
Master 2 Internship proposal

Functional and structural characterization of the autotaxin γ isoform

Project description:

Autotaxin (ATX) is a 99-125 kDa phospholipase involved in a large range of physiological and pathological processes. This enzyme is part of the nucleotide pyrophosphatase/phosphodiesterase family and is also referred to as ENPP2. ATX is mainly involved in the phospholipidic metabolism and the production of extracellular Lysophosphatidic Acid (LPA) from lysophosphatidylcholine acids (LPC). At least 5 human isoforms have been discovered so far. The beta isoform is the most abundant one, expressed in many parts of the body and accounting for the majority of ATX activity. The alpha and epsilon isoforms are less abundant and differ from ATX beta by a 52 aa polybasic insertion. ATX delta isoform is missing an exon of 19 tetrapeptides with unknown function. ATX gamma is brain specific and differs from ATX beta by a 25 aa insertion, while its activity is similar to the beta form. The ATX gamma structure has not been resolved so far, and no information is available on the structural modification arising from this insertion.

During the internship at EMBL Grenoble, the student will be in charge of i) the generation of a stable cell line expressing a deglycosylated version of ATX gamma ii) the expression and the purification of the secreted protein iii) the crystallization assays and the structure determination iv) the functional study of the various isoforms with biochemical assays and the screening of new inhibitors developed in collaboration with Pr Boumendjel lab

The student will be supervised daily by a predoctoral fellow, Mathias Eymery. The generation of a deglycosylated gamma ATX stable cell line will be handled with the HEK293 flp-in system and pcDNA5/FRT vector containing the deglycosylated ATX gamma sequence. Expression will be handled with roller bottles and purification of the secreted protein will be approached by an affinity column (POROS20MC) followed by a gel filtration with a Superdex 200 Increase 10/300 GL. For the biochemistry experiments, the assays are already implemented and the student will be involved in the testing of new ATX inhibitors synthesized in the partner lab. Finally, the student will have an introduction on how to perform crystallization assays and participate to the structural determination of this ATX gamma isoform. Furthermore, the candidate will also be involved in collaborative projects with other labs.

Candidate background: the project requirements can fit with any candidate with a background in biology and interested in wet lab experiments. Previous experience with cell culture, protein expression and purification are an advantage.

Duration and conditions of the stay: The candidate will be a member of the McCarthy team at EMBL Grenoble during the 6-month traineeship. Paid placement, competitive stipend.

Start date: Flexible, January or February 2022, can be adapted depending on university requirement.

For application please contact: meymery@embl.fr and andrewmc@embl.fr, including a CV and M1 transcript

Postal address: EMBL Grenoble, 71 avenue des Martyrs, 38000 Grenoble, France

Why join us

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What else you need to know

We are Europe's flagship research laboratory for the life sciences – an intergovernmental organisation performing scientific research in disciplines including molecular biology, physics, chemistry and computer science. We are an international, innovative and interdisciplinary laboratory with more than 1700 employees from many nations, operating across six sites, in Heidelberg (HQ), Barcelona, Hinxton near Cambridge, Hamburg, Grenoble and Rome. Our mission is to offer vital services in training scientists, students and visitors at all levels; to develop new instruments and methods in the life sciences and actively engage in technology transfer activities, and to integrate European life science research.