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**Title:** Synthesis and characterization of antimicrobial peptides

**Objectives:**

Peptides represent a promising alternative to antibiotics due to their low rate of acquired resistance, even though they are generally less stable than organic compounds. This project therefore focuses on the design of antibacterial peptides with improved stability and on the evaluation of their biological activity.

**Educational interests and targeted skills:**

This internship, positioned at the interface of chemistry and biology, will provide exposure to bioorganic chemistry, particularly peptide synthesis, along with associated characterization techniques such as liquid chromatography and mass spectrometry.

**Summary:**

Antibiotic resistance, a major global public health concern, was associated with approximately 4.7 million deaths in 2021. This phenomenon, defined as the ability of bacteria to develop survival mechanisms, is driven in particular by the widespread and often inappropriate use of antibiotics.

As part of a previous project focusing on the physicochemical properties of natural peptides, we synthesized antimicrobial peptides that demonstrated highly promising results on bacteria cells compared to currently available antimicrobial therapies. Building on these results, our objective is to design novel peptide derivatives through chemical modifications aimed at enhancing their biological activity, specificity, and stability. Structural optimization will be guided by alanine scanning and D-amino acid scanning to identify and eliminate potential cleavage sites, particularly those targeted by endopeptidases, and to pinpoint key functional groups involved in interactions with the target of interest. In this context, increased stability could be achieved through retro-inverso modification. Peptides of interest will be thoroughly characterized using circular dichroism spectroscopy and nuclear magnetic resonance (NMR) to elucidate their secondary structure, thereby providing insights into their potential structure–activity relationships.

**Approaches and materials used:**

Peptides will be synthesized both manually and using an automated synthesizer via Solid Phase Peptide Synthesis (SPPS). They will be analyzed and purified using liquid chromatography and mass spectrometry. Their secondary structures will be characterized through circular dichroism and NMR spectroscopy.

**Desired areas of expertise for the candidate:**

The candidate will have expertise in organic synthesis, with a particular focus on biomolecule synthesis, coupled with a robust understanding of fundamental biological concepts. Experience in integrating chemical and biological approaches will be highly valued.