KØBENHAVNS UNIVERSITET
UNIVERSITY OF COPENHAGEN
Department of Biomedical Sciences

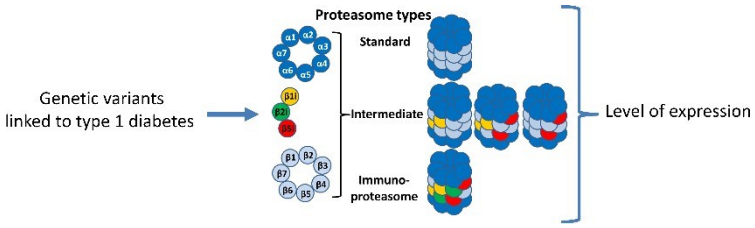
Master project in type 1 diabetes pathology: human genetic variability vs protein degradation and antigen presentation.

The project can be tailored to the 3-6 months ERASMUS exchange.

Type 1 diabetes (T1D) is a result of autoimmune attack directed at insulin producing pancreatic beta-cells that specifically targets insulin and proinsulin peptides. The peptides are visible to immune system through their presentation on MHC molecules on beta cell surface. Before their presentation they have to be processed by proteasomes. We have recently shown that non-standard proteasome is expressed in beta cells and is engaged in proinsulin degradation. Moreover, certain genetic variants are linked to higher expression of non-standard proteasomes and their inheritance co-segregates with HLA alleles predisposing to type 1 diabetes.

THE PROJECT

In this project, you will perform *in silico* analysis of genetic variants impact on the profile of transcription factors binding to proteasome subunits promoters. You will recreate selected genetic variants using CRISPR-Cas9 approach *in vivo* and analyze their impact on proteasome subunit expression and profile of transcription factors binding to the promoter(s) (via reverse ChiP).



Possible impact of type 1 diabetes linked genetic variation on the profile of proteasome expression.

Techniques you will learn during the project: analysis of transcription factor binding sites and genetic variants impact, CRISPR-Cas9 based genetic manipulation with creation of clonal cell lines, cell transfection and transduction with Lentiviral particles, reverse ChiP, primer design, PCR, protein analysis (SDS-PAGE, Western blot, immunoprecipitation), cell culture and freezing, literature search, critical analysis and presentation of the results.

THE GROUP

We are a small and dynamic research group at the Department of Biomedical Science (BMI, https://bmi.ku.dk/english/research/proinsulin-folding/). We are located at 12.6 in the old Panum building and we share office and lab spaces with 3-4 other groups. The project can be tailored to the interests of the candidate.

THE CANDIDATE

We are looking for a highly motivated candidate with an interest in cellular biology and/or diabetes. Ideally, the project is designed for a 10 months study. The project is suitable for a Master thesis for students of the study courses human biology, biomedical engineering, molecular biomedicine, biochemistry. If you wish to know more about this project, please contact associate professor Michal Marzec (michal@sund.ku.dk).