

A two-year Post-doctoral position in Molecular Modelling towards AAV gene therapy

Context

A Post-doctoral position is available within the frame of a collaborative project between the **Immunology and Liver Diseases team** from the **Genethon** and the **Catalysis and Molecular engineering team** from the **Toulouse Biotechnology Institute**. The project stands in the field of AAV gene therapy by focusing on the improvement of AAV-mediated gene transfer. Due to the human immune system recognition against AAV, low titer neutralizing anti-AAV antibodies were reported to have a large impact on AAV gene transfer efficacy. To address this issue, one promising strategy relies on a pre-treatment with immunoglobulin G-degrading enzyme isolated from *S.pyogenes* (IdeS) that has shown to reduce circulating anti-AAV neutralizing antibodies (Nabs) and allowed successful liver gene transfer in seropositive non-human primates (NHPs) (Leborgne et al., Nat. Med. 2020, 20:1096-1101). However, this approach has also shown some limitations related to the reduced activity of IdeS in NHPs where a significant amount of neutralizing, single-chain IgG still remained after prolonged exposure to the enzyme *in vitro* (Leborgne et al., Nat. Med. 2020, 20:1096-1101). By joining our respective expertise in immunology, computational structural biology and enzyme design and engineering, our goal will be to investigate and better understand molecular determinants involved in the IgG antibody recognition by bacterial enzymes with the aim *in fine* to design more efficient enzymes by computer-aided approaches and molecular modelling methods that will be subsequently experimentally evaluated.

Job description

The successful candidate will be in charge of conducting molecular modelling studies to get a better understanding of molecular determinants involved in the recognition of the IgG antibody by the enzyme and also to redesign enzyme mutants to improve their efficacy. This work will be carried out in tight interaction with experimentalists.

We are looking for a highly motivated scientist who has research background and expertise in a number of areas of Computational Biology, including protein modelling, molecular docking, molecular dynamics simulations and experience in computational protein design would be a plus.

A biology background and a sound understanding of protein modelling and protein-ligand and protein-protein interactions are required. Familiarity with UNIX and Linux is expected.

The candidate will be a key player in the project as He/She will ensure the tight interaction between the two collaborators. He/She will be based at Toulouse Biotechnology Institute, Toulouse (31), France.

Qualifications

- PhD in Molecular Modelling, Structural biology, Biophysics or related field.
- Strong communication and organizational skills and enjoy working in a team-oriented environment.
- Good English skills are required and notions of French would be a plus.
- The position is available starting in **September 2023 (at the earliest) and for a duration of up to 24 months.**

Applicants should send as soon as possible CV, summary of previous research and contact addresses of two references to:

Giuseppe Ronzitti (Genethon): gronzitti@genethon.fr

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