# NANOCARRIERS FOR SPECIFIC GUT FLORA MODULATION

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Nanoparticles can have a huge impact on a wide range of bio-applications, from food to pharmaceuticals. One of the most studied kind of nanoparticles in the last decade is represented by oil-in-water (O/W) emulsions. They consist in small oil droplets dispersed in an aqueous system, and can be found in many formulations, either in food or pharmaceutic products. Their compositions make them biodegradable and, in principle, nontoxic. However they are usually unstable systems, because there is a thermodynamic driven phase separation. Polymer coating is a known strategy helpful in preventing this process to occur.

In my research group we can count on a proprietary technology able to provide ultra-stable nanoemulsions (size ranging from 90 to 120 nm) meaning that they can keep their size distribution constant for >> 1 year.

These nanoemulsion-based carriers can be functionalized in order to express some peptidic sequences on the external wall, giving them the opportunity of targeting specific molecules.
Peptidic sequences can be manually produced by a technique named Solid-Phase Peptide Synthesis (SPPS), based on the stepwise assembly of peptides from amino acid precursors. In particular, Fmoc chemistry seems to be the best procedure to follow in order to achieve a faster and safer synthesis. In fact, this method can minimize side reactions in the peptidic chain, has less harsh cleavage conditions once the chain is concluded and has rigorous laboratory protocols.

Finally, the so-obtained peptide can be purified through the Reversed-Phase High-Performance Liquid Chromatography (RP-HPLC) and then added on the nanoemulsion surface.

The human gut is an ecosystem comprising trillions of microbes interacting with the host. The composition of the microbiota and their interactions play roles in different biological processes and in the development of human diseases, such as Chron's disease, inflammatory bowel disease, cardiovascular diseases, influencing even the brain through the brain-gut axis. Close relationships between dietary modifications, microbiota composition and health status have been established in the last years, but targeting a specific gut flora bacteria is still hard to do.

What has been done is to do fecal transplant from a healthy donor or to use prebiotics in order to stimulate microbioma growth, but little is known on how to modulate a single bacteria strain, naturally present in the human gut, i.e., to promote or inhibit its proliferation.

This PhD project's aim is to modulate the gut flora bacteria through the use of nanocarriers in the form of O/W nanoemulsions able to recognize the bacteria using specific peptides, either by promoting or, most importantly, inhibiting their growth, in order to improve the patient health status. The experiments will be performed in both static and dynamic conditions (gut-on-chip with the addition of bacteria and digestive juice chambers) in order to have a better view on the whole system, approaching the human in-vivo conditions.

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