Séminaire

ibs Institut de Biologie Structurale

CONFÉRENCIER INVITÉ

Vendredi 08 Septembre 2017 à 11h

Salle des séminaires

Institut de biologie structurale - 71 avenue des Martyrs CS 10090 38044 Grenoble Cedex 9 - T.+33 (0)4 57 42 85 00

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Golgi glycosylation and cellular Mn^{2+} homeostasis

Congenital disorders of glycosylation (CDG) are severe inherited diseases in which aberrant protein glycosylation is a hallmark. From this genetically and clinically heterogenous group, a significant subgroup due to Golgi homeostasis defects is emerging. We previously identified TMEM165 as a Golgi protein involved in CDG. Extremely conserved in the eukaryotic reign, the molecular mechanism by which TMEM165 deficiencies lead to Golgi glycosylation abnormalities was enigmatic. As GDT1 is the ortholog of TMEM165 in yeast, both gdt1Δ null mutant yeasts and TMEM165 depleted cells were used. We highlighted that the observed Golgi glycosylation defects due to Gdt1p/TMEM165 deficiency result from Golgi manganese homeostasis defect. We discovered that in both yeasts and mammalian Gdt1p/TMEM165 deficient cells, Mn^{2+} supplementation could restore a normal glycosylation. We also showed that TMEM165 was a Mn^{2+} sensitive protein. When exposed to high Mn^{2+} concentrations, we demonstrated that TMEM165 was targeted and degraded in lysosomes. Remarkably, the variant p.E108G recently identified in a novel TMEM165-CDG patient, was found to be insensitive to Mn^{2+} supplementation. This study not only provides novel insights into the molecular causes of glycosylation defects observed in TMEM165-deficient cells but also suggest that TMEM165 is a key determinant for the regulation of Golgi Mn^{2+} homeostasis.

Hôte : Hugues Lortat-Jacob (IBS/SAGAG)

L'accès au campus EPN nécessite un avis de rendez-vous

Contactez O. Cavoret (au moins 48h à l'avance) - T. 04 57 42 87 04 - email : ibs.seminaires@ibs.fr