

Diabetic microvascular complications – the role of the permeability layer.

The regulation of vascular permeability is a principal function of the microvasculature, and its disruption leads to vascular diseases from sepsis to diabetic complications. The endothelial cell surface coat (glycocalyx) is a key permeability mediator generated by proteins and carbohydrates that form a mesh over the cell surface. This mesh is disrupted in diabetes, resulting in kidney disease, neuropathy, retinopathy, and cardiomyopathy. This project will determine the relationship between the qualities of the glycocalyx (depth and coverage), and the permeability of individually perfused microvessels in vivo under normal and diabetic conditions. We will directly measure solute permeability in intact microvessels and simultaneously determine the glycocalyx properties using in vivo confocal microscopy, and then examine the ultrastructure by transmission electron microscopy tomography. Mesenteric exchange vessels (20-35 μ m) will be cannulated and perfused, and permeability measured before during and after selective enzymatic degradation of the terminal sialic acid residues of the glycocalyx by neuraminidase. This project will enable us to more clearly understand how this complex cell surface layer can regulate fluid and solute movement across the vessel wall in diabetes.

References

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