Elucidating Principles of Cortical Interneuron Synaptic Organization

June 4

Tuesday, 12:30 pm

Billings Building—Rosedale Room

SPEAKER:

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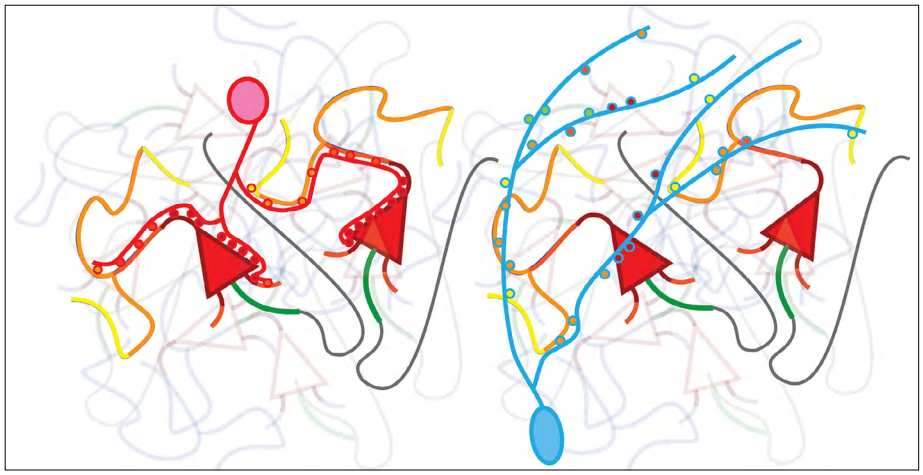
Abstract

Cortical interneurons represent the most transcriptionally and morphologically diverse set of neuronal subtypes, characterized in part by their striking degree of synaptic specificity. However, little is known about the extent of synaptic diversity due to the lack of unbiased methods to extract features of synaptic organization among interneuron subtypes. In this talk, I will introduce an approach we developed that combines imaging and computational extraction of synaptic features from genetically-identified interneuron synapses and their subcellular



specificity among postsynaptic targets. A machine-learning approach (1) reveals hundreds of spatial and structural features from each analyzed synapse, (2) constructs a multidimensional data set, consisting of millions of synapses, and (3) uncovers novel synaptic subgroups. By analyzing this dataset, we found that dendrite-targeting subgroups were clustered onto distinct subdomains of the dendrite along the proximal to distal axis; Soma-targeting subgroups were enriched onto different postsynaptic cell types; Finally, the two main subclasses of interneurons, basket cells and somatostatin interneurons, utilize distinct strategies to enact inhibitory synaptic coverage. Thus, we uncover previously unknown structural and topological features of inhibitory synaptic organization and establishes a conceptual framework for studying inhibitory synaptic diversity.

Publications

1. Genestine, M., Ambriz, D., Crabtree, G.W., Dummer, P., Molotkova, A., Quintero, M., Mela, A., Biswas, S., Feng, H., Zhang, C., et al. (2021). *Vascular-derived SPARC and SerpinE1 regulate interneuron tangential migration and accelerate functional maturation of human stem cell-derived interneurons.* Elife 10. 10.7554/eLife.56063.

2. McKenzie, M.G., Cobbs, L.V., Dummer, P.D., Petros, T.J., Halford, M.M., Stacker, S.A., Zou, Y., Fishell, G.J., and Au, E. (2019). *Non-canonical Wnt Signaling through Ryk Regulates the Generation of Somatostatin- and Parvalbumin-Expressing Cortical Interneurons.* Neuron 103, 853-864.e854. 10.1016/j.neuron.2019.06.003.

3. Nunnelly, L.F., Campbell, M., Lee, D.I., Dummer, P., Gu, G., Menon, V., and Au, E. (2022). *St18 specifies globus pallidus projection neuron identity in MGE lineage.* Nat Commun 13, 7735. 10.1038/s41467-022-35518-5.

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