SMART ANTIMICROBIAL HYDROGELS BASED ON SELF-ASSEMBLIES OF PEPTIDES

DIRECTEUR DE THESE : PHILIPPE LAVALLE
INSERM / CNRS / UNIVERSITE DE STRASBOURG, UMR_S 1121, BIOMATERIAUX ET BIOINGENIERIE, CRBS 1 RUE BOECKEL, 67000 STRASBOURG
TEL : 03 68 85 30 61 ; E-MAIL : philippe.lavalle@inserm.fr

The resurgence of antibiotic-resistant bacterial strains is becoming a major problem, especially in cases of nosocomial infections. More than 50% of these nosocomial infections are linked to medical devices such as implants, catheters, catheters, etc. Thus, there is an urgent need to develop new alternative strategies to conventional antibiotics and innovative antimicrobial materials. Moreover, chronic wounds, and more specifically diabetic wounds, are prone to infections and lead to major complications.

Our recent work on polypeptide-based coatings, including polyarginine (1-4), has shown the effectiveness of these molecules. However, at present, there is no specificity against only pathogenic bacteria and fungi. In this project, an entirely new family of smart antibacterial hydrogels. These hydrogels will provide antimicrobial activity exclusively in the presence of one specific microbial strains. The activity will based on the local production of antimicrobial peptides and in addition to their self-asembly ability forming locally a supramolecular network arounf the bacteria or fungi (5). It will result from the interaction of the peptides with the bacterial membrane and not to their action onto the bacterial metabolism as do conventional antibiotics. This will prevent bacterial resistance. Moreover, the peptide self-assembly will isolate the bacteria one from each other and thus will prevent biofilm formation and will facilitate their erradication. The specificity of the action will be obtained by tranforming precursor peptides into active self-assembling peptides through stimuli produce by a specific bacteria. The advantage of this specific activation of the targeted pathogens will be the preservation of the microbiota involved in many biological function. These innovative hydrogels will be a local alternative to systemic antibiotherapy. They will be used in many applications and could be incorporated in bandages or directly brought in contact with chronic wounds in a injectable form.

This work will be performed at the Biomaterials and Bioengineering lab (https://www.biomaterials-bioengineering.com) in close collaboration with clinicians and medical device companies.

1. Lebaudy E., Petit L., Nominé Y., Heurtault B., Ben Hadj Kaddour I., Senger B., Rodon Fores J., Vrana N. E., Barbault F., Lavalle P., “The antibacterial properties of branched peptides based on poly(l-arginine): In vitro antibacterial evaluation and molecular dynamic simulations”, Eur. J. Med. Chem., 2024, 268, 116224.
2. Knopf-Marques H., et al. "Multifunctional polymeric implant coatings based on gelatin, hyaluronic acid derivative and chain length-controlled poly(arginine)”, Mat. Sci. Engineer. C, 104, 109898, 2019.
3. Mutschler A., et al. "Nature of the polyanion governs the antimicrobial properties of poly(arginine)/polyanion multilayer films", Chem. Mater., 2017, 29, 3195.
4. Patent EP3962543B1 “Polypeptide and hyaluronic acid coatings”, Lavalle P., Calligaro C., Gribova V., Tallet L., Vrana E.
5. Muller C. et al. “Localized Enzyme-Assisted Self-Assembly of low molecular weight hydrogelators. Mechanism, applications and perspectives“, Adv. Coll. Int. Sci, 2022, 102660.