Chapter 2

CADHERINS: CELL ADHESION MOLECULES

Hasan ASKER[1]

Introduction

Cell adhesion molecules (CAMs) on the cell surface are molecules of protein structure that allow cells to attach to each other and to the extracellular matrix (Atabekoğlu, Engin, Üstün, & Aytaç, 2002). CAMs, which play an important role in the formation of cell-cell connections; the organization of many activities such as the activation, growth, migration, differentiation and death of the cell (Freemont, 1998; Juliano, 2002). Also CAMs provide for the transmission and regulation of intercellular signals. These molecules were studied in 4 main groups based on their structural similarities.

a. Immunoglobulin (Ig) Super Gene Family
b. Integrin Family
c. The Selectin Family
d. Cadherin Family

All members of the immunoglobulin supergene family serve as ligands for leukocyte integrin adhesion receptors where vascular endothelium is present. It is also known that they provide antigen recognition, complement binding and cell adhesion functions (Haznedaroğlu & Benekli, 1998).

Integrins are found in endothelial cells, epithelial cells, platelets, leukocytes and tumor cells and form cation-dependent adhesion. It is known that the intracellular part of these molecules is related to the intracellular skeleton of transmembrane proteins such as α-actinin, vinculin and talin (Adams & Shaw, 1994; Albelda & Buck, 1990).

The lectin region of the selectins is composed of a region similar to the epithelial growth factor and modules like the complement regulatory protein, and there are 3 types, E-selectin, P-selectin and L-selectin (Haznedaroğlu & Benekli, 1998).

[1]Assist Prof, Usak University, Faculty of Medicine, hasan.asker@usak.edu.tr

Catenins

Catenin has been reported to have cytoplasmic protein groups that interact with the intracellular region of the cadherin molecule and regulate cadherin functions. According to their electrophoretic fluidity, 3 main catenin types were identified. These are α, β, and γ catenin (Ozawa, Baribault, & Kemler, 1989).

Alfa (α) Catenin

α-catenin binds directly to actin filaments in cultured cells (Rimm, Koslov, Kebriaei, Cianci, & Morrow, 1995). α-catenin, β-catenin was attached to the amino terminus, γ-catenin was occasionally substituted for β-catenin in the cadherin-catenin complex (Funayama, Fagotto, McCrea, & Gumbiner, 1995).

Beta (β) Catenin

β-catenin is a protein encoded by the CTNNB1 gene in humans. In Drosophila, the homologous protein is called armadillonum. β-catenin was introduced as a subunit of the cadherin protein complex and an integral component of the Wnt signaling pathway (Kraus et al., 1994; MacDonald, Tamai, & He, 2009).

Gama (γ) Catenin

γ-catenin is an important component of desmosomes and is associated with desmosomal cadherins (Vleminckx & Kemler, 1999; Witcher et al., 1996).

References

Adsams, D. H., & Shaw, S. (1994). Leucocyte-endothelial interactions and regulation of leucocyte migration. *The Lancet*, 343(8901), 831–836.

Albelda, S. M., & Buck, C. A. (1990). Integrins and other cell adhesion molecules. *FASEB Journal: Official Publication of the Federation of American Societies for Experimental Biology*, 4(11), 2868–2880.

Anastasiadis, P. Z., & Reynolds, A. B. (2000). The p120 catenin family: complex roles in adhesion, signaling and cancer. *J Cell Sci,* 113(8), 1319–1334.

Atabekoğlu, C. S., Engin, Y., Üstün, Y., & Aytaç, R. (2002). Üreme Fizyolojisi ve Adezyon Molekülleri. *Ankara Üniversitesi Tıp Fakültesi Mecmuası,* 55(1), 85–92.

Blaschuk, O. W., Sullivan, R., David, S., & Pouliot, Y. (1990). Identification of a cadherin cell adhesion recognition sequence. *Developmental Biology*, 139(1), 227–229.

Bobryshev, Y. V., Cherian, S. M., Inder, S. J., & Lord, R. S. (1999). Neovascular expression of VE-cadherin in human atherosclerotic arteries and its relation to intimal inflammation. *Cardiovascular Research*, 43(4), 1003–1017.

Bradley, R. S., Cowin, P., & Brown, A. M. (1993). Expression of Wnt-1 in PC12 cells results in modulation of plakoglobin and E-cadherin and increased cellular adhesion. *The Journal of Cell Biology*, 123(6 Pt 2), 1857–1865.

Buhmeida, A., Pyrhönen, S., Laato, M., & Collan, Y. (2006). Prognostic factors in prostate cancer. *Diagnostic Pathology*, 1, 4.

Cepek, K. L., Shaw, S. K., Parker, C. M., Russell, G. J., Morrow, J. S., Rimm, D. L., & Brenner, M. B. (1994). Adhesion between epithelial cells and T lymphocytes mediated by E-cadherin and the alpha E beta 7 integrin. *Nature*, 372(6502), 190–193. https://doi.org/10.1038/372190a0

Fredette, B. J., & Ranscht, B. (1994). T-cadherin expression delineates specific regions of the developing motor axon-hindlimb projection pathway. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, 14(12), 7331–7346.

Freemont, A. J. (1998). Demystified ... adhesion molecules. *Molecular Pathology*, 51(4), 175–184.

Friedl, J., Puhlmann, M., Bartlett, D. L., Libutti, S. K., Turner, E. N., Gnant, M. F. X., & Alexander, H. R. (2002). Induction of permeability across endothelial cell monolayers by tumor necrosis factor (TNF) occurs via a tissue factor-dependent mechanism: relationship between the procoagulant and permeability effects of TNF. *Blood*, 100(4), 1334–1339.

Funayama, N., Fagotto, F., McCrea, P., & Gumbiner, B. M. (1995). Embryonic axis induction by the armadillo repeat domain of beta-catenin: evidence for intracellular signaling. *The Journal of Cell Biology*, 128(5), 959–968.

Gagliardi, G., Kandemir, O., Liu, D., Guida, M., Benvestito, S., Ruers, T. G., … Talbot, I. C. (1995). Changes in E-cadherin immunoreactivity in the adenoma-carcinoma sequence of the large bowel. *Virchows Archiv: An International Journal of Pathology*, 426(2), 149–154.

Gänzler, S. I., & Redies, C. (1995). R-cadherin expression during nucleus formation in chicken forebrain neuromeres. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, 15(6), 4157–4172.

Gumbiner, B. M. (1996). Cell Adhesion: The Molecular Basis of Tissue Architecture and Morphogenesis. *Cell*, 84(3), 345–357. https://doi.org/10.1016/S0092-8674(00)81279-9

Haznedaroğlu, İ. C., & Benekli, M. (1998). Adezyon molekülleri. *Türk Hematoloji - Onkoloji Dergisi*, 4(8), 252–254.

Hofmann, S., Grasberger, H., Jung, P., Bidlingmaier, M., Vlotides, J., Janssen, O. E., & Landgraf, R. (2002). The tumour necrosis factor-alpha induced vascular permeability is associated with a reduction of VE-cadherin expression. *European Journal of Medical Research*, 7(4), 171–176.

Ivanov, D. B., Philippova, M. P., & Tkachuk, V. A. (2001). Structure and functions of classical cadherins. *Biochemistry. Biokhimiia*, 66(10), 1174–1186.

Juliano, R. L. (2002). Signal Transduction by Cell Adhesion Receptors and the Cytoskeleton: Functions of Integrins, Cadherins, Selectins, and Immunoglobulin-Superfamily Members. *Annual Review of Pharmacology and Toxicology*, 42(1), 283–323. https://doi.org/10.1146/annurev.pharmtox.42.090401.151133

Kadowaki, T., Shiozaki, H., Inoue, M., Tamura, S., Oka, H., Doki, Y., … Mori, T. (1994). E-Cadherin and α-Catenin Expression in Human Esophageal Cancer. *Cancer Research*, 54(1), 291–296.

Kraus, C., Liehr, T., Hülsken, J., Behrens, J., Birchmeier, W., Grzeschik, K.-H., & Ballhausen, W. G. (1994). Localization of the Human β-Catenin Gene (CTNNB1) to 3p21: A Region Implicated in Tumor Development. *Genomics*, 23(1), 272–274. https://doi.org/10.1006/geno.1994.1493

Libby, P. (2012). History of Discovery: Inflammation in Atherosclerosis. Arteriosclerosis, Thrombosis, and Vascular *Biology*, 32(9), 2045–2051. https://doi.org/10.1161/ATVBAHA.108.179705

MacDonald, B. T., Tamai, K., & He, X. (2009). Wnt/β-catenin signaling: components, mechanisms, and diseases. Developmental *Cell*, 17(1), 9–26. https://doi.org/10.1016/j.devcel.2009.06.016

Matsui, S., Shiozaki, H., Inoue, M., Tamura, S., Doki, Y., Kadowaki, T., … Tsukita, S. (1994). Immunohistochemical evaluation of alpha-catenin expression in human gastric cancer. *Virchows Archiv: An International Journal of Pathology*, 424(4), 375–381.

Nakagawa, S., & Takeichi, M. (1995). Neural crest cell-cell adhesion controlled by sequential and subpopulation-specific expression of novel cadherins. *Development*, 121(5), 1321–1332.

Nose, A., Tsuji, K., & Takeichi, M. (1990). Localization of specificity determining sites in cadherin cell adhesion molecules. *Cell*, 61(1), 147–155. https://doi.org/10.1016/0092-8674(90)90222-Z

Ozawa, M., Baribault, H., & Kemler, R. (1989). The cytoplasmic domain of the cell adhesion molecule uvomorulin associates with three independent proteins structurally related in different species. *The EMBO Journal*, 8(6), 1711–1717.

Ozawa, M., Ringwald, M., & Kemler, R. (1990). Uvomorulin-catenin complex formation is regulated by a specific domain in the cytoplasmic region of the cell adhesion molecule*. Proceedings of the National Academy of Sciences*, 87(11), 4246–4250. https://doi.org/10.1073/pnas.87.11.4246

Rimm, D. L., Koslov, E. R., Kebriaei, P., Cianci, C. D., & Morrow, J. S. (1995). Alpha 1(E)-catenin is an actin-binding and -bundling protein mediating the attachment of F-actin to the membrane adhesion complex. Proceedings of the National Academy of Sciences of the United States of America, 92(19), 8813–8817.

Takai, Y., Shimizu, K., & Ohtsuka, T. (2003). The roles of cadherins and nectins in interneuronal synapse formation. *Current Opinion in Neurobiology,* 13(5), 520–526. https://doi.org/10.1016/j.conb.2003.09.003

Takeichi, M. (1991). Cadherin cell adhesion receptors as a morphogenetic regulator. *Science*, 251(5000), 1451–1455. https://doi.org/10.1126/science.2006419

Üre, İ., & Sözen, S. (2014). Prostat Kanserinde Doğal Seyir, Prognostik Etmenler ve Nomogramlar. *Turkiye Klinikleri Journal of Urology Special Topics*, 7(4), 35–40.

Vleminckx, K., & Kemler, R. (1999). Cadherins and tissue formation: integrating adhesion and signaling. *BioEssays*, 21(3), 211–220.

Williams, E. J., Furness, J., Walsh, F. S., & Doherty, P. (1994). Activation of the FGF receptor underlies neurite outgrowth stimulated by L1, N-CAM, and N-cadherin. *Neuron*, 13(3), 583–594. https://doi.org/10.1016/0896-6273(94)90027-2

Witcher, L. L., Collins, R., Puttagunta, S., Mechanic, S. E., Munson, M., Gumbiner, B., & Cowin, P. (1996). Desmosomal Cadherin Binding Domains of Plakoglobin. *Journal of Biological Chemistry*, 271(18), 10904–10909. https://doi.org/10.1074/jbc.271.18.10904

Yap, A. S., Brieher, W. M., & Gumbiner, B. M. (1997). Molecular and Functional Analysis of Cadherin-Based Adherens Junctions. *Annual Review of Cell and Developmental Biology*, 13(1), 119–146. https://doi.org/10.1146/annurev.cellbio.13.1.119