

The increasing occurrence of antibiotic-resistant bacteria combined with the slow discovery of new antibiotics will lead to an increase in deaths caused by bacterial infections. The estimated global number of annual deaths caused by drug-resistant infections is 10 million by 2050. Currently, antibiotic-resistant infections cause over 50,000 deaths annually in Europe. In 15 European countries over 10% of bloodstream *Staphylococcus aureus* infections are caused by methicillin-resistant strains (MRSA), with resistance rates close to 50% in several of these countries. The increasing occurrence of antibiotic-resistant bacteria will threaten public health not only by the increasing number of deadly infections. Lack of effective antimicrobial agents undermines all treatments that rely heavily on antibiotics, such as surgeries, organ transplants, or cancer therapies. Thus, bacterial infections are becoming a major threat to our modern health systems.

Despite immense effort devoted to the development of new antitumor therapies, tumors remain a major cause of death affecting millions of people. In many cases, chemotherapy is the first line of defense, but antitumor drugs present an insufficient selectivity and as a consequence, they cause many deleterious effects. Most antitumor drugs are designed to attack rapidly dividing tumor cells, which results in side-effects in nonmalignant tissues, where cells divide at the same rate (e.g., bone marrow, gastrointestinal tract, and hair follicles). Furthermore, many tumor cells developed resistance to antitumor drugs, which include transporting drugs outside of the cell, the ability to repair DNA damage, increased tolerance to stress, and increased expression of drug detoxifying enzymes

Antimicrobial peptides (AMPs) present a possible alternative for conventional antibiotics and antitumor drugs because selectivity and mechanism of action of AMPs are based on different molecular principles. Indeed, many AMPs have broad-spectrum antibacterial and antifungal activity as well as antiviral and antitumor activity, while having low toxicity.

However, natural AMPs show many limitations in their use as antibacterial or antitumor drugs, such as low stability due to rapid metabolism and proteolytic degradation, immunogenicity, and poor pharmacodynamic and pharmacokinetic properties. To overcome this obstacle, conjugates of short cationic peptides and lipophilic moieties are developed, which show potent antimicrobial or antitumor activity. These conjugates share basic structural principles with natural AMPs as they have a net positive charge and amphipathic structure.

The aim of this project is to harness extraordinary properties of metallacarboranes coupled with short cationic peptides to obtain potent antibacterial and/or antitumor conjugates.