

Master thesis project – Robert Kralovics Lab

The group of Robert Kralovics at CeMM is looking for a highly motivated Master's Student who is interested in identifying novel drugs and drug targets in myeloproliferative neoplasms (MPN).

MPN is a group of chronic hematopoietic malignancies characterized by excessive production of terminally differentiated blood cells and driven by somatic mutations in hematopoietic stem cells. In 2013, a breakthrough discovery made by our group identified CALR mutation as one of the three main driver mutations of MPN disease (Klampfl, Gisslinger et al. 2013). Together with our collaborators, we then uncovered the pathogenic mechanisms of mutant calreticulin, suggesting the important role of thrombopoietin receptor (MPL) in the activation of the downstream oncogenic pathways (Chachoua, Pecquet et al. 2016; Marty, Pecquet et al. 2016; Nivarthi, Chen et al. 2016). This brings us to our next research goal which is to identify novel drugs/drug targets specifically targeting mutant CALR-driven disease.

The project will focus on high-throughput drug screening and hits validation as well as CRISPR-Cas9 based genome-wide gene knock out screening. We are in collaboration with PLACEBO (Platform Austria for Chemical Biology) which provides us a highly elaborative drug library consisting of 92,000 compounds. The aim is to identify compounds which preferentially kill malignant cells with CALR mutation. Also, using genetic screening tools, we will try to further explore the disease pathogenesis and identify novel drug targets. The techniques that will be applied in the project include cell culture, cytotoxicity assay, molecular cloning, CRISPR-Cas9 genomic editing, western blot and next generation sequencing.

References

- Chachoua, I., C. Pecquet, et al. (2016). "Thrombopoietin receptor activation by myeloproliferative neoplasm associated calreticulin mutants." *Blood* 127(10): 1325-1335.
- Klampfl, T., H. Gisslinger, et al. (2013). "Somatic mutations of calreticulin in myeloproliferative neoplasms." *N Engl J Med* 369(25): 2379-2390.
- Marty, C., C. Pecquet, et al. (2016). "Calreticulin mutants in mice induce an MPL-dependent thrombocytosis with frequent progression to myelofibrosis." *Blood* 127(10): 1317-1324.
- Nivarthi, H., D. Chen, et al. (2016). "Thrombopoietin receptor is required for the oncogenic function of CALR mutants." *Leukemia* 30(8): 1759-1763.

Requirements and desired qualifications

- ✓ Bachelor degree in biology or equivalent
- ✓ Commitment to the project for a minimum of 10 months
- ✓ Strong interest in cancer therapeutics
- ✓ Experience in cell culture work considered as an advantage
- ✓ High accuracy and reliability
- ✓ Good interpersonal skills and passion for working in an international environment
- ✓ Solid written and oral communication skills in English

The successful applicant will be joining a dynamic laboratory with extensive experience in cancer genetics as well as in molecular and cellular biology and receives proper training in advanced biological technologies.

Application details

If you believe you fit the profile and would like to be part of our international, dynamic research group, please visit our website and apply using the link provided with your cover letter and CV including the contact details of two suggested referees. The application deadline is **September 17th, 2017**. The position is available from October 2017.

The Institute (www.cemm.at)

CeMM is a flagship institute for biomedical research in the heart of Europe, Vienna. We are committed to highest scientific standards as exemplified by recent publications in top journals including *Nature*, *Science* and *Cell*. CeMM offers a uniquely dynamic, interactive and international environment and is located in a beautiful building at the center of the Medical University campus, within walking distance of Vienna's historical city center. CeMM has been ranked among the top-5 best places to work in academia (<http://the-scientist.com/2012/08/01/best-places-to-work-academia-2012>). Vienna is frequently ranked the world's best city to live in. It is a United Nations city with a large English-speaking community. The official language at CeMM is English, and more than 40 different nationalities are represented at the institute. We are convinced that diversity and a multicultural work environment are clear advantages for successful research and are committed to attract, develop, and advance the most talented individuals regardless of their gender, race, sexual orientation, religion, age, disability status or any other dimension of diversity.