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Preface

Preface: The apical junctional complexes, composition, structure, and characteristics

In multicellular organisms, epithelial barriers, which promote organ homeostasis by restricting the flow of ions and solutes between cells, are fundamental to the physiology of organ systems. Epithelia form diffusion barriers between cellular compartments of very different fluid and solute composition not only through asymmetrically distributed transcellular transport mechanisms (transcellular pathway) but also by structures that regulate the diffusion of ions and small, noncharged solutes through the paracellular pathway. At the apical end of the paracellular space, adjacent cell membranes are indeed in close apposition, a site that was termed by early anatomists as the "terminal bar". These intercellular junctional complexes are composed of the tight junctions or zonula occludens, the adherens junctions or zonula adherens, and desmosomes or macular adherens, whereas gap junctions provide for intercellular communication. Tight junctions form an intercellular diffusion gate regulating the passage of ions, water, and various macromolecules through the paracellular spaces, and a fence restricting the apical/basolateral diffusion of membrane proteins and lipids whereas adherens junctions and desmosomes link membrane and cytoskeletal components at discrete contact regions. The present issue of *Biochimica et Biophysica Acta–Biomembranes* and the companion issue in preparation, titled "The apical junctional complexes, roles and dysfunctions," are designed to summarize some of the new information on some of the characteristics, composition, and structure of the apical junctional complexes. Adherens junctions mediate adhesion between neighboring cells by linking the actin cytoskeleton of one cell to that of the next cell via transmembrane adhesion molecules and their associated proteins complexes. The core of these junctions consists of two basic adhesive units, the interactions among transmembrane glycoproteins of the classical cadherin superfamily and the catenin family members (including p120-catenin, β-catenin, and α-catenin) and the nectin/afadin complexes. Niessen and Gottardi [1] highlight the diverse and extensive molecular complexity of this structure.

Desmosomes are adhesive intercellular junctions of epithelia and cardiac muscle that anchor the intermediate filament network to the plasma membrane. By functioning both as an adhesive complex and as a cell-surface attachment site for intermediate filaments, desmosomes integrate the intermediate filament cytoskeleton between cells and play an important role in maintaining tissue integrity. Garrod and Chidgey [2] consider the structure, composition, and function of desmosomes and their role in embryonic development and disease.

Tight junctions are the most apical component of the epithelial junctional complex and serve the major functional purpose of providing a "barrier" and a "fence" within the membrane, by regulating paracellular permeability and maintaining cell polarity. Tight junctions are built of three types of transmembrane proteins, of a number of peripheral membrane structural proteins, and are associated with a variety of regulatory proteins. The barrier itself is formed by continuous rows of transmembrane proteins from adjacent cells that contact in the intercellular space and is associated with a number of cortical and integral proteins functioning as scaffolds linking the integral proteins of tight junctions to the actin cytoskeleton, acting as cross linkers of transmembrane junctional proteins or being involved in vesicular trafficking to the tight junctions or in cell signaling. Chiba et al. [3] provide an overview of recent progress in studies on these proteins and highlight their roles and regulation, as well as their functional significance in human diseases, whereas Guillemot et al. [4] summarize the most recent advances in understanding the identity of the multimolecular protein complexes present in the cytoplasmic region underlying the tight junction, their domain organization, their protein interactions, and their functions in vertebrate organisms.

In epithelial and endothelial cells, tight junctions provide a physical border between apical and lateral domains, an asymmetrical distribution of molecules within the membrane referred to as "polarity". Proteins involved in epithelial cell polarization form evolutionarily conserved multiprotein complexes at the tight junction. These complexes regulate the architecture of epithelia throughout the polarization process, but the exact mechanisms underlying their roles remain poorly understood. Assémat et al. [5] focus their attention on establishing how these apical polarity complexes might regulate epithelial cell morphogenesis and functions, with particular emphasis on the latest findings on how these complexes regulate epithelial homeostasis.

Claudins are tetra-span transmembrane proteins which form the protein strands of the tight junctions and play a key selectivity role in the paracellular permeability for ions. Claudins can completely tighten the paracellular cleft for solutes, and they can form paracellular ion pores that have

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biophysical properties similar to those of traditional ion channel. Krause et al. [6] summarize structural and possible interaction features and properties of the claudin protein family

The composition of tight junctions is quite complex and diverse because they are built from about 40 different proteins, including members from multigenic families. These proteins include three transmembrane proteins (claudins, occluding, and JAMs), as well as cytoplasmic proteins fulfilling roles in scaffolding, cytoskeletal attachment, cell polarity, signaling, etc. Paris et al. [7] describe the interactions between the tight junction molecules to outline the general molecular architecture of the tight junctions and their dynamic changes in response to various signaling pathways, and stress their importance in the localized assembly of tight junctions and the establishment of cell polarity.

Adherens junctions and tight junctions are built of different proteins, but some of their components share similarities in the roles of specialized transmembrane proteins in forming extracellular adhesive contacts between cells, and intracellular links to the actin cytoskeleton. Hartsock and Nelson [8] present an overview of the formation and interactions of these two junctional complexes, of the mechanisms of regulation and dynamics of protein interactions, and how they interact with and regulate the actin cytoskeleton.

Tight junctions and adherens junction are structurally and functionally dependent on each other, and a circumferential belt of F-actin is associated with their cytoplasmic surfaces. The cytoskeleton is at least indirectly involved in the regulation of both the assembly and permeability of the tight junction in response to physiological and pathological effectors. Miyoshi and Takai [9] describe how subcellular protein interactions are coordinated to induce changes in actin organization and dynamics, in response to the status of apical junctions.

The ectoplasmic specialization (ES) is a testis-specific, actin-based hybrid anchoring and tight junction, confined to the interface between Sertoli cells at the blood-testis barrier (the "basal ES") as well as between Sertoli cells and developing spermatids (the "apical ES"). The ES shares features of adherens junctions, tight junctions, and focal contacts. By adopting the best features of each junction type, this hybrid nature of ES facilitates the extensive junction-restructuring events in the seminiferous epithelium during spermatogenesis and the migration of developing germ cells across the seminiferous epithelium. Wong et al. [10] discuss the biology and the unusual features of ES in AJ dynamics in the seminiferous epithelium.

The tight junction is a far more dynamic and complex structure than previously recognized and can undergo large reversible conductance changes in a matter of seconds and yet preserve its permselectivity, reflecting the interplay between a range of fundamental cellular processes, including surface organization of receptors, cytoskeletal organization, and cell trafficking, that all are coordinated by signaling events. Yu and Turner [11] summarize recent progress in understanding mechanisms and pathways of tight junction protein internalization and the relevance of these to tight junction regulation.

The assembly of tight junctions, which generally depends on the formation and maintenance of adherens junctions, is closely related to development, and the mechanisms of tight junction biogenesis within developmental models must be studied to gain insight into this process as an integral part of epithelial differentiation. Eckert and Fleming [12] review tight junction biogenesis in the early mammalian embryo (mouse, particularly) and relate it to inherent mechanisms of cell differentiation and biosynthesis occurring during cleavage of the egg and formation of the first epithelium.

Tight junctions form a physical barrier to control physiological flux; their components interacting with several signal transduction molecules, including G proteins (both trimeric and monomeric), protein kinases (e.g., PKA, PKC, CKII), a wide array of growth factors, cytokines, drugs, and hormones regulate tight junctions and barrier function. González-Mariscal et al. [13] describe how several signaling pathways modulate the barrier function of the junction and how particular molecular constituents of the tight junction are phosphorylated by diverse kinases.

The structure and permeability of tight junctions are dynamically regulated by intra- and extracellular cellular events and in particular influenced by the different channels, receptors, and transporters present in the membranes, either directly (e.g., through direct protein-protein interactions or via an intermediate partner protein) or indirectly (via changes in the ionic content of the cells able to alter tight junction structure and functions). Rajasekaran et al. [14] summarize the evidence obtained so far on such interactions and discuss possible functional implications as well as what is known about the molecular basis of these interactions.

The term polarity refers here to the subdivision of the plasma membrane of epithelial and endothelial cells into apical and basolateral domains. Tight junctions, localized at the boundary between these domains, may conceivably function as a "fence" to limit the diffusion of proteins and lipids within the plane of the membrane. Cereijido et al. [15] present evidence that polarization and tight junctions are dynamic features that change during development, in response to physiological and pharmacological challenges and in pathological situations such as infection

The vascular endothelial cell monolayer, critically localized at the interface between the blood and the vessel wall, fills vital functions of regulating tissue fluid balance and supplying the essential nutrients needed for the survival of the organism. These endothelial cells are exquisite "sensors" that respond to diverse signals generated in the blood, subendothelium, and interacting cells. Wallez and Huber [16] provide an up-to-date and precise picture of the specific mechanisms of endothelial tight and adherens junctions.

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References

[1] C.M. Niessen, C.J. Gottardi, Molecular components of the adherens junctions, Biochim. Biophys. Acta 1778 (2008) 562–571.
[2] D. Garrod, M. Chidgey, Desmosome structure, composition and function, Biochim. Biophys. Acta 1778 (2008) 572–587.

[3] H. Chiba, M. Osanai, M. Murata, T. Kojima, N. Sawada, Transmembrane proteins of tight junctions, Biochim. Biophys. Acta 1778 (2008) 588–600.
[4] L. Guillemot, S. Paschoud, P. Pulimeno, A. Foglia, S. Citi, The cytoplasmic plaque of tight junctions: a scaffolding and signalling center, Biochim. Biophys. Acta 1778 (2008) 601–613.
[5] E. Assémat, E. Bazellières, E. Pallesi-Pocachard, A. Le Bivic, D. Massey-Harroche, Polarity complex proteins, Biochim. Biophys. Acta 1778 (2008) 614–630.
[6] G. Krause, L. Winkler, S.L. Mueller, R.F. Haseloff, J. Piontek, I.E. Blasig, Structure and function of claudins, Biochim. Biophys. Acta 1778 (2008) 631–645.
[7] L. Paris, L. Tonutti, C. Vannini, G. Bazzoni, Structural organisation of the tight junctions, Biochim. Biophys. Acta 1778 (2008) 646–659.
[8] A. Hartsock, W.J. Nelson, Adherens and tight junctions: structure, function and connections to the actin cytoskeleton. Biochim. Biophys. Acta 1778 (2008) 660–669.
[9] J. Miyoshi, Y. Takai, Structural and functional associations of apical junctions with cytoskeleton, Biochim. Biophys. Acta 1778 (2008) 670–691.
[10] E.W.P. Wong, D.D. Mruk, C.Y. Cheng, Biology and regulation of ectoplasmic specialization, an atypical adherens junction type, in the testis, Biochim. Biophys. Acta 1778 (2008) 692–708.
[11] D. Yu, J.R. Turner, Stimulus-induced reorganization of tight junction structure: the role of membrane traffic, Biochim. Biophys. Acta 1778 (2008) 709–716.
[12] J.J. Eckert, T.P. Fleming, Tight junction biogenesis during early development, Biochim. Biophys. Acta 1778 (2008) 717–728.
[13] L. González-Mariscal, R. Tapia, D. Chamorro, Crosstalk of tight junction components with signaling pathways, Biochim. Biophys. Acta 1778 (2008) 729–756.
[14] S.A. Rajasekaran, K.W. Beyenbach, A.K. Rajasekaran, Interactions of tight junctions with membrane channels and transporters, Biochim. Biophys. Acta 1778 (2008) 757–769.
[15] M. Cereijido, R.G. Contreras, L. Shoshani, D. Flores-Benitez, I. Larre, Tight junction and polarity interaction in the transporting epithelial phenotype, Biochim. Biophys. Acta 1778 (2008) 770–793.
[16] Y. Wallez, P. Huber, Endothelial adherens and tight junctions in vascular homeostasis, inflammation and angiogenesis, Biochim. Biophys. Acta 1778 (2008) 794–809.

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