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INVESTIGATION ON DEVELOPMENTAL ROLES OF THE TWO ZEBRAFISH CLAUDIN5 FAMILY MEMBERS



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Cuvillier Verlag Nov 2010, 2010. Taschenbuch. Condition: Neu. Neuware - Tight junctions (TJs) are main structural elements of epithelial/endothelial cell layer barrier systems. Members of the Claudin (Cldn) family are transmembrane proteins that determine paracellular permeability properties. Much of what we have learned about barrier- and poreforming roles of Cldns stems from work in different cell lines. However, recent studies have provided evidence for roles of Cldns in development and disease. These latter functions cannot be adequately studied in tissue culture systems, which highlights the need to manipulate these proteins and to elucidate their functions within complex model organisms. In this study, the developmental functions of Cldn5a and Cldn5b were characterized during zebrafish (Danio rerio) embryonic morphogenesis. Expression analysis of both Cldn5 isoforms during zebrafish development revealed that Cldn5a is expressed within the embryonic neuroepithelium and within arterial endothelial cells, whereas Cldn5b is primarily expressed within arteries. Cldn5a is essential for the formation of an embryonic neuroepithelial-ventricular barrier which is required for brain ventricular expansion. Genetic analyses showed that Cldn5a functions downstream of tissue polarity cues which are essential for the establishment of the neuroepithelial-ventricular barrier. This barrier, together with the Na+,K+-ATPase ionic pump function, which generates the hydrostatic pressure within the ventricular lumen, contributes to embryonic brain ventricular expansion. The study also revealed that during zebrafish vasculogenesis, Cldn5a and Cldnb are essential for the separation of arterial and venous cells without affecting their differentiation. Functional rescue experiments with a TJ poreopening Cldn5a mutant complemented the loss of Cldn5 during vasculogenesis. This indicates a role of Cldn5s that is separate from TJ belt formation and sealing function, such as affecting cell motility or cell-cell adhesion behavior. 108 pp.

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