WWTF Project LS18-080

Protecting vascular barrier function across discipline and disease boundaries

Abstract

Vascular integrity is critical for blood flow and tissue homeostasis. A breach of the vascular barrier after injury can have serious, even fatal consequences, as seen in patients with burn injury or sepsis. The critical barrier for fluids, molecules and cells is safeguarded by the tight junction complex. A regulator of this barrier is cingulin, which links the tight junction complex to Rho signaling pathways. We have recently demonstrated that cingulin regulates claudin-5 levels and vascular permeability. Thus, the tight junction adaptor cingulin and its interaction with RhoGTPases could be targeted in inflammation. We aim A) to explore how cingulin controls barrier function, B) if the absence of cingulin at junctions aggravates diseases characterized by vascular leak and C) if this adapter protein could be used to attenuate vascular leak. The proposed project will use cutting-edge technology to combine basic and clinical research. We will monitor vascular barrier function in vitro and in vivo in real-time. The importance of interactions will be proven in mouse models of diseases characterized by vascular leak with full or endothelial cell specific knockout of cingulin. In combination with specific inhibitors, this will allow verification of identified pathways. We will investigate localized vascular barrier deficiency in patients with cancer, type-4 hypersensitivity and urticaria. This may serve as starting point for a novel treatment strategy to counteract vascular leak.

Scientific disciplines:
301306 - Medical molecular biology (50%) | 302011 - Dermatology (50%)

Keywords:
vascular leak, endothelial barrier function, cingulin, RhoGTPase exchange factors

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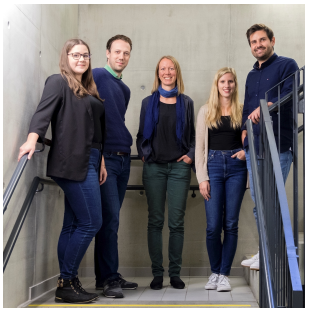

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Further links about the involved persons and regarding the project you can find at
https://archiv.wwtf.at/programmes/life_sciences/LS18-080