Synaptic Subgroup Identification - a high content method for synaptic disease modeling and its future applications

November 18

Tuesday, 12:30 pm

Billings Building—Rosedale Room

SPEAKER:

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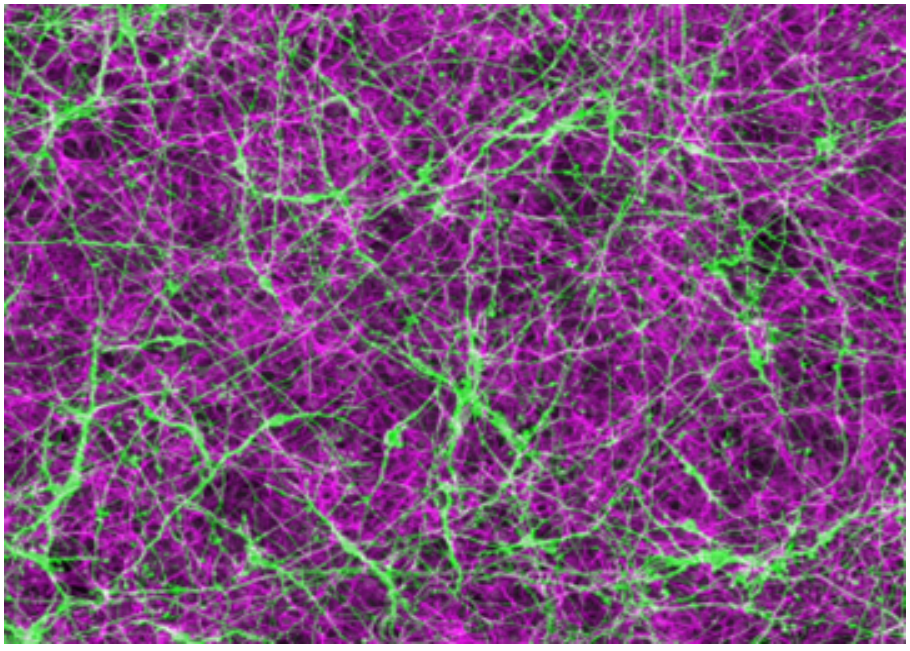
Abstract

Analyzing the broad, inhibitory network established by cortical interneurons requires high-content synaptic phenotyping beyond standard metrics. To meet this need, we developed Synaptic Subtype IDentification (SSID), a novel image-based machine learning method. SSID extracts hundreds of spatial and intensity features from each synapse to generate a deep phenotypic read-out, enabling the discovery, quantification, and spatial mapping of previously unrecognized synaptic subgroups. SSID has enabled us to glean novel insights into the functional organization of cortical interneuron synapses. Since our method is highly sensitive, we emplyed it to identify synaptic deficits in a mouse model of Fragile X Syndrome. Here, we observed significant shifts in synaptic subgroup composition and distribution in both cortical sections and dissociated culture. To extend this, we plan to use SSID to compare mouse and human FXS effects on interneurons generated by a rapid, highly efficient, and genetically controlled direct reprogramming (iPSC-to-iiN) system.



Publication:

Dummer PD, Lee DI, Hossain S, Wang R, Evard A, Newman G, Ho C, Schneider-Mizell CM, Menon V, Au E. Multidimensional analysis of cortical interneuron synaptic features reveals underlying synaptic heterogeneity. bioRxiv [Preprint]. 2024 Apr 17:2024.03.22.586340. doi: 10.1101/2024.03.22.586340. PMID: 38659827; PMCID: PMC11042224.