



Postdoctoral position available at the interface of Academia and Industry

In the frame of an ongoing funding scheme of the Walloon Region (DGO6; BEWARE FELLOWSHIPS *Academia*, co-financed by the COFUND program of the EU/FP7 - Marie Curie Actions), the Centre for Protein Engineering at the University of Liège (Belgium) is seeking for a collaborator holding a PhD degree. The aim is to apply for a postdoctoral fellowship to work on the project shortly described below and for which a good success rate is expected. This program focuses on technology transfer and a fellowship will hopefully be available to perform a research stay at the University, in partnership with the biotech company Eurogentec. Over the period covered by the mandate (30 months), eight months must be spent in the company. The call for proposals has just been launched and the deadline for submission is 30 October 2015. Note for the mobility criterion: all nationalities, including Belgian; the condition is to have spent less than 12 months over the last three years in Belgium.

Research program. Modern recombinant DNA methodologies give rise to high production of heterologous proteins, at relatively low cost. For the last three decades, a substantial number of proteins have been approved and are currently used in diagnostic tests and therapeutic treatments for e.g. cancers, infectious diseases, autoimmune diseases, and inflammatory diseases. In particular, monoclonal antibodies, alone or in combination with an active conjugate (e.g. toxic drug, radioisotope, cytokine) appear as “magic bullets” for a more efficient and specific therapeutic usage. Nowadays, the available drug arsenal has partly moved away from synthetic organic chemistry compounds towards recombinant proteins. Biologics are generally considered as less toxic and display *in vivo* activities that are more predictable. Nevertheless, development of suitable protein formulations is quite challenging and may require even more resources and time than for classical small organic molecules. Protein structures are highly dynamic and only marginally stable, and they are very sensitive to environmental factors (e.g. pH, temperature, interaction with surfaces, shear forces, shaking, presence of contaminants, protein concentration). Hence production, formulation and handling of proteins needs very special attention and this is particularly critical with large multidomain proteins, like antibodies.

The aim of protein formulation is to provide a final product that is safe, efficient and stable over a relevant period. Stability data are necessary to support formulation strategies for the development of any protein therapeutics. Common approaches for evaluation of protein stability to support formulation developments are often time-consuming (e.g. 6 months to 2 years), labor intensive and require significant quantity of material.

In this work, we will make use of our automated multi-channel pipetting workstation (Robotein[®], www.robotein.ulg.ac.be), in combination with a range of equipment for high throughput (HT) analysis (e.g. absorbance and fluorescence measurement, protein separation, analysis of interactions), to test large numbers of potential formulations. This will be achieved by screening various excipients under different conditions (e.g. concentration, pH, temperature, ionic strength) and evaluate the stability of proteins in terms of aggregation, denaturation, chemical degradation and any other structural changes. This will be feasible through the development of short term stability assays, based on real-time analysis and accelerated conditions for protein degradation. All experiments will be planned following a careful experimental design (DOE).

In an effort to develop safe, robust, rapid, and reproducible formulation protocols that are necessary to foster the successful development of protein-based pharmaceuticals, we also need to understand in more details the mechanisms by which protein structure and function can be altered during processing and storage. Thus, besides the HT screening approach available at Robotein[®], we will also make use of the wide range of biophysical and analytical techniques that are available at the Centre for Protein Engineering (e.g. UV/Vis absorbance, fluorescence, circular dichroism, bilayer interferometry, ITC, DSC, DLS) and through our collaborators (e.g. mass spectrometry and NMR) to provide a better understanding of the physico-chemical and biological properties of protein-based drugs, in particular their chemical and conformational stability.

This project is part of an ongoing collaborative effort between the group of Prof. André Matagne (contact person, see below) and Eurogentec, a renowned biotech company based in the Liège area.

Contact

Candidates should contact Prof. André Matagne, Laboratory of Enzymology and Protein Folding, Centre for Protein Engineering, Institut de Chimie B6, Allée de la Chimie, 3, University of Liège, B4000 Liège (Sart-Tilman), BELGIUM; email: amatagne@ulg.ac.be

