# 第327回 大阪大学神経科学懇話会

日時：**平成27年3月26日（木）18:00 – 19:00**

場所：**医学部　臨床研究棟　2階　階段横セミナー室**

演者：**Dr. Joaquim EGEA, PhD**

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演題：***FLRTing in the developing nervous system: novel molecular mechanisms of axon guidance and neuron migration***

要旨：

The correct migration of neurons and the correct projection of the growing axons during nervous system development are controlled by axon guidance cues that act through specific receptors located at the cell surface. How this restricted number of molecules can organize the entire nervous system connectivity is, however, poorly understood. In one hand, novel transmembrane proteins with extracellular leucine-rich repeats (eLRRs) have recently emerged as key regulators of these molecules and participate in the establishment of neuronal circuits:myelination (LINGO1), axon extension (Islr2/Linx), synaptic function (Trk, LRRTM, and SALM) and neuron migration (FLRTs). On the other hand, axon guidance molecules, when presented in a overlapping fashion (resembling more accurately an in vivo context), induce complex responses that cannot be predicted from their single effects.
Here we show one example of how one of the most studied axon guidance receptors, Robo1, can be modulated to fine tune its response to its cognate ligand Slit1. In the thalamocortical system, the topographical sorting of distinct axonal subpopulations relies on the emergent cooperation between Slit1 and Netrin-1 guidance cues presented by intermediate cellular targets. We show that the attractive response to the guidance cue Netrin-1 is controlled by Slit/Robo1 signaling and by FLRT3, a novel co-receptor for Robo1. While thalamic axons lacking FLRT3 are insensitive to Netrin-1, thalamic axons containing FLRT3 can modulate their Netrin-1 responsiveness in a context-dependent manner. In the presence of Slit1, both Robo1 and FLRT3 receptors are required to induce Netrin-1 attraction by the upregulation of surface DCC through the activation of protein kinase A. Finally, the absence of FLRT3 produces defects in axon guidance in vivo. These results highlight a novel mechanism by which interactions between limited numbers of axon guidance cues can multiply the responses in developing axons, as required for proper axonal tract formation in the mammalian brain. In addition to these findings, FLRTs have been previously shown to regulate neuron migration in the developing cortex. Taken together, these results strongly suggest a pivotal role for FLRTs in different aspects of the nervous system development.

※本講演は、医科学修士課程系別セミナーとして単位が認定されます

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