CAMD セミナー

(Center for Development of Advanced Medicine for Dementia)

Towards a Comprehensive Understanding of Molecular Interactions and Regulators in Alzheimer's Disease Using Multiscale Network Biology Approaches

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第1研究棟2階小会議室

Genetic, pathological, and neuroimaging data reveal that Alzheimer's disease (AD) involves many different pathways across many different brain tissues. Increasingly available large scale genetic, genomic, proteomic and pathophysiological data in AD have made it possible to more comprehensively address the complex mechanisms and effectors of AD through application of advanced systems biology approaches.

We have developed a multiscale network modeling framework to integrate multi-Omics data in AD. Towards this end, we constructed gene regulatory networks from thousands of postmortem brain tissue samples across many brain regions from AD and normal control subjects. Thousands of gene subnetworks were identified and systematically examined with respect to known pathways, AD related gene sets, and AD clinical and pathophysiological data. These subnetworks were rank-ordered by the degree of dysregulation and relevance to AD pathology. The network drivers were systematically identified based on network connectivity. Network structures of a number of top ranked subnetworks were systematically validated through *in vitro* or *in vivo* perturbations of key network driver genes.

Our integrative multiscale network analysis identified novel pathways and drivers that potentially regulate AD pathogenesis.