Institute of Molecular Genetics
of the Czech Academy of Sciences

Regular Wednesday IMG seminar

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"Tipping the lipid scales: negative feedback regulation via ORMDLs protein degradation ensures sphingolipid homeostasis"

Sphingolipids are essential lipid molecules that contribute to cellular structure and signaling. Their *de novo* synthesis is initiated in the endoplasmic reticulum (ER) and catalyzed by the multimeric serine palmitoyltransferase (SPT) complex. The ER-resident ORMDL proteins are well-established regulators of sphingolipid synthesis, directly inhibiting the SPT complex to control the pathway at its origin. Here, we identify a negative feedback loop that fine-tunes this regulatory mechanism. Using pharmacological inhibitors such as myriocin and fumonisin B1, which target different steps of the sphingolipid pathway, we demonstrate that reduced sphingolipid levels promote enhanced degradation of ORMDL proteins. This degradation alleviates SPT inhibition, thereby accelerating *de novo* sphingolipid biosynthesis and restoring metabolic balance.

The seminar will be held

on Wednesday 22nd January 2025 at 15:00

in the Milan Hašek Auditorium at IMG

(Institute of Molecular Genetics of the Czech Academy of Sciences, Vídeňská 1083, Prague 4)