



Three Ph.D. Positions

Analytical Characterization of Industrial Proteins and Biopharmaceuticals

Industrial, nutritional and therapeutic proteins have become key molecular entities used in the food industry and human/animal healthcare. Their role is rapidly increasing in this era of advanced biotechnology, with a large part of the newly approved drugs being already protein based. However, due to their large size, biology driven production, and complicated structural features therapeutic and nutritional proteins and industrial enzymes form some of the most challenging molecular entities to be functionally and structurally characterized. The main goal is to develop much-needed new analytical strategies enabling the separation, identification and quantification of all molecular forms of industrial enzymes, nutritional proteins and biotherapeutics in their intact native state. Distinctively, the novel analytical workflows to be developed within this program are aimed at the genuine intact proteins and will allow us to simultaneously establish structure-function relationships of proteoforms and aggregation states of proteins. The consortium is a collaboration between Utrecht University (Heck-lab), Leiden University Medical Center (Wuhrer-lab) and the companies DSM, FrieslandCampina and Roche. The project is (co)financed by the Netherlands Organisation for Scientific Research (NWO).

PhD1 (LUMC) will develop different native separation technologies for offline/online coupling to mass spectrometry using different types of industrial enzymes. The analytes will be enzymes exhibiting highly diverse and challenging modifications such as glycosylation and glycation. DSM will provide enzyme activity assays for demonstration of proof-of-concept for structure-function determination, materials and expertise and support in native enzyme analytical characterization.

PhD2 (UU) will further develop and employ high-resolution native mass spectrometry methods to characterize the complexity of dairy proteins, including the characterization of isoforms and co-occurring post-translational modifications. Integration of the gathered data with information measured by more conventional bottom-up, non-native approaches will be a prime objective. FrieslandCampina will provide support with *in vitro* digestion assays and immunological assays.

PhD3 (UU) will develop, and online couple, native separation and mass spectrometry methods applied to biopharmaceuticals such as immunoglobulins, fusion proteins and other antibody-based formats. Roche will provide expertise and materials for (affinity) columns and glyco-enzymes. Roche will in addition provide in-kind support with functional assays.

The three PhD students will work together in a team with principal investigators and post-docs of the involved groups and companies, and take secondments in industry to learn, but also transfer, new technologies. The PhD students will be appointed at the involved academic institutes, for a period of 4 years, and become embedded in the graduate schools and will perform practical work at both the UU and LUMC to allow a broad analytical technology toolbox development for structure-function determination of the different types of proteins.

We seek motivated students with a degree in Chemistry, Biology or Pharmaceutical Sciences with an interest and background in protein biochemistry and analytical method development and like to work in a team. Please send your applications (CV, letter of motivation and 2 references) in before May 1, 2018 via e-mail to Corine Heuzer (PA of Albert Heck) at c.c.heuzer@uu.nl. Enquiries about the positions can be made to Manfred Wuhrer (M.Wuhrer@lumc.nl) or Albert Heck (a.j.r.heck@uu.nl).