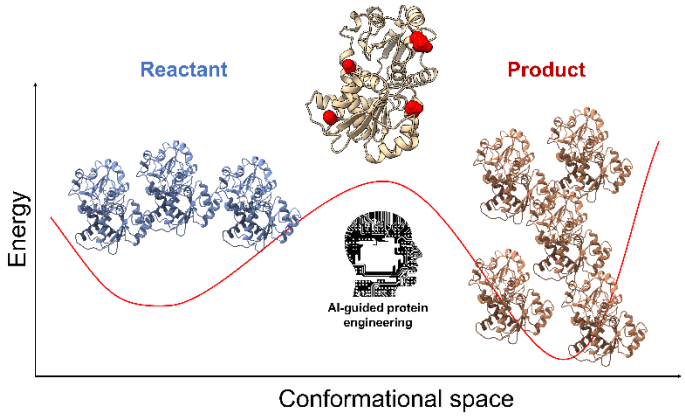
Master thesis project

Title: Computational design of Hyperactive Enzymes for Gene and Enzyme Replacement Therapies

Where: Telethon Institute of Genetics and Medicine, Pozzuoli

Duration: 9-12 months

Project description:
The present thesis project is focused on the computational design of enzymes used as treatment for lysosomal storage disorders (LSDs). LSDs are usually treated through enzyme replacement therapy (ERT) and liver-directed gene therapy. However, those treatments demand high vector doses or frequent injections to achieve therapeutic enzyme levels, increasing the risk of inflammation and liver toxicity. Recently, it has been proven that therapeutic proteins with enhanced specific activity can reduce vector doses, lower toxicity, and improve clinical outcomes.
During the thesis project, the student will learn how to integrate deep learning algorithms (e.g., ProteinMPNN, ESM2, active learning strategies, etc.) and biophysical simulations (e.g., enhanced sampling MD, constant-pH MD, etc.) to design hyperactive enzyme variants.
The ideal candidate has experience with Python or another programming language, is comfortable working in Linux environments, and possesses a basic understanding of molecular simulations and/or machine learning/deep learning techniques.



How to apply: please send an email with your CV and a motivational letter to Dr. Andrea Pasquadibisceglie a.pasquadibisceglie@tigem.it

TIGEM does not discriminate on the basis of sex, race, gender orientation, sexuality, or disability. The selection committee for this role encourages applicants from all backgrounds and will consider all applications equally irrespective of the aforementioned characteristics.