Cadherin

Mark Herbert, PhD

World Development Institute
39-06 Main Street, Flushing, Queens, New York 11354, USA, ma8080@gmail.com

Abstract: Cadherins (calcium dependent adhesion molecules) are a class of type-1 transmembrane proteins. They play important roles in cell adhesion, ensuring that cells within tissues are bound together. Their functions are dependent from calcium ions (Ca^{2+}). The cadherin superfamily includes cadherins, protocadherins, desmogleins, and desmocollins, etc. In structure, they share cadherin repeats, which are the extracellular Ca^{2+}-binding domains. There are multiple classes of cadherin molecule, each designated with a prefix (generally noting the type of tissue with which it is associated). It has been observed that cells containing a specific cadherin subtype tend to cluster together to the exclusion of other types, both in cell culture and during development. For example, cells containing N-cadherin tend to cluster with other N-cadherin expressing cells. However, it has been noted that the mixing speed in the cell culture experiments can have an effect on the extent of homotypic specificity. In addition, several groups have observed heterotypic binding affinity (i.e., binding of different types of cadherin together) in various assays. One current model proposes that cells distinguish cadherin subtypes based on kinetic specificity rather than thermodynamic specificity, as different types of cadherin homotypic bonds have different lifetimes.
[Mark Herbert, PhD. Cadherin**.** *Academ Arena* 2019;11(1):166-168]. ISSN 1553-992X (print); ISSN 2158-771X (online). http://www.sciencepub.net/academia. 4. doi:10.7537/marsaaj110119.04.

Keywords: cadherin; cell; protein; DNA; life

Cadherins (calcium dependent adhesion molecules) are a class of type-1 transmembrane proteins. They play important roles in cell adhesion, ensuring that cells within tissues are bound together. Their functions are dependent from calcium ions (Ca^{2+}).

The cadherin superfamily includes cadherins, protocadherins, desmogleins, and desmocollins, etc. In structure, they share cadherin repeats, which are the extracellular Ca^{2+}-binding domains. There are multiple classes of cadherin molecule, each designated with a prefix (generally noting the type of tissue with which it is associated). It has been observed that cells containing a specific cadherin subtype tend to cluster together to the exclusion of other types, both in cell culture and during development. For example, cells containing N-cadherin tend to cluster with other N-cadherin expressing cells. However, it has been noted that the mixing speed in the cell culture experiments can have an effect on the extent of homotypic specificity. In addition, several groups have observed heterotypic binding affinity (i.e., binding of different types of cadherin together) in various assays. One current model proposes that cells distinguish cadherin subtypes based on kinetic specificity rather than thermodynamic specificity, as different types of cadherin homotypic bonds have different lifetimes.

Different members of the cadherin family are found in different locations. E-cadherins are found in epithelial tissue; N-cadherins are found in neurons; and P-cadherins are found in the placenta. T-cadherins have no cytoplasmic domains and must be tethered to the plasma membrane.

E-cadherin (epithelial) is the most well-studied member of the family. It consists of 5 cadherin repeats (EC1 ~ EC5) in the extracellular domain, one transmembrane domain, and an intracellular domain that binds p120-catenin and beta-catenin. The intracellular domain contains a highly-phosphorylated region vital to beta-catenin binding and therefore to E-cadherin function.] Beta-catenin can also bind to alpha-catenin. Alpha-catenin participates in regulation of actin-containing cytoskeletal filaments. In epithelial cells, E-cadherin-containing cell-to-cell junctions are often adjacent to actin-containing filaments of the cytoskeleton.

E-cadherin is first expressed in the 2-cell stage of mammalian development, and becomes phosphorylated by the 8-cell stage, where it causes compaction. In adult tissues, E-cadherin is expressed in epithelial tissues, where it is constantly regenerated with a 5-hour half-life on the cell surface.

Loss of E-cadherin function or expression has been implicated in cancer progression and metastasis. E-cadherin downregulation decreases the strength of cellular adhesion within a tissue, resulting in an increase in cellular motility. This in turn may allow cancer cells to cross the basement membrane and invade surrounding tissues.

Other cadherins

- CDH1 - E-cadherin (epithelial)
- CDH2 - N-cadherin (neural)
- CDH3 - P-cadherin (placental)

- CDH4 - R-cadherin (retinal)
- CDH5 - VE-cadherin (vascular endothelial)
- CDH6 - K-cadherin (kidney)
- CDH7 - cadherin 7, type 2
- CDH8 - cadherin 8, type 2
- CDH9 - cadherin 9, type 2 (T1-cadherin)
- CDH10 - cadherin 10, type 2 (T2-cadherin)
- CDH11 - OB-cadherin (osteoblast)
- CDH12 - cadherin 12, type 2 (N-cadherin 2)
- CDH13 - T-cadherin - H-cadherin (heart)
- CDH15 - M-cadherin (myotubule)
- CDH16 - KSP-cadherin
- CDH17 - LI cadherin (liver-intestine)
- CDH18 - cadherin 18, type 2
- CDH19 - cadherin 19, type 2
- CDH20 - cadherin 20, type 2
- CDH23 - cadherin 23, (neurosensory epithelium)

Human proteins containing cadherin domain

CDH1; CDH10; CDH11; CDH12; CDH13; CDH15; CDH16; CDH17; CDH18; CDH19; CDH2; CDH20; CDH22; CDH23; CDH24; CDH26; CDH28; CDH3; CDH4; CDH5; CDH6; CDH7; CDH8; CDH9; CELSR1; CELSR2; CELSR3; CLSTN1; CLSTN2; CLSTN3; DCHS1; DCHS2; DSC1; DSC2; DSC3; DSG1; DSG2; DSG3; DSG4; FAT; FAT2; FAT4; LOC389118; PCDH1; PCDH10; PCDH11X; PCDH11Y; PCDH12; PCDH15; PCDH17; PCDH18; PCDH19; PCDH20; PCDH7; PCDH8; PCDH9; PCDHA1; PCDHA10; PCDHA11; PCDHA12; PCDHA13; PCDHA2; PCDHA3; PCDHA4; PCDHA5; PCDHA6; PCDHA7; PCDHA8; PCDHA9; PCDHAC1; PCDHAC2; PCDHB1; PCDHB10; PCDHB11; PCDHB12; PCDHB13; PCDHB14; PCDHB15; PCDHB16; PCDHB17; PCDHB18; PCDHB2; PCDHB3; PCDHB4; PCDHB5; PCDHB6; PCDHB7; PCDHB8; PCDHB9; PCDHGA1; PCDHGA10; PCDHGA11; PCDHGA12; PCDHGA2; PCDHGA3; PCDHGA4; PCDHGA5; PCDHGA6; PCDHGA7; PCDHGA8; PCDHGA9; PCDHGB1; PCDHGB2; PCDHGB3; PCDHGB4; PCDHGB5; PCDHGB6; PCDHGB7; PCDHGC3; PCDHGC4; PCDHGC5; PCLKC; RESDA1; RET;

Cadherins (named for "calcium-dependent adhesion") are a class of type-1 transmembrane proteins. They play important roles in cell adhesion, forming adherens junctions to bind cells within tissues together. They are dependent on calcium (Ca2+) ions to function, hence their name.

The cadherin superfamily includes cadherins, protocadherins, desmogleins, and desmocollins, and more. [1] [2] In structure, they share cadherin repeats, which are the extracellular Ca2+-binding domains. There are multiple classes of cadherin molecule, each designated with a prefix (in general, noting the type of tissue with which it is associated). It has been observed that cells containing a specific cadherin subtype tend to cluster together to the exclusion of other types, both in cell culture and during development. [3] For example, cells containing N-cadherin tend to cluster with other N-cadherin-expressing cells. However, it has been noted that the mixing speed in the cell culture experiments can have an effect on the extent of homotypic specificity. In addition, several groups have observed heterotypic binding affinity (i.e., binding of different types of cadherin together) in various assays. One current model proposes that cells distinguish cadherin subtypes based on kinetic specificity rather than thermodynamic specificity, as different types of cadherin homotypic bonds have different lifetimes.

Structure and Function [edit] Cadherins are synthesized as polypeptides and undergo many post-translational modifications to become the proteins which mediate cell-cell adhesion and recognition. These polypeptides are approximately 720–750 amino acids long. Each cadherin has a small cytoplasmic component, a transmembrane component, and the remaining bulk of the protein is extra-cellular (outside the cell). To date, over 80 types of cadherins in humans have been identified and sequenced.

Cadherins behave as both receptors and ligands and other molecules. During development, their behavior assists in properly positioning cells: they are responsible for the separation of the different tissue layers, and for cellular migration. [10] In the very early stages of development, E-cadherin (epithelial cadherin) is most greatly expressed. During the next stage, the development of the neural plate, N-cadherin (neural cadherin) is expressed and there is a decrease in E-cadherin. Finally, during the development of the notochord and the condensation of somites, E- P- and N-cadherin expression increases. After development, cadherins play a role in maintaining cell and tissue structure, and in cellular movement. [9] Regulation of cadherin expression can occur through promoter methylation among other epigenetic mechanisms.

Ribbon representation of a repeating unit in the extracellular E-cadherin ectodomain of the mouse (Mus Musculus). There are said to be over 100 different types of cadherins found in vertebrates, which can be classified into four groups: classical, desmosomal, protocadherins, and unconventional. This large amount of diversity is accomplished by having multiple cadherin encoding genes combined with alternative RNA splicing mechanisms. Invertebrates contain fewer than 20 types of cadherins.

Different members of the cadherin family are found in different locations.

References

1. Baidu. http://www.baidu.com. 2019.

2. Cancer Biology. http://www.cancerbio.net. 2019.
3. Google. http://www.google.com. 2019.
4. Journal of American Science. http://www.jofamericanscience.org. 2019.
5. Life Science Journal. http://www.lifesciencesite.com. 2019.
6. Ma H, Chen G. Stem cell. The Journal of American Science 2005;1(2):90-92. doi:10.7537/marsjas010205.14. http://www.jofamericanscience.org/journals/am-sci/0102/14-mahongbao.pdf.
7. Ma H, Cherng S. Eternal Life and Stem Cell. Nature and Science. 2007;5(1):81-96. doi:10.7537/marsnsj050107.10. http://www.sciencepub.net/nature/0501/10-0247-mahongbao-eternal-ns.pdf.
8. Ma H, Cherng S. Nature of Life. Life Science Journal 2005;2(1):7-15. doi:10.7537/marslsj020105.03. http://www.lifesciencesite.com/lsj/life0201/life-0201-03.pdf.
9. Marsland Press. http://www.sciencepub.net. 2019; http://www.sciencepub.org. 2019.
10. National Center for Biotechnology Information, U.S. National Library of Medicine. http://www.ncbi.nlm.nih.gov/pubmed. 2019.
11. Nature and Science. http://www.sciencepub.net/nature. 2019.
12. Stem Cell. http://www.sciencepub.net/stem. 2019.
13. Wikipedia. The free encyclopedia. http://en.wikipedia.org. 2019.

1/25/2019