CDB SEMINAR

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14:00~15:00 A7F Seminar Room

Defining the spatiotemporal origins of GABAergic cortical interneuron subtypes

The mammalian neocortex contains a large diversity of GABAergic interneurons, which collectively regulate overall network activity by locally modulating neuronal excitation. In order for interneurons to function properly in the cortical network, each of the interneuron subtypes must be integrated within the developing excitatory network in a very precise manner. Cortical GABAergic interneurons, at least in rodents, are not generated locally in the cortex but originate in the embryonic ventral telencephalon and migrate tangentially up into the neocortex. Specifically, by employing *in vivo* transplantation techniques, spatially distinct domains of the ventral telencephalon, the MGE and CGE (medial and caudal ganglionic eminence) have been shown to produce most if not all of cortical interneurons.

Recently, we have developed an inducible genetic strategy to label temporally distinct cohorts of interneuron precursors specifically derived from the MGE at early and late embryonic stages (Miyoshi et al., 2007). We have found that MGE-derived cortical interneurons adopt inside-out layering pattern and most of the interneuron subtypes, except for the fast-spiking basket cells, have distinct temporal origins. Furthermore, we have combined these alleles to conditional loss-of-function allele of homeodomain containing transcription factor *Nkx2-1*, which is selectively expressed in the MGE progenitors. This study have shown that *Nkx2-1* plays a critical role for specifying MGE- vs CGE-derived subtypes of interneurons (Butt et al., 2008). While the majority of cortical interneurons are thought to arise from the MGE, many of the less abundant subtypes arise exclusively from the CGE. We again took advantage of inducible genetic strategy and labeled temporally distinct cohorts emerging from the CGE. I will demonstrate that CGE-derived interneurons behave very differently than those from the MGE. Unlike pyramidal cells or MGE-derived interneurons, CGE-derived GABAergic cortical interneurons do not follow inside-out layering pattern. Consistent with this observation, similar subtypes of cortical interneurons are produced from the CGE throughout development.

In a separate study, I have generated a conditional loss-of-function allele of the master regulatory gene *FoxG1*, a transcriptional repressor expressed in both embryonic progenitors and adult neurons of the mammalian forebrain. Interestingly, mutations or deletions in the human homolog of *FoxG1* (*FoxG1B*) were identified in a subset of Rett syndrome patients. I will demonstrate that *FoxG1* is required for the proper migration and positioning of pyramidal cells and interneurons. When *FoxG1* is removed from neuronal precursors at the time they are becoming postmitotic, mutant cells fail to migrate into cortical plate and remain below the subplate.

Host:
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