Review Article

Cell adhesion molecules

N. C. Indhu Rekka[1], R. Sarah Sathiyawathie[2]*, R. Abilasha[3]

ABSTRACT

One of the areas of biomedical science that has recently advanced tremendously is understanding of signaling the cell surface. It is becoming increasingly clear that the body's tissues rely on its integrity, function, spatial organization, and interactions at its cell surface. Multicellular organisms require efficient mechanisms by which information can be transmitted between cells. To exchange information, cells interact with each other. Cell adhesion molecules (CAMs) belong to these class of molecules. They form the platform for cell-to-cell interactions and adhesion between cells. There are totally about 25 different types of CAMs.

KEY WORDS: Cadherins, Cell communication, Immunoglobulin superfamily, Integrins, Selectins

INTRODUCTION

Cell adhesion molecules (CAMs) are proteins located on the cell surface involved in binding with other cells or with the extracellular matrix (ECM) in the process called cell adhesion. In essence, CAMs help cells stick to each other and their surroundings.[1,2] These proteins are typically transmembrane receptors and are composed of three domains: An intracellular domain that interacts with the cytoskeleton, a transmembrane domain, and an extracellular domain that interacts either with other CAMs of the same kind (homophilic binding) or with other CAMs or the ECM (heterophilic binding).[3]

CELL-CELL ADHESION AND COMMUNICATION

Adhesion of like cells is a primary feature of the architecture of many tissues. A number of cell surface proteins (the CAMs) mediate such homophilic (like binds like) adhesion between cells of a single type and heterophilic adhesion between cells of different types.[4,5] For cells to function in an integrated manner, specialized junctions consisting of clustered cell adhesion molecules are essential.[6] There are four major classes of junctions: The tight, gap, cell-cell, and cell-matrix junctions.[7] They carry out this role by connecting the internal cytoskeleton directly to the cell exterior, either another cell or the ECM, through two cell-adhesion molecules – cadherins and integrins.[8] All cytoskeleton-associated junctions are organized into three parts: Cell-adhesion molecules, adapter proteins, and the bundle of cytoskeletal filaments itself.[9,10] They are classified as calcium-dependent and calcium-independent CAMs.[11] Calcium-independent CAM includes immunoglobulin superfamily (IgSF). Calcium-dependent CAMs include the integrins, the cadherins, and the selectins.[12]

Access this article online

Website: jprsolutions.info | ISSN: 0975-7619

CALCIUM DEPENDENT – CADHERIN CAM

Cadherins are a class of type-1 transmembrane proteins. They play important roles in cell adhesion, forming adherens junctions to bind cells within tissues together.[13] They are dependent on calcium (Ca2+) ions to function.[14] The cadherin superfamily includes cadherins, protocadherins, desmogleins, and desmocollins.[15] In structure, they share cadherin repeats, which are the extracellular Ca2+-binding domains. There are multiple classes of cadherin molecule.[16] Each cadherin has a small cytoplasmic component, a transmembrane component, and the

[1]Departemnt of Research, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Chennai, Tamil Nadu, India, [2]Department of Research, Saveetha Dental College and Hospital, Saveetha Institute of Medical and Technical Sciences, Chennai, Tamil Nadu, India, [3]Department of Oral and Maxillofacial Pathology, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Chennai, Tamil Nadu, India

***Corresponding author:** Dr. R. Sarah Sathiyawathie, Department of Research, Saveetha Dental College and Hospital, Saveetha Institute of Medical and Technical Sciences, 162, Poonamallee High Road, Chennai–600 077, Tamil Nadu, India. Phone: +91-9884156513. E-mail: dr.sarahrobin@gmail.com

Received on: 08-09-2018; Revised on: 14-11-2018; Accepted on: 26-01-2019

remaining bulk of the protein is extracellular (outside the cell).[17] 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.[18]

CALCIUM DEPENDENT – INTEGRIN CAM

Integrins are transmembrane receptors that are the bridges for cell-cell and cell- ECM interactions.[19] When triggered, integrins, in turn, trigger chemical pathways to the interior, such as the chemical composition and mechanical status of the ECM, which results in a response such as regulation of the cell cycle, cell shape, and/or motility, or new receptors being added to the cell membrane.[20,21] Ligands for integrins include fibronectin, vitronectin, collagen, and laminin. Integrins have two different chains, the alpha (α) and beta (β) subunits, and are called obligate heterodimers. The α and β subunits each penetrate the plasma membrane and possess small cytoplasmic domains.[22] Integrins have two main functions: (i) Attachment of the cell to the ECM and (ii) signal transduction from the ECM to the cell. Cell attachment to the ECM is a basic requirement to build a multicellular organism.[23] Integrins are not simply hooks but give the cell critical signals about the nature of its surroundings. They enforce a cellular decision on what biological action to take, be it attachment, movement, death, or differentiation. Thus, integrins lie at the heart of many cellular biological processes.[24]

CALCIUM DEPENDENT – SELECTINS CAM

The selectins (cluster of differentiation 62 or CD62) are a family of CAMs.[25] All selectins are single-chain transmembrane glycoproteins that share similar properties to C-type lectins due to a related amino terminus and calcium-dependent binding.[26] Selectins bind to sugar moieties and so are considered to be a type of lectin, cell adhesion proteins that bind sugar polymers. Selectins are involved in constitutive lymphocyte homing and chronic and acute inflammation processes.[27] There are three subsets of selectins:

- Selectin P is expressed in endothelial and metamegakaryocytes. It affects white blood cell movement and is increased in atherosclerotic plaques.
- Selectin E has both lectin and epidermal growth factor (EGF)-like domains. It is involved in interactions between leukocytes and endothelial and in atherosclerosis.
- Selectin L has one lectin and 1 EGF domain and is involved in neutrophil adhesion (the purple cell below is a human neutrophil).[28]

CALCIUM INDEPENDENT – IgSF CAM

IgSF CAMs are a class of CAMs.[29] They are either homophilic or heterophilic and bind integrins or different IgSF CAMs.[30] The IgSF is a large group of cell surface and soluble proteins that are involved in the recognition, binding, or adhesion processes of cells.[31] Molecules are categorized as members of this superfamily based on shared structural features with immunoglobulins; they all possess a domain known as an immunoglobulin domain or fold.[32] They are commonly associated with roles in the immune system. It includes neural CAMs (NCAMs), intercellular CAMs (ICAMs), vascular CAM (VCAM), platelet-endothelial CAM (PECAM-1), endothelial cell-selective adhesion molecule (ESAM), junctional adhesion molecule (JAMs), nectins, and other CAMs.[33] Each IgSF CAM has an extracellular domain, which contains several Ig-like intrachain disulfide-bonded loops with conserved cysteine residues, a transmembrane domain, and an intracellular domain that interacts with the cytoskeleton.[34,35] It has also been suggested that CAMs may have a role in the pathogenesis of atherosclerotic vascular disease in diabetes.[36]

CONCLUSION

Adhesion molecules play major role in many fields of medicine including embryology, immunology, and malignancy and have been referred to as “the glue of life.” Cell adhesion and adhesion molecules have been shown to contribute to the pathogenesis of a large number of common human disorders and tumor cell metastasis in cancer. The CAMs are up to open new therapeutic avenues for many pathologic conditions which are currently associated with high morbidity and mortality.

REFERENCES

1. Gassmann P, Enns A, Haier J. Role of tumor cell adhesion and migration in organ-specific metastasis formation. Onkologie 2004;27:577-82.
2. Brackenbury R, Rutishauser U, Edelman GM. Distinct calcium-independent and calcium-dependent adhesion systems of chicken embryo cells. Proc Natl Acad Sci U S A 1981;78:387-91.
3. Brown K, Yamada K. The role of integrins during vertebrae development. Dev Biol 1995;6:69-77.
4. Halbleib JM, Nelson WJ. Cadherins in development: Cell adhesion, sorting, and tissue morphogenesis. Genes Dev 2006;20:3199-214.
5. Steinberg MS. Adhesion in development: An historical overview. Dev Biol 1996;180:377-88.
6. Alrawi SJ, Schiff M, Carroll RE, Dayton M, Gibbs JF, Kulavlat M, *et al.* Aberrant crypt foci. Anticancer Res 2006;26:107-19.
7. Betson M, Lozano E, Zhang J, Braga VM. Rac activation upon cell-cell contact formation is dependent on signaling from the epidermal growth factor receptor. J Biol Chem 2002;277:36962-9.
8. Alexander NR, Tran NL, Rekapally H, Summers CE, Glackin C, Heimark RL, *et al.* N-cadherin gene expression in

prostate carcinoma is modulated by integrin-dependent nuclear translocation of twist1. Cancer Res 2006;66:3365-9.
9. Edelman GM, Gallin WJ, Delouvée A, Cunningham BA, Thiery JP. Early epochal maps of two different cell adhesion molecules. Proc Natl Acad Sci U S A 1983;80:4384-8.
10. Derycke LD, Bracke ME. N-cadherin in the spotlight of cell-cell adhesion, differentiation, embryogenesis, invasion and signalling. Int J Dev Biol 2004;48:463-76.
11. Clevers H. Wnt/beta-catenin signaling in development and disease. Cell 2006;127:469-80.
12. Desai BV, Harmon RM, Green KJ. Desmosomes at a glance. J Cell Sci 2009;122:4401-7.
13. Hulpiau P, van Roy F. Molecular evolution of the cadherin superfamily. Int J Biochem Cell Biol 2009;41:349-69.
14. Angst BD, Marcozzi C, Magee AI. The cadherin superfamily: Diversity in form and function. J Cell Sci 2001;114:629-41.
15. Bello SM, Millo H, Rajebhosale M, Price SR. Catenin-dependent cadherin function drives divisional segregation of spinal motor neurons. J Neurosci 2012;32:490-505.
16. Tesche C, Duguay TM, Schoepf UJ, van Assen M, De Cecco CN, Albrecht MH, *et al.* Current and future applications of CT coronary calcium assessment. Expert Rev Cardiovasc Ther 2018;16:441-53.
17. Niessen CM, Gumbiner BM. Cadherin-mediated cell sorting not determined by binding or adhesion specificity. J Cell Biol 2002;156:389-99.
18. Gumbiner BM. Regulation of cadherin-mediated adhesion in morphogenesis. Nat Rev Mol Cell Biol 2005;6:622-34.
19. Lodish H, Berk A, Kaiser C, Krieger M, Bretscher A, Ploegh H, *et al*. Molecular Cell Biology. 7th ed. New York: Worth Publication; 2013. p. 934.
20. Xiong JP, Stehle T, Diefenbach B, Zhang R, Dunker R, Scott DL, *et al.* Crystal structure of the extracellular segment of integrin alpha Vbeta3. Science 2001;294:339-45.
21. Hynes RO. Integrins: Bidirectional, allosteric signaling machines. Cell 2002;110:673-87.
22. Humphries MJ. Integrin structure. Biochem Soc Trans 2000;28:311-39.
23. Nermut MV, Green NM, Eason P, Yamada SS, Yamada KM. Electron microscopy and structural model of human fibronectin receptor. EMBO J 1988;7:4093-9.
24. Smith JW. Cilengitide merck. Curr Opin Investig Drugs 2003;4:741-5.
25. Calderwood DA. Talin controls integrin activation. Biochem Soc Trans 2004;32:434-7.
26. Harburger DS, Bouaouina M, Calderwood DA. Kindlin-1 and -2 directly bind the C-terminal region of beta integrin cytoplasmic tails and exert integrin-specific activation effects. J Biol Chem 2009;284:11485-97.
27. Delcommenne M, Streuli CH. Control of integrin expression by extracellular matrix. J Biol Chem 1995;270:26794-801.
28. Gullingsrud J, Sotomayor M. Mechanosensitive channels. Theoretical and Computational Biophysics Group, Beckman Institute for Advanced Science and Technology. Champaign: University of Illinois at Urbana; 2019.
29. Cotran RS, Kumar V, Collins SL. Robbins Pathologic Basis of Disease. Philadelphia: W.B Saunders Company; 1998.
30. Parham P. The Immune System. 2nd ed. New York: Garland Science; 2005. p. 244-5.
31. Ley K. The role of selectins in inflammation and disease. Trends Mol Med 2003;9:263-8.
32. Cheung LS, Raman PS, Balzer EM, Wirtz D, Konstantopoulos K. Biophysics of selectin-ligand interactions in inflammation and cancer. Phys Biol 2011;8:015013.
33. Springer TA. Adhesion receptors of the immune system. Nature 1990;346:425-34.
34. Lajtha A, Banik NL, Banik N. Handbook of Neurochemistry and Molecular Neurobiology: Neural Protein Metabolism and Function. New York: Springer; 2007. p. 698.
35. Barclay AN. Membrane proteins with immunoglobulin-like domains – a master superfamily of interaction molecules. Semin Immunol 2003;15:215-23.
36. Carter RA, Wicks IP. Vascular cell adhesion molecule 1 (CD106): A multifaceted regulator of joint inflammation. Arthritis Rheum 2001;44:985-94.

Source of support: Nil; Conflict of interest: None Declared