MIT Bioinformatics Seminar

Neurotyping: An integrated computational-experimental paradigm to develop targeted therapeutics for Parkinson's and other CNS diseases.

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Date: Monday, Nov. 14, 2022

Zoom URL: `https://mit.zoom.us/j/92936688687`

For diseases of a privileged organ like the brain – whose pathologic examination has typically been post-mortem – the era of somatic cell reprogramming has brought hope. iPS cells and derivative CNS tissues offer inroads into patient-specific biology, and the promise of targeted disease-modifying therapies for complex and heterogeneous CNS diseases. In our group, we have directed this technology toward understanding and treating neurodegenerative proteinopathies, especially "synucleinopathies" including Parkinson's disease, dementia with Lewy bodies and multiple system atrophy. In synucleinopathies, no matter what the cause, there is always pathologic accumulation of alpha-synuclein in CNS cells. We have thus intensely studied the biology of this protein, its native and pathologic interactions and the consequences of pathogenic mutations in iPSC-derived CNS cells. These investigations have led to the discovery of novel functions for alpha-synuclein relevant to disease, genetic and

physical cellular interactions linking alpha-synuclein to other disease-causing Parkinson's genes, insights into gene-environment interactions and the advancement of candidate disease-modifying therapies to clinical trials. In this talk, I will review our work and focus on emerging efforts to integrate iPSC discovery with computational and genomics approaches to molecularly stratify patients in "neurotypes." We anticipate insights from our work will engender targeted therapeutic strategies for complex CNS diseases, Parkinson's and beyond.