Exploring the outer limits of ATP-dependent DNA ligase sequence space. The recently discovered class of crAssphages.

In all forms of life, essential enzymes called DNA ligases play a key role in joining strands of DNA whenever new DNA is being made or when damaged DNA is being repaired. There are two classes of DNA ligases, which use ATP or NAD as a cofactor. As they enable recombinant DNA technologies, there are a variety of commercially available ligases with different properties and preferential use in specific methods. Highly divergent organisms occupying diverse ecological niches are a rich source of novel enzyme activities for the biotech industry. Biotechnologies are promising means of tackling global issues and they attracted even more attention over the course of the global pandemic.

This curiosity-driven project supervised by Dr Stuart MacNeill would explore the properties of two (with some more luck even four) unstudied ATP-dependent DNA ligases with the potential to improve the efficiency of existing recombinant DNA technologies and inspire novel tools. The enzymes, derived from crAssphages, the most abundant phages in the human gut, will be expressed in recombinant form from synthetic genes and purified. This will be followed by investigation of their activity under varying conditions and on different substrates. The commercial potential of the novel enzymes will be explored through contact with biotech companies.

The experimental work will be supplemented with a phylogenetic reconstruction of the DNA ligase distribution across different organisms under the supervision of Dr Carolin Kosiol. This aspect of the research might give an insight into the factors acting on the evolution of DNA ligases and identify possible events of horizontal gene transfer involving crAssphages.