Nottingham BBSRC DLA Programme : (NE)B-Family DNA polymerases for Biotechnology

University of Nottingham, School of Life Sciences

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About

Thanks to £14m of funding awarded by the Biotechnology and Biological Sciences Research Council (BBSRC), the University of Nottingham and Nottingham Trent in partnership with the National Biofilms Innovation Centre (NBIC) are offering fully funded innovative four-year cohort-based training in frontier science.

Postgraduate researchers will be recruited to a research cluster within each of the overarching research areas:

- Alternative and Emerging Protein sources for Sustainable food and feed (Sustainable Agriculture and Food Security) - Cluster lead Professor John Brameld
- RIC@N-DLA: Multiscale RNA Science from mechanisms to applications (Bioscience for Human Health) – Cluster lead Dr Federico Dajas-Bailador
- Future Genomes Across Life – Engineering biology for sustainability and innovation (Biotechnology for Sustainable Growth) – Cluster lead Professor Thorsten Allers

Project description

We invite applications for a BBSRC fully funded CASE studentship to investigate (NE)B-Family DNA polymerases for Biotechnology. This sits under our Biotechnology for Sustainable Growth theme and is offered through partnership with New England Biolabs.

Archaeal family B DNA polymerases are a cornerstone of biotechnology. Enzymes such as Vent, Deep Vent, Phusion, and Q5 are family B DNA polymerases (PolB) that originate from Archaea – they have been developed by New England Biolabs (NEB) for PCR amplification and next-generation DNA sequencing applications. Such enzymes require robust strand displacement activities, which are found in PolB but not PolD, the D-family DNA polymerase exclusive to Archaea. However, PolB lacks any specific motif to associate with the replicative helicase complex – such a motif is found in PolD and has to potential to develop a new class of DNA polymerase for biotechnology.

Archaea encode two replicative DNA polymerases. PolB is a family B polymerase with similarity to eukaryotic Pol alpha, its catalytic core has a Klenow fold found in all B family polymerases. PolD belongs to the D family and is exclusive to Archaea, its catalytic core is homologous to the double-psi beta-barrel motif found in RNA polymerases. PolB has 3'–5' exonuclease and polymerase activities in one polypeptide, but PolD separates them in the DP1 and DP2 subunits, respectively. The DP1 exonuclease subunit of PolD is a structural homolog of subunit 2 of eukaryotic replicative DNA polymerase, which facilitates a tight association of PolD to the replicative helicase complex and tethers DNA polymerase to the replisome. However, unlike PolB, PolD is not capable of the robust strand displacement activity necessary for lagging strand synthesis.

An ideal polymerase for biotechnological applications would feature the robust strand displacement activity of PolB, and an association with the replicative helicase found in the DP1

subunit of PolD; such an association with the replicative helicase may provide enhanced processivity in DNA synthesis reactions on complex templates. We have constructed such a hybrid DNA polymerase in the halophilic archaeon Haloferax volcanii, the most tractable species for archaeal genetics. H. volcanii strains where PolB is fused to the N-terminal helicase-binding domain of DP1 are viable and exhibit near-wild type growth. In parallel, we have established that in the absence of replication origins, DNA synthesis in H. volcanii is initiated by homologous recombination, and that recombination-dependent replication uses PolD while origin-dependent replication uses PolB.

The goal of the PhD project is to develop a new class of DNA polymerase for biotechnology, while providing functional insights into assembly of the archaeal DNA replication machinery and the unique mechanisms of DNA replication in Archaea.

Why choose this project?

The lab of Thorsten Allers works on DNA replication, recombination, and repair in Archaea. We use Haloferax volcanii as a model for archaeal genetics – this species is easy to grow and has a wide range of genetic tools, most of which have been developed in our lab. H. volcanii is ideal to investigate the rules of life and to develop new tools for biotechnology. In initial phase of the project, the student will acquire experimental skills in microbial genetics, molecular biology, and bioinformatics. The project will involve the generation of plasmids and strains to carry out genetic screens of H. volcanii PolB and PolD variants. Strains with polymerase variants will be tested for the efficiency and accuracy of DNA synthesis in vivo, using microbiological techniques including growth competition and mutation accumulation assays, microscopy and flow cytometry, pulsed-field gel electrophoresis, and genomic technologies including nanopore DNA sequencing.

The lab of Ed Bolt investigates the biochemistry of DNA processing enzymes that are required for DNA repair, homologous recombination, replication and CRISPR immunity systems. These include DNA polymerases, DNA/RNA helicases, and RNA/DNA nucleases. The Bolt group has a track record of expertise in understanding protein mechanism, and how these translate into their cellular behaviour. Bolt has studied DNA processing in CRISPR-Cas systems since 2007 and has expertise in CRISPR/Cas9 triggered genome editing in human cells. His lab is equipped with FPLC systems for protein purification and analysis, and equipment for protein-nucleic acid processing assays in real time kinetics (e.g., by anisotropy and FRET in a FLUOstar Omega), and end-point analyses in gel systems. Using these analyses, the student will gain experience of methods within a project integrating genetics, biochemistry and in-cell methods.

New England Biolabs (NEB) is world-renowned biotechnology company that makes and supplies enzymes, reagents, and tools used in molecular biology and genetic research. Headquartered in Ipswich MA, USA, and having subsidiaries world-wide including Hitchin, UK, NEB not only produces a wide variety of molecular biology reagents but also houses and funds a basic research department. The lab of Kelly Zatopek in the research department of NEB studies nucleic acid maintenance in extremophilic archaea to understand the mechanisms these organisms utilize to repair, remove or recycle DNA.

Our expertise is in in vitro biochemical and structural characterization of archaeal enzymes, including DNA polymerases such as PolB and PolD. In later phases of the project, the student will express, purify and biochemically characterize the new class of archaeal DNA polymerases to understand their catalytic efficiency, fidelity and association with replisome components.

Further, the student will apply these enzymes in DNA amplification workflows to understand their ability to carry-out high fidelity, processive DNA amplification.

For informal enquiries about the project please contact Professor Thorsten Allers

Requirements

Applications are invited from candidates with backgrounds in Bioscience, Biochemistry, Microbiology, Biotechnology, Chemistry, Chemical/Biochemical/Process Engineering, Environmental Science, Pharmacy, Computer Science, Maths or related disciplines who have/expect to graduate with a first/upper-second UK honours degree, or equivalent qualifications gained outside the UK.

Applications are also welcome from candidates with a 2:2 undergraduate degree or lower, who hold a Masters degree in a relevant area or three or more years of full-time work experience relevant to your undergraduate degree, or to the PhD projects you are applying for.

Funding details

Funding is available for four years from October 2026. The award covers tuition fees at the UK rate, plus an annual stipend. The UK Research and Innovation (UKRI) stipend is tax free and was set at £20,780 for 2025/26 entry.

UK and International candidates are eligible to apply.