the molecule at the plasma membrane. This is of considerable importance with respect to EpCAM variants expressed in normal tissue, where it might reveal to be less stable and thus may have repercussions on functionality.

O'Shaughnessy, T. J., et al. (2009). "Passaged neural stem cell-derived neuronal networks for a portable biosensor." Biosens Bioelectron **24**(8): 2365-2370.

We have previously demonstrated a portable biosensor that utilizes networks of mammalian neurons on microelectrode arrays (MEAs) as the sensing element. These neuronal cultures on MEAs are derived from primary neuronal tissues and are short-lived. In order to extend the shelf life of neuronal networks for use in a fieldable sensor technology, a renewable source of networks is needed. Neural stem and progenitor cells are capable of self-renewal and differentiation into functional neuronal networks. The purpose of this study was to develop a strategy for growing passaged neural stem and progenitor cells on MEAs under controlled conditions to produce differentiated neurons and glia comprising functional neuronal networks. Primary and passaged neuroepithelial stem and progenitor cells dissociated from embryonic day 13 rat cortex were seeded on MEAs and maintained with serum-free medium containing basic fibroblast growth factor (bFGF) combined with brain-derived neurotrophic factor (BDNF). These culture conditions lead to abundant neurons, with astrocytes as supportive cells, forming synaptically linked networks of neurons. Spontaneous action potentials were best recorded from networks derived from primary or passaged progenitor cells 4-5 weeks after initial culture. The passaged progenitor cell-derived networks on MEAs responded to the GABA(A) antagonist bicuculline, the NMDA glutamate inhibitor APV, and the non-NMDA glutamate antagonist CNQX indicating active synapses were present. Passaged neural stem and progenitor cell-derived networks on MEAs have properties similar to networks derived from primary neuronal cultures and can serve as a renewable supply of sensor elements for detection of environmental threats.

Outka, G. (2002). "The ethics of human stem cell research." Kennedy Inst Ethics J **12**(2): 175-213.

The medical and clinical promise of stem cell research is widely heralded, but moral judgments about it collide. This article takes general stock of such judgments and offers one specific resolution. It canvasses a spectrum of value judgments on sources, complicity, adult stem cells, and public and private contexts. It then examines how debates about abortion and stem cell research converge and diverge. Finally, it proposes to extend the principle of "nothing is lost" to current debates. This extension links historical discussions of the ethics of direct killing with unprecedented possibilities that in vitro fertilization procedures yield. A definite normative region to inhabit is located, within a larger range of rival value judgments. The creation of embryos for research purposes only should be resisted, yet research on "excess' embryos is permissible by virtue of an appeal to the "nothing is lost" principle.

Tramontin, A. D., et al. (2003). "Postnatal development of radial glia and the ventricular zone (VZ): a continuum of the neural stem cell compartment." Cereb Cortex **13**(6): 580-587.

The germinal neuroepithelium, or ventricular zone (VZ) of the developing fetal brain, was once thought to transform into the non-germinal ependymal zone of the postnatal and adult brain. Persistence of neural stem cells and neurogenesis throughout postnatal life, however, suggests a continuum between embryonic and adult germinal brain centers. Here, we suggest that developmental changes in anatomy and molecular marker expression in the ventricular walls (the principal germinal centers of the brain) may have misled us into current interpretations of VZ transformation from a germinal to a non-germinal epithelium. We review previous studies and present new data indicating that a germinal layer with characteristics similar to those of the embryonic VZ persists in lateral ventricular walls of the postnatal mouse brain, a region where the adult

subventricular zone (SVZ) develops and where neurogenesis persists into adult life. The early postnatal VZ is largely composed of radial glial cell bodies that remain proliferative, display interkinetic nuclear migration and serve as progenitors of new neurons. Ependymal cells then progressively populate the walls of the lateral ventricle but a subpopulation of astrocytes, derived from radial glia, remain in contact with the ventricle lumen, into which they extend a single cilium similar to that found on neuroepithelial cells and radial cells. We propose that a VZ 'compartment' is retained postnatally and that this niche may be essential for stem cell function.

Tsai, D. F. (2005). "Human embryonic stem cell research debates: a confucian argument." J Med Ethics **31**(11): 635-640.

Human embryonic stem cell research can bring about major biomedical breakthroughs and thus contribute enormously to human welfare, yet it raises serious moral problems because it involves using human embryos for experiment. The "moral status of the human embryo" remains the core of such debates. Three different positions regarding the moral status of the human embryo can be categorised: the "all" position, the "none" position, and the "gradualist" position. The author proposes that the "gradualist" position is more plausible than the other two positions. Confucius's moral principle of jen, which proposes a unique theory of "love of gradation", and the principle of yi, which advocates "due treatment for persons", are then explored. The author then argues that our moral obligations to do good to other living organisms, persons, and our families are different. Putting together the "gradualist" position on the human embryo, and Confucius's theories of "love of gradation" and "due treatment for persons", the author concludes that the early embryo has less ethical significance than the later fetus and adult human. The moral obligation we have toward persons is clearer and stronger than that which we have toward human embryos. Embryo research is justifiable if it brings enormous welfare to human persons that cannot be otherwise achieved. The "love of gradation" requires us, however, to extend love and respect towards other entities according to their different status. We should therefore be very cautious in using human embryos for research, acknowledging the gradualist nature of their moral status.

Zhou, T., et al. (2011). "Dominant-negative C/ebpalpha and polycomb group protein Bmi1 extend short-lived hematopoietic stem/progenitor cell life span and induce lethal dyserythropoiesis." Blood **118**(14): 3842-3852.

The primitive hematopoietic stem/progenitor cells (HSPCs) during embryonic hematopoiesis are thought to be short-lived (SL) with limited self-renewal potential. The fate and consequence of these short-lived HSPCs, once reprogrammed into "long-lived" in a living animal body, remain unknown. Here we show that targeted expression of a dominant-negative C/ebpalpha (C/ebpalphaDN) in the primitive SL-HSPCs during zebrafish embryogenesis extends their life span, allowing them to survive to later developmental stage to colonize the definitive hematopoietic sites, where they undergo a proliferative expansion followed by erythropoietic dysplasia and embryonic lethality because of circulation congestion. Mechanistically, C/ebpalphaDN binds to a conserved C/EBP-binding motif in the promoter region of bmi1 gene, associated with a specific induction of bmi1 transcription in the transgenic embryos expressing C/ebpalphaDN. Targeted expression of Bmi1 in the SL-HSPCs recapitulates nearly all aberrant phenotypes induced by C/ebpalphaDN, whereas knockdown of bmi1 largely rescues these abnormalities. The results indicate that Bmi1 acts immediately downstream of C/ebpalphaDN to regulate the survival and self-renewal of HSPCs and contribute to the erythropoietic dysplasia.

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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