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All about claudins

Kursad Turksen

Regenerative Medicine Program; Sprott Centre for Stem Cell Research; Ottawa Hospital Research Institute; Ottawa, ON Canada

Since the discovery of Claudins more than a decade ago, much has been learned about their structure-function relationships. Claudins are tetraspan membrane proteins responsible for the formation of tight junctions. In this capacity, Claudins form a tissue-specific selective permeability barrier that is critical for the function of the tissue. Claudins are developmentally regulated and expressed in a tissue- and cell-specific manner; chronic changes in their expression are associated with various disease states. The studies that have been put together in this Special Issue provide updates on both current knowledge as well as some of the unanswered questions and challenges in the field.

Tight junctions (TJ), as described in the seminal work of Farquhar and Palade in 1963, are intercellular structures that function as "fence and gate" permeability barriers in polarized epithelial cells.[1] Understanding of the already known tissue-specific selective permeability barrier took a significant leap forward with the discovery of the Claudin family of integral membrane proteins by Tsukita and his colleagues in 1998.[2] In a brief introduction to this specific issue, I will emphasize some of the most pertinent directions that papers in these special issues are covering.

The review by Koval covers the intriguing area of how Claudins assemble into fibrils in a cell-specific manner[3] But Claudins do not act alone to constitute TJ formation and barrier function, and considerable advances have been made in understanding the interactions between the Claudins and various sub cortical proteins of polarized cells, as highlighted by Van Itallie and Anderson.[4]

Although initially Claudins were identified in mammalian cells, it very quickly became apparent that the Claudin family of TJ proteins exists in all vertebrates. Studies in worms, fish and birds, have provided invaluable insights into Claudin biology and function. Simke[5] covers some of the critically important aspects of the pfam00822 super family of proteins in worms. Similarly, Kolosove et al.[6] outline current understanding of a very large family of Claudins in teleosts and their tissue-specific expression and barrier function that complements studies in mammals.

Changes that occur developmentally with cell fate selection and differentiation leading to organogenesis are known to be associated with changes in cell polarity and compartmentalization.[7,8] These changes are accompanied by very distinct Claudin expression profiles as outlined for the chick embryo by Collins et al.[9] This and other contributions to this issue underscore that the Claudin story is a story in progress and emphasize both the excitement and the need for continued discovery. Nowhere is this more evident than in the striking advances made in understanding normal Claudin-based TJ formation and barrier function in a number of tissues as summarized by Hou in kidney,[10] by Lu et al. in intestine,[11] Goncalves et al. the blood-brain barrier[12] and by Peltonen et al. in the peripheral nervous system.[13] On the other hand, studies by Martin et al.[14] provide insights in to the role of Claudins in disease state such as breast cancer. The corollary, however, is that much work remains to uncover the mechanisms underlying changes in Claudin expression and barrier function in various disease states.[11-13,15] Hopefully, contributors and readers of this issue will take up the remaining challenges.

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Correspondence to: Kursad Turksen; Email: kursadturksen@gmail.com.
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