生命科学セミナー

Perivascular Neurons Instruct Three-Dimensional Vascular Lattice Formation via Piezo2-mediated Contact

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Tue. 20th August 16：00 - 17：00

KUIAS Main Building 2nd floor, Seminar Room

(Kyoto University Campus map #77)

The vasculature in the central nervous system is assembled into the 3D lattice network to provide nutrients and oxygen for accurate neural functions. However, the mechanisms controlling 3D vascular lattice patterning are largely unknown in contrast to 2D vascular growth. Combining viral labeling, genetic marking, and single-cell transcriptomics profiling in the mouse retina, we identified a subset of Fam19a4/Nts-positive retinal ganglion cells (Fam19a4/Nts-RGCs) as perivascular neurons that physically contact endothelial cells with unique perisomatic endfeet. Genetic ablation of Fam19a4/Nts-RGCs led to disoriented growth of penetrating vessels near the RGC layer, leading to abnormal 3D vascular lattice formation. We further identified Piezo2, a mechanosensitive channel, as a Fam19a4/Nts-RGCs-enriched protein during retinal vascular development. Pan-neuronal and Fam19a4/Nts-RGC specific deletion of Piezo2 led to the loss of Fam19a4/Nts-RGC-vascular contacts and phenocopied the vascular defects upon the Fam19a4/Nts-RGC ablation. These abnormal 3D vascular lattice structures lead to reduced capillary perfusions, chronic hypoxia, and progressive RGC loss in the adult retina. Additionally, we identified a cerebellar granule cell subset regulating cerebellar vascular scaffold patterning using a similar Piezo2-dependent mechanism, generalizing a unique neuronal role in guiding the three-dimensional vascular patterning during neural circuit assembly. Taken together, we uncovered a specific and unexpected neuron-type role in instructing 3D vascular lattice formation via direct neurovascular interaction mediated by Piezo2.

Reference:
Toma K,…, Duan X et al. Perivascular neurons instruct 3D vascular lattice formation via neurovascular contact. Cell (187)11: 2767-2784.E23 (2024)

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