Title: The role of gut-liver axis in Amanita species mushroom poisoning (NCN/SONATA)

Supervisor: Dr Aleksandra A Kołodziejczyk
Institute: International Institute of Molecular and Cell Biology in Warsaw
Laboratory: Laboratory of Cellular Genomics
www: https://olab.com.pl/ https://shorturl.at/JNT69

Project description:
Death cap Amanita phalloides poisoning is a life-threatening condition, with treatment options limited to supportive care and liver transplantation. Amanita phalloides produces three classes of peptide toxins: amatoxins, phallotoxins, and virotoxins. The most studied and believed to be the deadliest of these molecules is bicyclic peptide α-amanitin.
Due to close anatomical connection gut microbiota may act on the liver through several mechanisms including production of functional metabolites and degradation of ingested molecules, thus regulating what is absorbed into portal circulation and directly transported to the liver. The role of gut microbiota has been demonstrated in several liver diseases including liver cancer and acute liver failure due to paracetamol overdose. Hence, we hypothesize that gut microbes also play role in pathophysiology of liver failure in α-amanitin poisoning. Interestingly, amatoxins are poorly absorbed into the blood, while similar in structure phallotoxins are believed not to be absorbed at all. This suggests that there may be either differential absorption or microbiota are capable of efficient degradation of phallotoxins, but not as efficient of amatoxins, enabling the latter deadly potential. Moreover, in other contexts cyclic peptides were shown to be degraded by bacteria.
The overarching aim of the project is to gain comprehensive understanding of the molecular and cellular mechanisms underlying the pathophysiology of Amanita phalloides poisoning with goal in mind to improve clinical outcomes.

Aim:
The goals of this study are: (1) test for a potential role of microbiota in poisoning, (2) to find bacteria degrading α-amanitin and (3) to characterise mechanisms of cellular responses to Amanita phalloides poisoning in the liver. To address these questions, we will study human tissue explants, and use *in vitro* and *in vivo* models of disease.
In this project you will learn – advanced genomics (single cell RNAseq, metagenomics), mammalian cell cultures, mouse models of liver failure, and advanced microbiological techniques such as anaerobic bacteria culturing.

Requirements:
- MSc degree in biology, biotechnology, biochemistry, genetics, medicine or related field
- Knowledge of molecular and cell biology
- Proficiency in written and spoken English
- Excellent interpersonal skills, initiative, good work organization, good collaboration skills
- Hands-on experience in laboratory work
- Prior experience in following techniques will be an advantage (but not prerequisite):
    a) sequencing libraries generation (Illumina, RNAseq, single cell genomics, metagenomics)
    b) cell culture (cell lines, organoids, CRISPR-based cell line modification techniques)
    c) microbiology (culturing bacterial isolates, phenotyping, working anaerobically)
    d) working with mice
    e) FACS, cell sorting
- This is a mainly ‘wet-lab’ position, however experience in sequencing data analysis will be a plus

Number of positions available: 1

Contact: akolodziejczyk@iimcb.gov.pl

The application system will be activated from July 29, 2023 to August 11, 2023