## XXXI JCET LECTURE, 28.02.2014, 9.00

# The role of ENaC in the vascular endothelium – implications from mouse models

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The expression of the epithelial sodium channel (ENaC) was mainly assigned to the kidneys, colon and sweat glands where it was considered to be the main determinant of sodium homeostasis. Recently, indirect evidence for the possible existence of ENaC in a non-epithelial tissue was derived from the observation that the vascular endothelium is a target for aldosterone. Inhibitory actions of aldosterone receptor blockers and, more directly, by ENaC blockers such as amiloride supported this view. This was followed by direct data on the expression of ENaC in vascular endothelium. To study the role of ENaC in the vascular endothelium three different mouse models were probed for the mechanical stiffness of endothelial cells with an Atomic Force Microscope and ENaC expression: (i) endothelium-specific αENaC knockout (ii) aldosterone synthase knockout and (iii) a mouse model for the Liddle syndrome. It was found that that the membrane insertion of ENaC via a mineralocorticoid receptor-dependent pathway determines the nanomechanical properties of the endothelial cortex, a layer 50 – 200 nm beneath the plasma membrane. This compartment has been shown to play a crucial role as it controls the production of the endothelium-derived vasodilator nitric oxide (NO) which directly affects the tone of the vascular smooth muscle cells. In contrast to soft endothelial cells, stiff endothelial cells release reduced amounts of NO, the hallmark of endothelial dysfunction.

Thus, it is concluded that the channel acts as a major regulator of cellular mechanics which is a critical parameter in differentiating between vascular function and dysfunction.

**CURRICULUM VITAE**

Kristina Kusche-Vihrog is a principle investigator at the Institute of Physiology II, University of Muenster (Director: Prof. Hans Oberleithner). After completing her study in 1999 at the Biological Faculty, University of Mainz, Germany, and University of Umeå (Sweden) she started her PhD training which was completed in 2001. After a postdoctoral period she changed 2002 to the University of Muenster, Institute of Animal Physiology and 2008 finally arrived at the Medical Faculty, Institute of Physiology II, University of Muenster. She finished her Habilitation in April 2013.

She is mainly interested in the role of aldosterone and sodium in endothelial function/dysfunction. Together with Hans Oberleithner she identified the epithelial sodium channel (ENaC) as a new player in the vascular endothelium. With the help of genetically modified endothelial cells and different mouse models it was possible to define a new role for endothelial ENaC, namely as a modifier of endothelial nanomechanics. To address the topics of her research interest she applies molecular biological methods, protein biochemical methods, advanced immune fluorescence microscopy and atomic force microscopy with living endothelial cells. In a further development of the AFM technique her group is now specialized in the detection of the nanomechanical properties of *ex vivo* endothelial cell from *in situ* preparations of either mouse or human arteries. This allows the investigation of (patho)physiological mechanisms in an experimental system close to the native environment. She collaborates with a number of national and international groups and is member of the COST Action ADMIRE BM1301.

Selected Literature

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