2 PhD positions in Chemistry/Chemical Biology

The Rubini Group in the School of Chemistry at University College Dublin (UCD) is seeking 2 Ph.D. students in the field of Chemistry/Chemical Biology to work on the engineering of the therapeutic protein human Interferon-gamma. These Ph.D. studentships would ideally start in **September 2024** and are for a period of four years.

The scholarship consists of a stipend of €22,000 per annum for up to 4 years and is funded by Science Foundation Ireland. Fees (EU level) will be also covered.

Human Interferon-gamma is a glycosylated pleiotropic cytokine that is crucial for the innate and adaptive immune response. In Nature, Human Interferon-gamma displays two highly heterogeneous N-glycosylations at Asn25 and Asn97, the role of which remains elusive in pharmacokinetics or clinical applications. For therapeutic purposes, unglycosylated human Interferon-gamma is produced in *E. coli*, resulting in a product with a short half-life. Current molecular biology and synthetic methods cannot give access to homogeneous glycoforms of human Interferon-gamma in good yields. Here we propose to combine the benefits of bacterial recombinant production with the precision of chemical methods, exploiting the reactivity of cysteine thiols introduced at the glycosylation sites. A range of thiol-selective conjugation reactions will be exploited for coupling to defined synthetic glycans with different compositions. The glycoconjugates will be characterised and their stability and bioactivity will be assessed, together with the role played by the conjugation linker. Further, we will compare the stability and bioactivity of site-specific PEGylated human Interferon-gamma variants with the glycoconjugates. These results will greatly increase the understanding of the potential of PEGylation vs glycosylation for the development of robust human Interferon-gamma variants with improved therapeutic profiles.

Applications are welcome from students from Ireland/EU with, or expecting to gain, a first class Honours degree (or equivalent) or a Master degree in Chemistry/Biochemistry/Chemical Biology or other relevant scientific discipline. In particular, candidates with experience in protein engineering and glycochemistry are strongly encouraged to apply.

Applications should include a cover letter, CV, detailed academic transcripts and the contact details for at least two academic referees and should be sent by email to Dr. Marina Rubini (**marina.rubini@ucd.ie**). Interviews will be held either online or in-person depending on circumstances. Applications will be handled on a rolling basis until the positions have been filled.