Invitation à la soutenance publique de thèse de
Louise THINES
Master bioingénieur : chimie et bio-industries à finalité spécialisée

Pour l’obtention du grade de Docteur en sciences agronomiques et ingénierie biologique

« The yeast protein Gdt1p is a newly-identified actor in manganese homeostasis at the Golgi »

qui se déroulera
le jeudi 21 novembre 2019 à 16h15
Salle Jean-Baptiste Carnoy
Place Croix du Sud, 4-5
1348 Louvain-la-Neuve

Jury members:

Prof. Pierre Morsomme (UCLouvain), supervisor
Prof. Patrice Soumillon (UCLouvain), chairperson
Prof. Pascal Hols (UCLouvain), secretary
Prof. Emile Van Schaftingen (UCLouvain)
Prof. Marc Boutry (UCLouvain)
Prof. Kyle Cunningham (John Hopkins Univ., USA)
Prof. Mélanie Boeckstaens (Univ. Libre de Bruxelles, Belgium)

Congenital disorders of glycosylation (CDGs) are a group of hereditary diseases characterized by deficiencies in glycosylation. In 2012, some CDGs were linked to mutations in the human gene TMEM165. TMEM165 belongs to the uncharacterized protein family 0016 (UPF0016) whose members were poorly characterized and their function, unknown. This project studies the S. cerevisiae UPF0016 member Gdt1p as a model protein of the family. Previous data showed that Gdt1p localizes at the Golgi membrane and is involved in Ca²⁺ and pH homeostasis through its transport activity. More recently, plant and bacterial UPF0016 members were shown to be involved in Mn²⁺ homeostasis, but without providing any direct proof of transport. In this context, this work mainly investigated whether Gdt1p transports Mn²⁺. To do so, we exploited the fact that manganese quenches the fluorescence of Fura-2 to develop a Mn²⁺ transport assay in Fura-2 loaded L. lactis cells producing Gdt1p. With this approach, we highlighted Mn²⁺ transport by Gdt1p, in addition to its previously reported Ca²⁺ transport ability. In parallel, we found in yeast that Gdt1p confers resistance to high Mn²⁺ concentration, controls the cellular Mn²⁺ stores, and modulates the activity of the Mn²⁺-dependent enzyme Sod2p. Similar techniques were used to demonstrate that conserved motifs of the family seem essential for proper transport. Our data further enabled us to assume that Gdt1p would work as a Ca²⁺-Mn²⁺/H⁺ antiporter, importing both divalent cations in the Golgi lumen in exchange of protons. Apart from illustrating how yeast regulates its Golgi Mn²⁺ concentration, this work reinforces the suggested link between the UPF0016 family and Mn²⁺ homeostasis, and provides insights into the molecular causes of TMEM165-CDGs.