GQBB LABORATORY OF BIOCHEMISTRY

LABORATORY OF BIOCHEMISTRY
GROUP OF BIOLOGICAL CHEMISTRY AND BIOTECHNOLOGY
BIOENGINEERING DEPARTMENT

IQS UNIVERSITAT RAMON LLULL

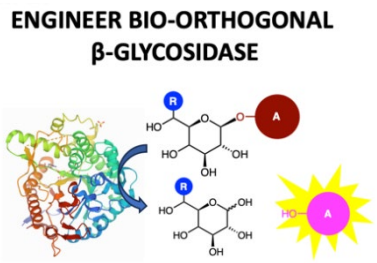
Proposed project for internship 2025-26

Project:
NEW-TO-NATURE GLYCOSIDASES AS BIO-ORTHOGONAL TOOLS IN METABOLIC LABELLING AND MICROBIOME STUDIES

Vacancies: 1 Master research project (6-9 months)
1 undergrad internship (12-15 weeks)

Summary: Non-natural modified sugars (such as C6-modified glycosides or ring expanded sugars) have the potential to be transformative glycomimetics with application in chemical biology and medicinal chemistry. Glycosides of such modified sugars are insensitive to degradation by hydrolytic enzymes. Therefore, engineering the active site of a glycosidase to be active on these non-natural glycosides will generate a bio-orthogonal non-natural sugar/engineered hydrolase pair. Transfected cells expressing the engineered glycosidase will allow the highly selective and time-resolved delivery of molecular cargoes (from precursor glycosylated cargos with the modified sugars) inside cells. Applications in chemical biology are diverse: a) microbiome studies, where selective access to a metabolic nutrient conferred by a bio-orthogonal substrate-enzyme pair will give the producing organism a competitive advantage over others in the community and enable its engraftment into a microbiome (dysbiosis therapies), b) metabolic labelling, where a masked metabolite precursor will be selectively released by the bio-orthogonal system in a time-resolve fashion.

Objective: In this project, you will contribute to engineer a novel (new-to-nature) glycosyl hydrolase (bioorthogonal glycosidase) that selectively cleaves non-natural modified glycosides *in vitro* and in cells that recombinantly produce the enzyme. We have recently shown that fluorescent-labelled septanosides are uptaken by cells (Pote et al.2021) enabling *in vivo* selection strategies. You will develop and implement a directed evolution approach combined with fluorescence-assisted cell sorting (FACS) screening of large libraries using the fluorogenic substrates recently synthesized in collaboration with Dr. M. Peczuh (University of Connecticut, USA. The novel bioorthogonal hydrolase will be characterized for the bioorthogonal unmasking of functional probes *in vivo*.



Methodology: *molecular biology, gene library preparation, HTS by FACS, protein expression, enzyme kinetics.*

More information at: https://planaslab.iqs.edu/

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