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The NO-Age and NO-AD Seminar Series 059

Harnessing Endophenotypes and Network Medicine for Discovery of Pathobiology and Drug Repurposing in Alzheimer's Disease

by

Dr. Feixiong Cheng

Department of Molecular Medicine, Cleveland Clinic Lerner College of Medicine, *U.S*

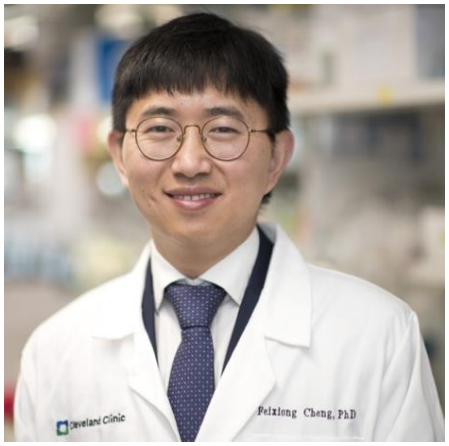
at

14:00-15:15 (CET), Monday, 05th Sep. 2022

Register in advance:
https://uio.zoom.us/webinar/register/WN_CaJV5b_dSYqHK5GPkkpTfg

Evandro F. Fang (UiO), Jon Storm-Mathisen (UiO), Lene Juel Rasmussen (KU), W.Y. Chan (CUHK)

Queries: e.f.fang@medisin.uio.no
Previous recorded talks are available here: https://noad100.com/videos-previous-events/



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Speaker: Prof. Feixiong Cheng

Title: Harnessing Endophenotypes and Network Medicine for Discovery of Pathobiology and Drug Repurposing in Alzheimer's Disease

Abstract:
High-throughput DNA/RNA sequencing technologies have rapidly led to a robust body of genetic and genomic data in multiple national Alzheimer's disease (AD) genome projects, such as the Alzheimer's Disease Sequencing Project (ADSP) and the Alzheimer's Disease Neuroimaging Initiative (ADNI); however, the predisposition to AD involves a complex, polygenic, and pleiotropic genetic architecture. Recent advances in genetics and systems biology have showed that AD is governed by network-associated molecular determinants (termed disease module) of common endotypes or endophenotypes (e.g., Amyloid and Tau). Approaching AD with a simplistic single-target approach has been demonstrated effective for developing symptomatic therapies but ineffective when attempted for disease modification. Therapeutic approaches by specifically modulating genetic risk genes are essential for development of disease-modifying treatments in AD. However, existing data, including genomics, transcriptomics, proteomics, and interactomics (protein-protein interactions [PPIs]), have not yet been fully utilized and integrated to explore the roles of targeted therapeutic development for AD. Understanding AD from the point-of-view of how human interactome perturbations underlie the disease is the essence of network medicine. The main hypothesis of the AD network medicine is that cellular networks altered by genetic variants gradually rewire throughout disease pathogenesis and progression. Systematic identification and characterization of underlying AD pathogenesis and disease modules will serve as a foundation for identifying disease-modifying targets for AD. Integration of the genome, transcriptome, proteome, and the human interactome are essential for such identification. This seminar will introduce protein-protein interactome network-based, multimodal omics analysis technologies established by Cheng's lab to identify novel drug targets and repurpose existing drugs for Alzheimer's disease. Dr. Cheng will illustrate how his team combines tools from network medicine, endophenotype models, artificial intelligence (AI), multi-omics (GWAS, genomics, transcriptomics, and proteomics), and electronic health records (EHRs), to identify potential drug targets and repurposable drugs using Alzheimer's disease as a prototypical example.

Biography:

Dr. Feixiong Cheng is a systems pharmacologist and data scientist by training, with extensive expertise in analyzing, visualizing, and mining multimodal, high-dimensional heterogeneous data from real-world (e.g., electronic health records (EHRs) and health care claims) and experiments that profile the molecular state of human cells and tissues by genetics, genomics, transcriptomics (single-cell), proteomics, metabolomics, and interactomics (protein-protein interactions [PPIs] and chromatin interactions), for drug discovery and patient care with 15 years' experience. The primary goal of his lab is to combine tools from neurocomputation, artificial intelligence (AI), genetics and genomics (DNA/RNA sequencing), EHRs, network medicine, and experimental systems biology (PPIs) assays, to address the challenging questions toward understanding of human complex diseases (in particular for Alzheimer's disease), which could have a major impact in identifying novel real-world data-driven diagnostic biomarkers and therapeutic targets for precision medicine drug discovery and patient care (Two phase II trials have been initialized). Dr. Cheng has extensive experience in various aspects of large-scale human genome sequencing and multi-omics studies, including the Alzheimer's Disease Sequencing Project (ADSP), The Cancer Genome Atlas (TCGA), TopMed, PVDOMICS, and others. Dr. Cheng has created multiple multi-omics and EHR methodologies and successfully applied them for Alzheimer's disease drug discovery: (1) in silico network medicine-based discovery combined with insurance records data mining and patient iPSC-derived models identifies sildenafil (Viagra) as a candidate drug for Alzheimer's disease (Nature Aging 2021, PMID: 35572351) and a Phase II trial has been initialized; (2) multimodal single-cell/nucleus transcriptomics analysis combined with insurance records data mining identifies fluticasone and mometasone (approved asthma drugs) as candidate treatments for Alzheimer's disease (Genome Research 2021, PMID: 33627474); (3) insurance records data mining combined with mouse models identifies salsalate and diflunisal as candidate treatments for Alzheimer's disease and Traumatic brain injury (TBI) via reducing acetylated tau (Cell 2021, PMID: 33852912); and (4) AI-based multimodal analysis of genetic and genomic combined with EHR data identified pioglitazone (anti-diabetic drug) as candidate treatment for AD (Alzheimer's Research & Therapy 2022, PMID: 35012639). He has served as keynote speakers or invited speakers in over 30 international and national conferences, including the FDA Scientific Computing Board 2020 and 2021 NIH Alzheimer's Research Summit: Path to Precision Medicine for Treatment and Prevention. He has received several Awards, including 2021 HHMI Gilliam Graduate Mentor Award (mentor graduate students under-represented background), 2020 ADDF Scholarships Winners, and NIH Pathway to Independence Award (K99/R00). In summary, his lab has established cutting-edge network medicine and systems pharmacology methodologies (Nature Biotechnology 2022, Nature Aging 2021, Nature Genetics 2021, PLOS Medicine 2021, Genome Biology 2021, PLOS Biology 2020, Lancet Digital Health 2020, Nature Communications 2019a, 2019b and 2018) to identify novel targets and repurposed drugs and combination therapies for a variety of human diseases, in particular for Alzheimer's disease.