NSI

名古屋大学 高等研究院

Group of Brain function and development, NSI

Research unit for developmental disorders, B3 unit

Seminar

Investigating Molecular and Subcellular Mechanisms Underlying Subcerebral Axon Projection

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How CNS circuits sculpt their axonal arbors into spatially and functionally organized domains is not well understood. Segmental specificity of corticospinal connectivity is an exemplar for such regional specificity of many axon projections. Corticospinal neurons (CSN) innervate spinal and brainstem targets with segmental precision, controlling voluntary movement. Multiple molecularly distinct CSN subpopulations innervate cervical cord for evolutionarily enhanced precision of forelimb movement. We identify that Lumican, previously unrecognized in axon development, controls balance of cervical innervation between distinct lateral and medial CSN subpopulations. Lumican, an extracellular proteoglycan expressed by lateral CSN, non-cell-autonomously suppresses cervical collateralization by multiple medial CSN subpopulations. This newly identified axon guidance mechanism– inter-axonal molecular crosstalk between CSN subpopulations– controls corticospinal circuitry, target density, and competitive specificity. Such crosstalk is generalizable beyond the corticospinal system for evolutionary incorporation of new neuron populations into pre-existing circuitry.

Complementing above work, to comprehensively elucidate related axon projection mechanisms functioning at tips of growing CSN axons *in vivo*, I am currently applying experimental and analytic approaches recently developed in my postdoc lab (Poulopoulos*, Murphy* et al) to quantitatively and subcellularly "map" RNA and protein molecular machinery of subtype-specific growth cones, in parallel to their parent somata, isolated directly *in vivo* from developing subcerebral projection neurons (SCPN; the broader cortical output neuron population targeting both brainstem and spinal cord; includes CSN). I am investigating both normal development and GC-soma dysregulation with mutation of central CSN-SCPN transcriptional regulator Ctip2/Bcl11b. This "subcellular RNA mapping" identifies distinct, subcellularly-specific transcriptomic changes in the growth cone or/and soma compartments of *Ctip2*-mutant SCPN.

Reference

Itoh*, Sahni* et al., ***bioRxiv***, 2021; Sahni… Itoh… et al., ***Cell Reports***, 2021a; Sahni, Itoh, et al., ***Cell Reports***, 2021b; Poulopoulos*, Murphy* et al., ***Nature***, 2019; Arlotta*, Molyneaux* et al., ***Neuron***, 2005; Itoh et al., in prep

Date: July 14, 2022 (Thursday) 16:00-17:00

2022年7月14日(木) 16:00～17:00

Place: 1F seminar room, Science South Building (NEO PLACE)

理学南館1Fセミナー室(NEOREX PLACE)

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