Deciphering the cellular effects of edema on the vasculature

Research area:

Vascular Biology

Brief description

The project tests the hypothesis that increased interstitial pressure leads to specific cytoskeletal and junctional rearrangements in endothelial cells to adjust the balance between vascular leakage and lymphatic drainage, which is prerequisite for normal vascular development and function.

Aim

We aim to investigate the consequences of (lymph)edema on vascular development, organization of the endothelial cell cytoskeleton, junctions as well as vessel function by combining *in vivo* studies on genetic mouse models and *in vitro* cell culture systems.

Background

Edema formation is frequently encountered in clinics and characterized by an abnormal accumulation of interstitial fluid and consequently increased interstitial pressure due to altered blood vessel function and/or insufficient lymphatic drainage. Besides its physiological function in maintaining the integrity of the body by increasing leukocyte recruitment to promote wound healing and to prevent infection, edema occurs in the context of various diseases and can lead to severe organ dysfunction.

Moreover, it has previously been suggested that a certain vascular leakage is required for proper lymphatic development as well as maturation and that increased lymphatic drainage may in turn regulate blood vessel permeability. However, the mechanisms involved in the coupling of lymphatic drainage and regulation of blood vessel permeability are grossly elusive.

Project plan

The student will investigate the mechanisms coupling vascular leakage to lymphatic drainage and *vice versa*, by specifically interfering with either blood vessel permeability or lymphatic drainage capacity.

Preliminary *in vitro* studies revealed that knockdown of certain integrins in endothelial cells results in cytoskeletal alterations, disruption of cell contacts and

consequently increased endothelial permeability. The student will further characterize the cellular effects of integrin knockdown under static and dynamic culture conditions *in vitro* using confocal microscopy and biochemical methods.

Next, increased blood vessel permeability or impaired lymphatic drainage will be induced genetically in blood and/or lymphatic endothelium-specific integrin deficient animals. The student will quantitatively assess blood and lymph vessel density, architecture, endothelial cell proliferation, as well as characterize cell junction organization in the ear skin of adults, or back skin and mesentery of embryos by confocal microscopy, biochemical methods and flow cytometry.

These studies will help to decipher edema-induced changes in the vasculature with a particular focus on endothelial cell junctions, vascular permeability and lymphatic drainage capacity and could identify novel targets for the specific treatment of increased vascular leakage or impaired lymphatic drainage.

If you are highly motivated, dedicated to research and would like to answer these challenging questions, please contact us.

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