A synthetic biology magnetic toolkit for detecting bacteria

Supervisory team:
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Project description:
Detection and identification of bacteria quickly and at low cost brings benefits in both healthcare and wider public health settings. In the former case, identifying infecting organisms in patient samples such as urine or sputum will permit practitioners to make informed decisions about prescribing antibiotics, so slowing the spread of antimicrobial resistance (AMR) by reducing unnecessary or inappropriate antibiotic use, and improving patient outcomes by ensuring timely use of effective treatments. In the latter, bacterial identification in water sources can reduce the spread of infections by assuring the safety of water for human consumption or recreational use. One method to identify, and potentially remove, bacteria from liquid samples involves magnetic tagging followed by capture on e.g. magnetic beads or similar supports. Achieving this in turn requires the ability to label bacteria with magnetic nanoparticles with high affinity, and ideally species specificity.

This project seeks to achieve this goal using the biological iron storage protein ferritin as the basis for magnetic nanoparticles that can be decorated with specific receptors, in particular sugars, known to bind target bacteria with high affinity. The goal of the project is to produce such particles and evaluate their binding to a panel of target bacteria. Bacterial ferritins are formed from a single protein chain that self-assembles into a 24-subunit cage-like structure containing a central iron core. The student will first develop methods for generating ferritin-based magnetic nanoparticles by expressing ferritins from a range of bacterial species in recombinant E. coli; and either reconstituting purified proteins in the presence of iron in vitro, or manipulating bacterial growth conditions (e.g. through iron supplementation) to generate magnetic particles within the bacterial cell. Assembly, iron content and magnetic properties of the recombinant nanoparticles will be assessed by a range of biophysical methods. The student will then trial methods for tagging ferritin particles with bacteria-specific ligands, expressing ferritins as fusions with either peptide-based systems (SpyCatcher-SpyTag) that can be modified with molecules such as sugars (glycans) known to be bound by bacterial surface receptors, or the adhesin proteins used by bacteriophages to attach to their specific bacterial targets. Demonstrating assembly of magnetic nanoparticles based on ferritin fusions will then enable testing for adhesion to, and capture of, target bacteria under conditions mimicking those in patient or environmental (water) samples. Achieving this goal will then justify future efforts, beyond the anticipated lifetime of the project, to develop this system for practical implementation.

Our aim as the SWBio DTP is to support students from a range of backgrounds and circumstances. Where needed, we will work with you to take into consideration reasonable project adaptations (for example to support caring responsibilities, disabilities, other significant personal circumstances) as well as flexible working and part-time study requests, to enable greater access to a PhD. All our supervisors support us with this aim, so please feel comfortable in discussing further with the listed PhD project supervisor to see what is feasible.