令和6年度 第5回 NCNP 国際セミナー

日時:令和6年7月17日(水)13:00~

場所:研究所本館第一·第二会議室

演者: Prof. Eran Perlson, Ph.D

Sagol School of Neuroscience, Dept. of Physiology and Pharmacology Faculty of Medicine, Tel Aviv University, Israel

演題: Unlocking ALS: Muscle Exosome Control TDP-43 Local Synthe sis at the NMJ

内容紹介:

Amyotrophic lateral sclerosis (ALS) is characterized by the disruption of neuromuscular junctions (NMJs) and neurodegeneration. Recent research underscores the significanc e of TDP-43 in the formation of axonal pathological condensates, contributing to NMJ disruption by inhibiting local protein synthesis. However, the mechanisms driving local TDP-43 accumulation remain elusive. In this study, we unveil TDP-43 axonal accumula tion in peripheral nerves of both SOD1 patients and mice, attributable to aberrant loc al synthesis. This phenomenon is instigated by the misregulation of muscle-derived m iR-126a-5p exosomes in ALS. Intervention targeting muscle exosomes or miR-126a-5p inhibition prompts presynaptic TDP-43 synthesis and accumulation, culminating in axon al translation disruption and NMJ degeneration. Intriguingly, the introduction of miR-12 6 to SOD1G93A mice and co-cultures exhibits neuroprotective effects, delaying motor decline. These findings illuminate a novel transcellular communication axis between mu scles and axons, orchestrating local synthesis and NMJ maintenance at single synaps e resolution.

(This work is under revision in Nature Neuroscience.)

担当·連絡先:荒木 敏之(疾病研究第五部:内線5151)