Title: Exploration and validation of new method for identification of DDP-IV inhibitors from protein hydrolysates

Supervisors: Henrik Franzyk / Dan Stærk (main supervisor)

Description: Type 2 diabetes (T2D) is a multiparametric metabolic disease affecting more than 400 million people worldwide. It is characterized by decreased insulin sensitivity in the liver, muscles, and adipose tissues and/or reduced insulin secretion by the pancreatic β-cells. This leads to elevated blood glucose, causing severe complications such as retinopathy, neuropathy, and cardiovascular diseases. The incretins are a group of metabolic peptide hormones that are released after a meal, and they stimulate production of insulin, which leads to lowering of blood glucose. The incretins are cleaved by the enzyme dipeptidyl peptidase-IV (DPP-IV), and DPP-IV inhibitors are therefore important targets in the search for new blood glucose lowering drugs.
In this project new methods will be developed for identifying peptide-based DPP-IV inhibitors from protein-rich food waste products (i.e., it is a green/sustainable approach).
Based on early work on isolation and characterization of peptide inhibitors of DDP-IV from protein hydrolysates, a number of these will be synthesized, purified and characterized in a hyphenated assay. This will include spiking of crude extracts/hydrolysates with these known pure inhibitors (typically proline-containing peptides with 3-5 residues) to perform proof-of-concept experiments for the feasibility of "fishing out" and identifying these as potent hits. Also, libraries of variants of known peptide hits may be investigated for proof-of-concept that high-affinity inhibitors are not "out-competed" by the presence of numerous medium/low-affinity inhibitors. The project will be highly interdisciplinary involving peptide synthesis, analytical chemistry, spectroscopy and pharmacological assaying.

Contact: Dan Stærk (ILF; Build. 30, room 140); e-mail: ds@sund.ku.dk

Henrik Franzyk (ILF; Build. 30, room 136); e-mail: henrik.franzyk@sund.ku.dk