東京大学大学院医学系研究科神経病理学
卓越大学院・特別セミナー

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演題: *NGF brain metabolism, Amyloid pathology and Alzheimer's D*isease

日時: 2019 年 9 月 20 日(金) 午後 2 時 30 分-3 時 30 分
場所：東京大学医学部教育研究棟 13 階 第 6 セミナー室

Cuello 教授は、中枢神経系におけるアセチルコリン性神経伝達と、それを支える NGF シグナル経路に関する先駆的な業績を通じて、アルツハイマー病におけるコリンエステラーゼ阻害療法に貢献された神経薬理学の重鎮です。故・金澤一郎教授らとオクスフォード大で進められたサブスタンス P の局在に関する古典的業績に始まり、最近では NGF の細胞外腔における成熟化過程や、細胞内アミロイドβの病態解析でも、数々の重要な知見を発信されております。今回来日された機会に、特別に講演をお願いする機会に恵まれました。多数のご来聴をお待ち致します。

Our lab is interested in the early Alzheimer's disease (AD) pathology. We have made contributions regarding the early intraneuronal Aß burden, the early AD inflammation and experimental therapeutics in rat and mice transgenic models of the AD-like amyloid pathology. On this presentation I will discuss a novel brain metabolic pathway responsible for the activity-dependent release of proNGF from cortical neurons, its conversion to mature NGF (mNGF) and subsequent degradation by metalloproteases. This metabolic pathway was validated pharmacologically to regulate the cholinergic phenotype of basal forebrain cholinergic neurons.

We have found that this pathway is deregulated in AD and in Down syndrome, with AD pathology producing a "trophic factor-disconnect" and thus explaining the cholinergic atrophy in AD. Our lab is currently investigating the extent of the brain NGF metabolic deregulation at preclinical stages of AD and whether NGF pathway-related molecules could be used as potential biomarkers of pre-symptomatic AD pathology.

参考文献

Welikovitch LA, Do Carmo S, Maglóczky Z, Freund T, Cuello AC. Evidence of intraneuronal Aβ accumulation preceding tau pathology in the entorhinal cortex. ***Acta Neuropathol*** 136:901-917, 2018

Bruno MA, Cuello AC. Activity-dependent release of precursor nerve growth factor, conversion to mature nerve growth factor, and its degradation by a protease cascade. ***Proc Natl Acad Sci USA*** 103: 6735-6740, 2006

Cuello AC, Jessell TM, Kanazawa I, Iversen LL. Substance P: localization in synaptic vesicles in rat central nervous system. ***J Neurochem*** 29:747-751, 1977

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