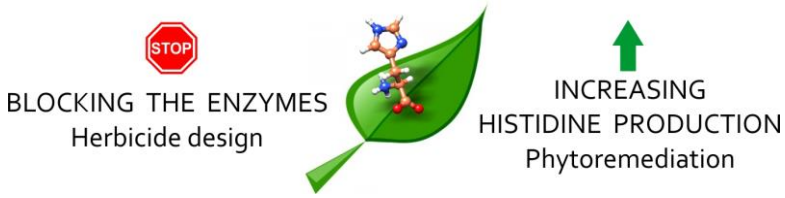
Histidine Biosynthetic Pathway in Plants: Structural and Functional Studies as a Framework for the Design of Inhibitors and Activators

Plants are vital to life on Earth. Either directly or indirectly they are a major source of nutrition for heterotrophic organisms, including humans. This is because plants are autotrophs, able to biosynthesize the entire landscape of the twenty amino acids that occur in proteins. Plant biosynthetic pathways of the essential amino acids are particularly important, as they contain unique enzymes that do not occur in animals. This project is focused on the plant histidine biosynthetic pathway. Unlike the corresponding route of bacteria, which is targeted in antibiotic design, the plant pathway has been rather neglected by research. This is a missed opportunity because the plant histidine biosynthetic pathway appears as a good target for herbicide discovery. Rising herbicide resistance is becoming a serious threat to global agriculture, and changes in the climate will likely make the situation worse. Therefore, research that may open new possibilities and guide herbicide discovery—such as this project—is much needed. The plant histidine biosynthesis pathway has yet another application, this time related to increasing the cellular histidine concentration. Such plants could be used for phytoremediation of heavy metal contaminated soil because elevated free histidine pool rises, e.g., nickel tolerance.



However, in order to rationally tackle, impact, and exploit the pathway we need to fully understand its enzymes at a molecular level. Such a degree of details is brought by macromolecular crystallography, a method second to none in revealing of enzyme structures. Currently, structural information regarding the pathway enzymes is limited, which “inhibits” discoveries. By using crystallography, complemented with biochemical, biophysical, and computational methods, this project will be a milestone in our understanding of the plant histidine biosynthetic pathway. It is expected that the much-needed results will guide future inventions which will secure sustainability of this project.