# Structure-function studies of the bacterial plasmid defence system Wadjet

**Supervisory team:**
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**Project description:**
Microbes are found in many environments, and in almost all cases are under constant attack from bacteriophages and other selfish genetic elements. To avoid infection, bacteria have evolved a wide range of defence mechanisms. These different systems are found clustered on the genome in what are called “defence islands”. The defence systems include the well-know restriction enzymes and CRISPR-Cas9, which have been exploited for molecular biology and gene editing, respectively. Yet there are many other uncharacterised systems within the defence islands that may provide yet more tools for scientists to exploit. This project aims to use biophysical analysis and structural biology to explore the mechanism of one such system, named after the Egyptian goddess Wadjet.

The Wadjet system prevents bacterial transformation by plasmids. It comprises four genes: jetA, jetB, JetC and JetD. jetABC encode gene products that are related at a sequence level to bacterial condensins. Condensins are widespread across all organisms, and are ATP-dependent molecular machines that help to regulate the process of genome segregation during cell division. Their exact mechanisms and roles are still debated. They form large protein complexes that use ATP hydrolysis to drive large-scale changes in DNA conformation, including tethering DNA together, or actively extruding DNA loops as molecular motors. In this collaborative project between the Szczelkun and Berger-Schaffitzel labs, you will determine the overall structure of the Wadjet JetABCD complex, show how it interacts with DNA, and determine the role for ATP hydrolysis. We propose that DNA capture or loop extrusion blocks plasmid replication. These activities will be directly distinguished and measured in real time using a single molecule magnetic tweezers assay.