



# MSc Thesis in Molecular Biology

## Computer-aided design of thrombolytic enzymes

We are looking for a motivated **MSc Student** to join our laboratory of **Computer-Aided Molecular Design** (Division of Physiological Chemistry, Medical University of Graz). The successful MSc Student candidate will participate in the **experimental part** of the project **Computer-aided design of thrombolytic enzymes**.

**Background:** Amongst different actors, the von Willebrand factor (vWF) and its physiological partner, the metalloproteinase ADAMTS13 (a disintegrin-like and metalloprotease with thrombospondin type 1 motif 13), have been proven to mediate the thrombolysis of occlusions in ischemic stroke that are resistant to the tissue plasminogen activator (tPA), the standard drug in thrombolytic treatment. ADAMTS13 is a metalloprotease that counterbalances the von Willebrand factor (vWF) by means of cleaving it into smaller, less adhesive multimers within nascent platelet-rich thrombi. vWF bridges subendothelial collagen at the site of vascular injury with platelets' glycoprotein Ib $\alpha$  during the initiation of hemostasis. Upon presence of vessel injury, the circulating globular form of vWF anchors to collagen via its A3 domain and - like a flag in the wind - stretches and exposes its A1 domain for the binding of platelets and its A2 domain to ADAMTS13. Thus, ADAMTS13 has emerged as an attractive enzyme that could be used as thrombolytic drug in the clinic.

**Goal:** The MSc Project will consist of the **expression, purification and enzymatic assay of the full-length zinc metalloprotease ADAMTS13**, a key player in the regulation of blood clots formation. The MSc Student will focus her/his efforts in the expression of the wild-type full-length ADAMTS13 in *E. coli* and in the yeast *P. pastoris*, the purification of the expressed protein using chromatographic methods, and the *in vitro* measurement of the enzymatic activity. In collaboration with the laboratory of Dr. Gerhard Cvirn (Med Uni Graz), the effect of the recombinant protein on the formation and breakdown of blood clots will be evaluated on whole blood too.

**Timing and facilities:** We offer a position for the MSc Thesis for 6 months starting from now. Our research group counts with a molecular biology lab and the MSc Student will be fully supported by our team.

**Questions?** Feel free to visit [CAMDgraz.com](http://CAMDgraz.com) or to send an Email to: [pedro.murcia@medunigraz.at](mailto:pedro.murcia@medunigraz.at)

