大学院特別講義

デンマーク・オーフス大学研究者による オンラインセミナーの御案内

BRI-DANDRITE online joint lecture

日　　時：令和３年 10 月６日(水) 17:00～18:00

開催方法：**Zoom**

The role of patient specific alpha-synuclein aggregates in Parkinson's disease related disorders – challenge or opportunity for disease modifying therapies?

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Aggregation of the presynaptic protein alpha-synuclein (a-syn) plays a pivotal role in the group of so-called synucleinopathies dominated by Parkinson's disease, Lewy body dementia and multiple systems atrophy. It is hypothesized the disease progression is driven by a spreading of a-syn aggregates from "sick" neurons to healthy neurons, where they template the aggregation of the neurons native a-syn and thus perpetuate the disease process in a step-wise manner.
Recent cryo-electron microscopic studies demonstrate the presence of different folding strains of a-syn in patient brains. We engineered a two structurally different strains and demonstrated they exhibit different functional effects in cells, human neurons and two mouse models. The strain mimicking multiple systems atrophy exhibited a stronger degenerative phenotype.
This may have consequences for our attempts to make disease modifying treatments. We have demonstrated that the ER calcium pump is activated by a-syn aggregates and targeting this activation and its subsequent calcium accumulation in the endoplasmic reticulum slows disease progression in cell and in vivo models. Current experimental approaches allow amplification of patient specific a-syn aggregates from CSF samples and we find they differ functionally. Future experiments will have to prove if experimentally demonstrated pathogenic effects of a-syn aggregates are valid across different patient derived a-syn strains or if they are specific to a-syn aggregates present in subgroups of the synucleinopathies. Such stratification will enhance the chance for positive outcomes of clinical trials targeting a-syn aggregate specific mechanisms.

どうぞ奮ってご参加ください。

（司会：脳研究所　脳病態解析分野　教授・松井　秀彰）