

New insights into the development of epithelial cells

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Scientists of the Max Delbruck Center for Molecular Medicine (MDC) Berlin-Buch and the Experimental and Clinical Research Center (ECRC) of MDC and Charite in Berlin-Buch have gained new insights into the development of epithelial cells and their molecular repertoire. Dr. Max Werth, Katharina Walentin and Professor Kai Schmidt-Ott have identified a transcription factor (grainyhead-like 2, Grhl2), which regulates the composition of the molecular "bridges" that link adjacent epithelial cells. The authors were able to demonstrate that Grhl2, via DNA-binding, directly regulates the expression of two such cell junctional molecules, E-cadherin and claudin 4.

This could be important for understanding the mechanisms of various diseases. For example, Grhl2-deficient mice die early in embryonic development and display defects of neural tube closure, including spina bifida.

Spina bifida is a common human congenital disease that is often associated with severe disabilities. Little is known about how the disease develops, and Grhl2 may be an important player in its pathogenesis.

Furthermore, the authors hypothesize that Grhl2 may also have important functions in <u>internal organs</u>, such as the kidney. Epithelial cells line the renal tubular system, which in humans is several kilometers long.

This system of renal tubules, together with the renal corpuscles, forms



the basic structural and functional unit of the kidney – the nephron. The human kidney filters waste products from 1700 liters of blood per day, of which 180 liters are collected as primary urine and of which finally one to two liters are excreted as urine.

The studies of the authors show that Grhl2 is produced in nephron segments that are relatively impermeable to water and solutes and that fine-tune the composition of urine.

A dysfunction of Grhl2 in these cells may affect epithelial barrier formation and other cell characteristics and, thereby, contribute to various diseases, including congenital abnormalities of the kidney or the development of hypertension.

More information: The transcription factor grainyhead-like 2 (Grhl2) regulates molecular composition of the epithelial apical junctional complex, *Development*, doi:10.1242/dev.055483

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