Antimicrobial resistance (AMR) has emerged as one of the leading public health threats of the 21st century. As a result of drug resistance, antibiotics and other antimicrobial medicines become ineffective and infections become increasingly difficult or even impossible to treat. Fearfully, researchers claimed that AMR in bacteria caused an estimated **1.27 million deaths in 2019**. The review on Antimicrobial Resistance, commissioned by the UK Government, argued that AMR could kill **10 million people per year by 2050**, thus I hope everyone could agree that the spread of AMR is an **urgent issue requiring a scientific plan** to implement.

Transition metals are significant for the survival of all organisms. Pathogens have developed highly efficient transport systems, which rely on (i) **chaperones** – metal chelating molecules presented in the microorganism in order to efficiently bind a metal ions, and (ii) **transmembrane transporters (importer and exporter)** – interacting with specific chaperones and able to transport metal ions into the periplasm and cytoplasm. Effective acquisition of metal ions is crucial for the **survival and virulence** of many pathogens, thus **maintaining metal homeostasis** is a critical process that must be precisely coordinated by them. To achieve this, bacteria need to use numerous of diverse metal uptake and efflux systems. **Understanding a novel metal-acquisition mechanisms in microbes** will make a significant contribution to the development and design of **new therapeutics against resistant pathogens**, which could be a good alternative for commonly used drugs.

The aim of the project is to **understand and fully characterize the bioinorganic chemistry of biologically significant copper transporters in bacteria -** to elucidate different binding sites, thermodynamic features and structural details. There is a **significant gap** in our understanding of copper importing systems in many prokaryotic organisms. I decided to start from **the prediction and synthesis** of metal binding sites in bacterial transporters and then perform a **detailed thermodynamic characteristics** of their copper complexes defining metal binding donors and complex geometries. In parallel, **the stability comparison** between copper and zinc complexes formed by potential zinc binding copper transporters will be also investigated. I will move into the further steps of the proposed project concerning **NMR structure analysis** of copper transporters complexes and **ternary chaperone-copper-transporter interactions**. In the last step of the project I will focus on **understanding antibiotic-chaperone interactions** and their potential antimicrobial activities.

The impact of the results of this project will be a large input into the fascinating research field of the not yet well explored bioinorganic chemistry of metal binding sites for novel copper chaperones in bacteria. There is a significant limitation in our understanding of bacterial copper transport. The challenges that we will face are: (i) Which are the precise copper binding sites? (ii) Can they be blocked with other metal ions, such as zinc? (iii) Can we use chaperones as targeting molecules, to which we can attach conventional antibiotics which could then in such a way be specifically delivered to a precise bacterial copper transporter? My ambition is to clarify different binding sites, thermodynamical features and structural details, which, what is even more important, will really **be a milestone in understanding the mechanism of metal pathway** and finally may help to find new, specific antimicrobial drugs.