Perivascular astrocyte endfeet

The perivascular astrocyte endfoot is a specialized and diffusion-limited subcellular compartment that fully ensheathes the cerebral vasculature. Despite their ubiquitous presence, a detailed understanding of endfoot physiology remains elusive, in part due to a limited understanding of the proteins that distinguish the endfoot from the greater astrocyte body.

Stokum et al. developed a technique to isolate astrocyte endfeet from brain tissue, which was used to study the endfoot proteome in comparison to the astrocyte somata. In this approach, brain microvessels, which retain their endfoot processes, were isolated from mouse brain and dissociated, whereupon endfeet were recovered using an antibody-based column astrocyte isolation kit. The findings expand the known set of proteins enriched at the endfoot from 10 to 516, which comprised more than 1/5th of the entire detected astrocyte proteome. Numerous critical electron transport chain proteins were expressed only at the endfeet, while enzymes involved in glycogen storage were distributed to the somata, indicating subcellular metabolic compartmentalization. The endfoot proteome also included numerous proteins that, while known to have important contributions to blood-brain barrier function, were not previously known to localize to the endfoot. The findings highlight the importance of the endfoot and suggest new routes of the investigation into endfoot function [1)].

To examine the three-dimensional structure of the astrocyte endfeet and their relationships with the endothelial cells, coronal rat brain sections immunolabeled for the two astroglial markers [glial fibrillary acidic protein (GFAP)/S-100beta] and the endothelial glucose transporter (GLUT1) were analyzed under the confocal microscope. Double immunolabeling of GFAP and S-100beta showed numerous well-defined astrocytes sending one or more endfeet to the vasculature. Examination of GFAP immunolabeling at higher magnification showed that this endfeet consists of well-defined rosette-like structures lying on the vessel wall. Double immunostaining of GFAP and GLUT1 showed that the endothelial cells were the main targets of these repeated geometrical units formed by the astrocyte endfeet. When three-dimensional images were reconstructed, obvious privileged anatomical relationships were observed between endfeet and individual endothelial cells. These anatomical data provide strong support for the involvement of astrocytes in cerebral metabolic coupling. The finger-like appearance of astrocyte endfeet could allow direct metabolic exchanges between intracerebral vessels and non-glial elements such as nerve terminals [2)].

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Stokum JA, Shim B, Huang W, Kane M, Smith JA, Gerzanich V, Simard JM. A large portion of the astrocyte proteome is dedicated to perivascular endfeet, including critical components of the electron transport chain. J Cereb Blood Flow Metab. 2021 Apr 4:271678×211004182. doi: 10.1177/0271678×211004182. Epub ahead of print. PMID: 33818185.
2)
Kacem K, Lacombe P, Seylaz J, Bonvento G. Structural organization of the perivascular astrocyte endfeet and their relationship with the endothelial glucose transporter: a confocal microscopy study. Glia. 1998 May;23(1):1-10. PMID: 9562180.