

Title: The role of gut-liver axis in Amanita species mushroom poisoning

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 toxins: amatoxins, phallotoxins, and virotoxins. The most studied and believed to be the deadliest of these molecules is α -amanitin, which is very resistant to cooking and freezing. As a result of mistaken identification of the mushroom, consumption of a meal containing Death cap results in profound liver damage, by halting transcription of RNA which leads to cell death and inability to regenerate.

In the body, toxins from the mushroom enter from the stomach into the intestine, and then together with nutrients they go to the liver, which is the first organ in the body that receives nutrient rich blood directly from the intestine. Liver functions as a filter for molecules that come from the intestine, which makes it particularly affected by the toxin.

Food, on its path to the blood, encounters gut microbiota. This term denotes populations of bacteria, fungi, protozoa, and viruses that live inside the intestine. These microbes are important for human health and have several roles including instruction of immune system and aiding digestion of indigestible molecules such as fibers. The microbiome (collective of all genomes of the microbiota) carries several magnitudes of more genes than human, and hence has capabilities to degrade or produce molecules that humans cannot.

Interestingly, microbiota was shown by us and others to play a role in several liver diseases including liver cancer and acute liver failure due to paracetamol overdose. Hence, we hypothesize that in case of Death cap poisoning, they also may play a role.

In this study we plan to test whether microbiota affects the extent of the liver damage and what are the mechanisms behind it.

To sum up, the overarching aim of the project is to gain comprehensive understanding of the mechanisms underlying the pathophysiology of Death cap poisoning with goal in mind to improve clinical outcomes.