Cortical Interneurons: from birth to networks

Developmental trajectories of cortical inhibitory neurons

Lynette Lim
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The focus of the introductory talk will be on mechanisms controlling interneuron (cIN) migration and axon targeting. We will provide evidence that different classes of cINs use distinct routes of migration to reach the cortex, that define the IN-subtype specific axonal pattern and function. We suggest that migration and axon targeting programmes are coupled to optimize the assembly of inhibitory circuits in the cerebral cortex.

Lim, L., Mi, D., Llorca, A., Marín, O. (2018) Development and Functional Diversification of Cortical Interneurons. Neuron Oct 24;100(2):294-313. doi: 10.1016/j.neuron.2018.10.009.

Lim, L., Pakan, JMP, Selten, MM., Marques-Smith, A., Llorca, A., Bae, SE., Rochefort, NL., Marín, O. (2018) Optimization of interneuron function by direct coupling of cell migration and axonal targeting. Nat Neurosci. 21(7):920-931. doi: 10.1038/s41593-018-0162-9.

Mechanisms controlling the postnatal development of cortical interneurons

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The place of origin determines certain aspects of cortical interneuron (cIN) fate, but it is only when they reach their target lamina and form contacts with the local circuitry that their number is defined and their mature properties are established. Recent evidence suggest that network activity and activity-dependent genetic programs are implicated in these late stages of cIN development. In this talk we will present work that addresses mechanisms controlling the development of distinct-IN subtypes during this critical time window of the first two postnatal weeks.

Denaxa, M.*, Neves, G., Burrone, J., Pachnis, V. (2018). Homeostatic control of interneuron apoptosis during cortical development. J Exp Neurosc. 5(12):1-3 *corresponding author https://pubmed.ncbi.nlm.nih.gov/30013387/

Denaxa M* ^, Neves G*^, Rabinowitz A, Kemlo S, Liodis P, Burrone J*, Pachnis V*. (2018) Modulation of apoptosis controls inhibitory interneuron number in the cortex. Cell Reports 12(7):1710-1721 *corresponding authors ^ equal contribution
https://pubmed.ncbi.nlm.nih.gov/29444425/

The integration of upper layer cortical interneurons into the cortical circuits

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Upper layer interneurons are involved in modulating barrel cortex activity and perception during active whisking. We will discuss our work on the identification of structural and functional connectivity motifs that allow these interneurons to respond to distinct sensory stimuli during development.

Kastli R, Vighagen R, van der Bourg A, Argunsah AÖ, Iqbal A, Voigt FF, Kirschenbaum D, Aguzzi A, Helmchen F, Karayannis T. (2020) Developmental divergence of sensory stimulus representation in cortical interneurons. Nat Commun. 11(1):5729. doi: 10.1038/s41467-020-19427-z.

The emergence and plasticity of axo-axonic synapses at the axon initial segment

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The activity-dependent rules that govern the wiring of GABAergic interneurons are not well understood. Chandelier cells (ChCs) are a type of GABAergic interneuron that control pyramidal cell output through axo-axonic synapses that target the axon initial segment. Increases in the activity of either pyramidal cells or individual ChCs during a critical temporal window result in a reversible decrease in axo-axonic connections. We will discuss work supporting the hypothesis that the direction of ChC synaptic plasticity follows homeostatic rules that depend on the polarity of axo-axonic synapses.

Pan-Vazquez A, Wefelmeyer W, Gonzalez Sabater V, Neves G, Burrone J. (2020) Activity-Dependent Plasticity of Axo-axonic Synapses at the Axon Initial Segment. Neuron 106(2):265-276.e6. doi: 10.1016/j.neuron.2020.01.037.

Wefelmeyer W, Cattaert D, Burrone J. Activity-dependent mismatch between axo-axonic synapses and the axon initial segment controls neuronal output. Proc Natl Acad Sci U S A. 2015 Aug 4;112(31):9757-62.