KJELDGAARD Lecture - Steve Finkbeiner

Wednesday 25 September 2024 at 13:15—14:00

Followed by PhD-session at 14:30—15:00

(Coffee and cake will be served between lecture and PhD-session)

Venue: 1871-120 (NUCLEUS)

Host: Poul Nissen

Steve Finkbeiner, MD, PhD

Gladstone Institute, UCSF

San Francisco, US

Disentangling complex biology to create blueprints for CNS disease interventions with stem cells, robotics and AI

The human brain has been described as the most complex machine in the universe. So perhaps it is unsurprising that that it has been so challenging to understand the root causes and discover effective treatments for many CNS diseases. To help unravel causal mechanisms, we developed faithful models of several adult-onset neurodegenerative diseases from patient-derived stem cells, including models of amyotrophic lateral sclerosis, frontotemporal dementia, Huntington's, Parkinson's and Alzheimer's disease. We then examined these models with robotic microscopy, a high throughput automated imaging platform we developed that can visualize and monitor pathobiology as it emerges over time in individual brain cells until the fates of those cells are determined. These studies have revealed that neurons mount significant coping responses to disease-causing misfolded proteins, and that bolstering protein homeostasis might be a broadly effective therapeutic strategy in many neurodegenerative diseases. Recently, we developed and applied artificial intelligence (AI) tools to the microscopy imaging data we generate, which revealed patterns and phenotypes that were undetectable to the unaided human observer. New AI approaches may help make intelligible the tremendous complexity of the human brain in health and disease, and enable progress toward overcoming CNS diseases.

References:

1. Finkbeiner S. et al (2004) Inclusion body formation reduces levels of mutant huntingtin and the risk of neuronal death. Nature 431:805–810.
2. Finkbeiner S. et al (2014) Autophagy induction enhances TDP43 turnover and survival in neuronal ALS models. Nat. Chem. Biol. 10:677–685.
3. Finkbeiner S. et al (2018) In silico labeling: Predicting fluorescent labels in unlabeled images. Cell 173:1–12.
4. Finkbeiner S. et al (2021b) Superhuman cell death detection with biomarker-optimized neural networks. Sci. Adv. 7:eabf8142.

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