**pH-Responsive Micelles for Controlled Enzyme Inhibitor Release**

In this project, we will design pH-repsonsive micelles, loaded with the anticancer agent SAHA, to target effective drug deliver at the tumour site.

**Names of Supervisors:**

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**Themes**: polymer synthesis; micelle synthesis; molecular enzyme inhibitor synthesis; polymer and micelle characterization; pH-response analysis; enzyme inhibition assays; in vitro cell viability assays.

**Background**

The histone-deacetylase enzymes (HDACs) are an important class of molecular targets in cancer therapy. SAHA is a HDAC inhibitor, which is known to have some off-target effects, such as genotoxicity. As such, it would be desirable to design delivery systems for SAHA that lead to active molecule only at the tumour. To deliver the drug selectively to the tumour, we can exploit its **lower pH** compared to the typical extracellular environment.

pH-responsive micelles have been reported based on hydrophobic polyurethane cores with hydrogen bonding carbamate groups and hydrophilic poly(ethylene glycol) groups. In water, these species will self-assemble into micelles. Lowering the pH leads to protonation of the carbamates and breakdown of the micelles, which then release their cargo.3

**Project Details**

In this project, we will synthesis and analyse pH-responsive micelles that give controlled release of HDAC inhibitors. The project will involve **Synthetic Chemistry** (polymer synthesis and the synthesis of SAHA and other novel HDAC inhibitors), **Micelle Analysis** (fluorescence assays, polymer characterization by SEC, DLS, SEM and TEM, release assays) and **Biological Assays** (HDAC enzyme activity assays and *in vitro* anticancer assays). As shown below, several components of the polymer can be tuned to improve pH response and biological properties.



Beyond the practical training, the student on this project will join a dynamic research team and develop skills in collaboration, teamwork and communication. For more details, contact james.walton@durham.ac.uk and clare.mahon@durham.ac.uk