The cellular and molecular basis of ageing in bacteria

Supervisory team:
Main supervisor: Dr Tobias Bergmiller (University of Exeter)
Second supervisor: Dr Bertram Daum (University of Exeter)
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Host institution: University of Exeter (Streatham/St Luke's)

Project description:

Ageing or senescence is the inevitable process leading to deterioration of biological function with increased age. Entropy and macromolecular damage are regarded as the drivers that shapes ageing and life span in many organisms. In general, our understanding of molecular ageing processes remains highly incomplete and restricted to model organisms such as Drosophila melanogaster, Caenorhabditis elegans or Saccharomyces cerevisiae.

Until recently, bacteria had been overlooked in ageing research, mostly because they were supposed to be immortal due to the absence of a complex body plan or differentiation. Research in recent years and work in the Bergmiller lab have shown that Escherichia coli can be distinguished into ageing mother cells and rejuvenated offspring at the level of the single cell. Old mother cells can display hallmarks of ageing and genetic limitation of life span (Boehm et al., PLoS Genetics 2016), and increased fitness in environments with antibiotics (Bergmiller et al., Science 2017). Nevertheless, while single-cell microfluidic techniques such as “mother machines” have greatly advanced our understanding of ageing in bacteria, the molecular mechanisms of ageing and the presence of molecular markers of ageing in bacteria remain elusive.

In this interdisciplinary PhD studentship, you will use a range of methods spanning bacterial genetics, biochemistry, microfluidics and cryo-electron microscopy to study the consequences of ageing in bacteria across scales on the molecular, cellular and population level. You will use a combination of single-cell microfluidics and novel assays to investigate links between population fitness and mother cell age, and the genetic determinants of replicative life span. Using single particle cryoEM and cryo Electron Tomography, you will study the impact of ageing on the structure and function of molecular machines central to the cell’s fitness and survival: The ribosome and the ATP synthase. By combining population, single cell and structural techniques, you will investigate the impact of ribosome and ATP-synthase targeted antibiotics on aging cells to gain a wider understanding of how antibiotic strategies can be engineered to have a greater effect on bacterial populations.

The successful candidate will be supervised by Dr. Tobias Bergmiller and Dr. Bertram Daum, both at the University of Exeter/Living Systems Institute. Both combine a range of complementary skills such as molecular biology, quantitative single-cell microbiology and cryo-electron microscopy and tomography. Prof. Paul Verkade from the University of Bristol will act as external supervisor to complement the project with expert skills and infrastructure in correlative light and electron microscopy (CLEM).