



第 494 回つくば分子生命科学セミナー

TSUKUBA MOLECULAR LIFE SCIENCE SEMINAR

演題：Catastrophic Hepatokine FGF X: From the Liver to Muscle Stem Cell Dysregulation and Sarcopenia

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日時：2025 年 12 月 22 日（月） 16:00–17:00

会場：医学系学系棟 4 階 483 室

要旨：(abstract)

Metabolic dysfunction-associated steatohepatitis (MASH) is increasingly recognized as a chronic liver disease that exerts detrimental effects beyond the liver. Among these, sarcopenia—the progressive decline in skeletal muscle mass and function—represents a critical complications with profound clinical consequences. While previous studies have largely focused on proteostatic regulation within myofibers, the contribution of liver-derived hepatokines to muscle regeneration remains underexplored. In this study, we newly present fibroblast growth factor X (FGFX) as a pathogenic hepatokine to induce sarcopenia elevated under MASH conditions. We demonstrate that circulating FGFX impairs muscle regeneration by disrupting the balance between proliferation and differentiation of muscle stem cells (MuSCs) through FGFR4-mediated signaling. Mechanistically, FGFX–FGFR4 activation suppresses dystrophin-glycoprotein complex (DGC) and MEF2C expression, leading to aberrant nuclear translocation of YAP, atypical hyperplasia of MuSC, and failure of myogenic differentiation. These maladaptive responses culminate in impaired skeletal muscle regeneration and functional decline. Our findings reveal a novel liver–muscle axis in which FGFX functions as a “catastrophic hepatokine,” linking chronic liver injury to muscle wasting. This work provides new mechanistic insight into the pathogenesis of sarcopenia in MASH and suggests potential therapeutic strategies targeting the FGFX–FGFR4 pathway.

本セミナーは、医学学位プログラム（博士）「医学セミナー」（担当：専攻各教員）、及び、フロンティア医科学学位プログラム（修士）「医科学セミナーII」（担当：入江賢児）の関連セミナーに相当します。

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