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この公開講座・セミナー・シンポジウム等は大学院医学研究科の単位認定対象となっております。単位認定の条件や対象科目等は下記をご確認ください。

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代謝内分泌内科学セミナー

日　時　令和 8年 12月 17日（木）18:00～19:00

場　所　7号館 1 階 カンファレンスルーム

★大学院医学研究科の単位認定あり　★参加申込不要

座長

順天堂大学大学院医学研究科 代謝内分泌内科学
教授　綿田 裕孝 先生

講演

1. Pathological phenotypes of astrocytes in Alzheimer's disease.

Professor Jong-Seok Moon, Ph.D.

Department of Pathology, College of Medicine, Soonchunhyang University

2. TFEB-mediated lysosomal enhancement ameliorates stress-induced mitochondrial DNA release in microglia & hypothalamic inflammation, resulting in improved metabolic profile & weight loss

Chair Professor Myung-Shik Lee, M.D., Ph.D.

Department of Integrated Biomedical Science, Soonchunhyang Institute of Medi-bio Science & Div. of Endocrinology, Dept. of Internal Medicine, Soonchunhyang University.

韓国の Soonchunhyang University（順天郷大学）から2名の研究者をお招きし、ご講演いただきます。Moon 先生には、アルツハイマー病の病態形成におけるアストロサイトの機能変容とその役割について、Lee 先生には、TFEBを介したオートファジー・リソソーム機能の制御と、ミクログリアを介した視床下部炎症および肥満の病態について、それぞれご講演いただきます。神経変性疾患および代謝性疾患の病態を、グリア細胞の機能制御という観点から紐解く、最先端の研究をご紹介いただきます。

主催
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（大学院医学研究科）

Abstracts

1. Pathological phenotypes of astrocytes in Alzheimer's disease.

Professor Jong-Seok Moon, Ph.D.

Astrocytes are involved in various processes in the central nervous system (CNS). As the most a bundant cell type in the CNS, astrocytes play an essential role in neuronal maintenance and sup port, synaptic activity, neuronal metabolism, and amyloid-beta (Aβ) clearance. Alzheimer's disea se (AD) is a neurodegenerative disorder associated with cognitive and behavioral impairment. T he transformation of astrocytes is involved in various neurodegenerative diseases, such as AD. Since astrocytes have functional diversity and morphological and physiological heterogeneity in t he CNS, AD-related astrocytes might show various pathological phenotypes during AD. Astrocyt es developing pathological phenotypes could contribute to AD progression. In our study, we sug gest the pathological phenotypes of astrocytes in the context of AD, highlighting recent findings i n human and mouse AD.

2. TFEB-mediated lysosomal enhancement ameliorates stress-induced mitochondrial DNA release in microglia & hypothalamic inflammation, resulting in improved metabolic profile & weight loss

Chair Professor Myung-Shik Lee, M.D., Ph.D.

Mitochondrial dysfunction and metabolic inflammation are key contributors to metabolic disorder s. Hypothalamic inflammation-associated microglial activation is also increasingly recognized as an important element in obesity. We studied whether amelioration of mitochondrial dysfunction o f microglia through enhancement of autophagy/lysosome function could reduce hypothalamic infl ammation and metabolic dysregulation in obesity. When microglial cells were treated with palmiti c acid, mitochondrial DNA (mtDNA) was released into the cytoplasm, accompanied by mitochon drial ROS accumulation, mtDNA oxidation, IFN-β induction and IRF3 phosphorylation, suggestin g activation of the cGAS/STING pathway. mtDNA release and IFN-β induction after palmitic acid treatment were attenuated by adenoviral expression of TFEB, a master regulator of autophagy g ene expression and lysosomal biogenesis. Released mtDNA was colocalized with TFAM and L C3, and was decreased by TFEB expression, suggesting its clearance by mitochondrial nucleoid -phagy in addition to mitophagy. TFEB-CAMG-Tg mice expressing constitutively active human T FEB in microglia exhibited significantly reduced body weight gain, improved glucose tolerance a nd lower HOMA-IR than non-transgenic littermates fed a high-fat diet (HFD). Immunofluorescenc e analysis revealed a significantly decreased number of $Iba1^{+}$ microglia, reduced C1q accumulat ion and diminished IRF3 phosphorylation in TFEB-CAMG mice. Decreased POMC neuronal acti vity under HFD, indicated by decreased cFos signal in POMC cells, was restored in the hypothal amus of TFEB-CAMG mice, leading to enhanced leptin sensitivity and diminished food intake. T FEB overexpression mitigated lysosomal stress associated with HFD, as indicated by reduced li pofuscin accumulation and restored LAMP1, CHMP2B, and CHMP4B signals. These findings su ggest that metabolic stress in microglia leads to mtDNA release, followed by STING-mediated IF N-β induction and hypothalamic inflammation, lysosomal stress, leptin resistance and obesity. T his process can be ameliorated by enhancing autophagy/lysosome function in microglia, likely th rough mitochondrial nucleoid-phagy. Microglial autophagy/lysosome enhancement may represe nt a promising therapeutic strategy against metabolic dysfunction due to obesity and also neurod egenerative diseases associated with microglial stress.