Electric axon guidance in embryonic retina: Involvement of integrins

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The axons of embryonic brain, spinal cord, and retina extend along the extracellular voltage gradient towards the cathode in a process known as galvanotropism. In embryonic nervous tissues, positive direct current (DC) potentials are generated by neuroepithelial cell's sodium transport1, of which disruption results in erroneous axon path-finding4, suggesting that electric fields play a pivotal role in orienting newborn axons. However, the experimental evidence was lacking for the cell surface molecule that is activated asymmetrically in an electric field. Here I show that integrin activation mediates electric axon guidance. Retinal strips of chick embryos were embedded in Matrigel®, and cultured in the electric field of the same strength as that in vivo (15 mV/mm)4. Matrigel® contained the same extracellular matrix proteins as in the embryonic retina, laminin and collagen, to which integrins bind. Retinal ganglion cell axons extended towards the cathode2. A monoclonal anti-chicken integrin antibody (TASC), which enhances integrin-ligand binding, accelerated the cathodal growth. A reduction in the extracellular free Ca2+ with EGTA also enhanced the cathodal growth, which suggested that millimolar Ca2+ inhibits axon growth, and also that the influx of Ca2+ was unlikely to be essential for cathodal steering. In the presence of Mn2+, which non-specifically activates integrin-ligand binding, the axons formed local meshes. These results suggested that the inhibition of integrins by the extracellular Ca2+ underlies electric axon guidance.

Recent Publications:

1. Yamashita M (2016) Epithelial sodium channels (ENaC) produce extracellular positive DC potentials in the retinal neuroepithelium. Data in Brief, 6: 253-256.

2. Yamashita M (2015) Weak electric fields serve as guidance cues that direct retinal ganglion cell axons in vitro. Biochemistry and Biophysics Reports, 4: 83-88.

3. Yamashita M (2015) Electrophysiological recordings from neuroepithelial stem cells. Stem Cell Renewal and Cell-Cell Communication (Ed. Turksen K), Methods in Molecular Biology, Springer Protocols, 1212: 195-200.

4. Yamashita M (2013) Electric axon guidance in embryonic retina: Galvanotropism revisited. Biochem Biophys Res Commun, 431: 280-283.

5. Yamashita M (2013) From neuroepithelial cells to neurons: Changes in the physiological properties of neuroepithelial stem cells. Arch Biochem Biophys, 534: 64-70.

6. Yamashita M (2012) Ion channel activities in neural stem cells of the neuroepithelium. Stem Cells International, 2012: doi: org/10.1155/2012/247670.

Speaker Biography

Masayuki Yamashita is a professor of physiology at International University of Health and Welfare. He received his PhD at the Department of Neurophysiology, Institute of Brain Research, School of Medicine, University of Tokyo in 1986. He moved to National Institute for Physiological Sciences (Okazaki, Japan) as a JSPS fellow and a research associate. In 1989, he started physiological studies of retina at the Department of Neuroanatomy, Max-Planck-Institute for Brain Research (Frankfurt/M). After the reunification of Germany, he moved to the Department of Physiology, Osaka University Medical School. He studied the calcium signaling systems in embryonic chick retina. Then, he moved to the Department of Physiology, Nara Medical University as a professor (1999-2014). He has been interested in the electrophysiological properties of neuroepithelial cells and newborn neurons. The retina is a nice model for studying the early development of central nervous systems.

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