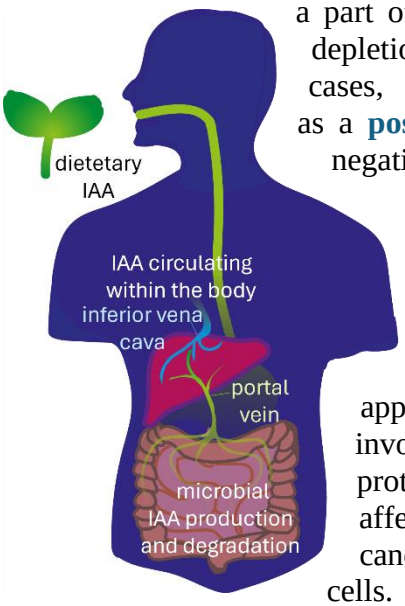
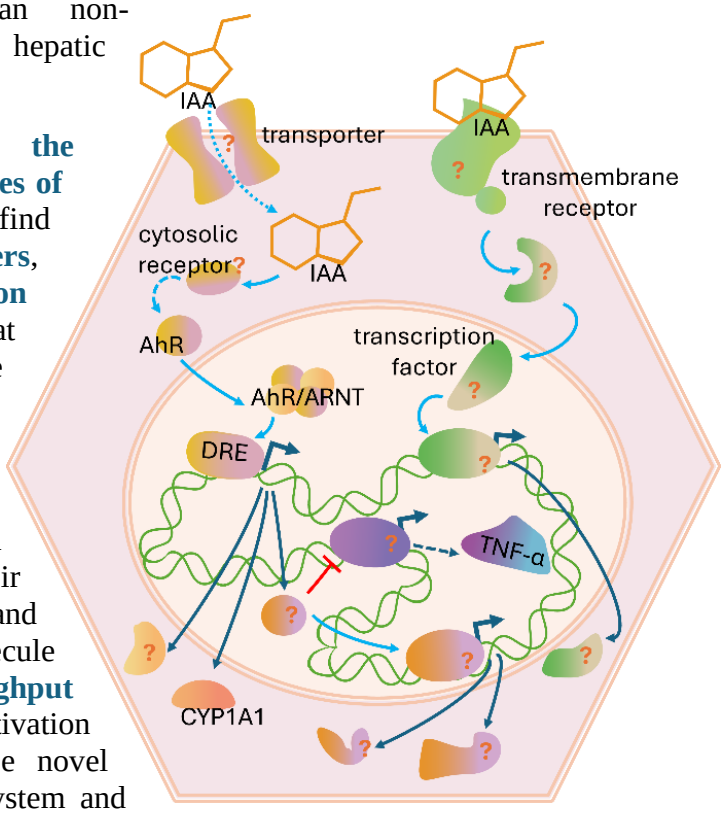
Decoding the molecular mechanisms of indole-3-acetic acid influence on liver cells

Indole-3-acetic acid (IAA, I3A, 3-IAA) is a tryptophan derivative. It serves as one of the most important plant hormones as an auxin. It is produced by plants, archaea, bacteria, and fungi. Humans and animals cannot produce it, but they obtain it from food and their gut microbiota.

While IAA's effect on plants has been studied profoundly since its discovery one hundred years ago, less is known about how it affects humans and animals. In some publications, IAA is seen as a part of the blood and fecal **metabolome of healthy subjects**, and its depletion is associated with a high-fat diet or ethanol binging. In other cases, such as uremia, the prevalent high levels of IAA are seen as a **possibly toxic** factor, with a low understanding of has a positive, negative, or neutral effect on the disease.



Animal studies have shown, that IAA supplemented, injected, or made by introduced microbes **altered the liver disease outcomes**. Many publications leave the question of the mechanism unknown, while others try to explain focusing on a few pathways highlighted already for other tryptophan metabolites. This approach has no chance to picture a holistic view of all processes involved in IAA liver cell response. To this day, no transcriptomic nor proteomic studies have been made to address how this compound affects human non-cancerous hepatic cells.



In my research, I will **describe the mechanisms** that happen in **various types of liver cells** upon IAA treatment. I aim to find the **transmembrane transporters**, **receptors**, enzymes and **transcription factors** involved in its action. With that information, it will be possible to create treatments for patients with hepatic diseases aiming to raise or lower IAA levels.

I propose studying the IAA response in liver cells by investigating their **transcriptome**, looking for crucial, and probably, never assigned to this molecule **signaling pathways,** and **high-throughput screening** for genes necessary for their activation and transduction. For this, I will use novel methods utilizing the **CRISPR-Cas9** system and **next-generation sequencing**. This data-driven approach will lead to discoveries beyond the hypotheses possible today.