

The Mechanisms and Evolution of Senescence in Microbes

Supervisory team:

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Project description:

Senescence, the accumulation of biomolecular damage leading to age-related declines in reproduction and survival, is pervasive across the animal kingdom and has become a key focus of research in evolutionary biology and biomedicine. It has long been thought that unicellular organisms typically do not senesce, because without a clear germ-soma divide any damage accumulated by one generation would be passed to the next, leading to the progressive deterioration and ultimate extinction of the lineage. However, the advent of high resolution live-imaging techniques that allow researchers to track the life-histories of individual cells and lineages within clonal *E. coli* populations has revealed evidence of clearly structured variation in both reproduction and survival among cells, which is now widely interpreted as evidence that bacteria do senesce (Stewart et al. 2005 PLOS Biology). This discovery has triggered a surge of interest in the possibility of bacterial senescence (Moger-Reischer & Lennon 2019 Nature Reviews Microbiology), both among evolutionary biologists and applied microbiologists.

This project will combine cutting-edge microbiology with experimental evolution to critically assess whether this complex phenotype in *E. coli* does indeed show the key mechanistic and evolutionary hallmarks of senescence. The project will have two main strands. First, as recent work has questioned whether the observed variation in performance actually does arise via damage accumulation (Lapinska et al. 2019 Philosophical Transactions of the Royal Society B), we will couple high resolution live-imaging of dividing cell lineages with novel fluorescent markers that allow us to observe damage occurring in real time, to experimentally test whether the variation arises via damage accumulation or novel alternative mechanisms unrelated to senescence. Second, we will develop evolutionary models of microbial senescence, to investigate whether the true pattern of variation in cellular performance is consistent with what one would expect of senescence. We will then test the key predictions of these models by conducting experimental evolution using *E. coli* populations.

This ambitious project is expected to significantly advance our understanding of senescence in microbes, shed new light on the evolutionary origin of senescence, and yield novel insights relevant to the global effort to combat antimicrobial resistance. The candidate will gain cutting-edge research skills in senescence biology, microbiology, evolutionary modelling and experimental evolution, under the mentorship of a supervisory team with expertise in these areas. They will be based at Exeter's renowned Penryn Campus in Cornwall, collaborating closely with colleagues at Exeter's Streatham campus and in Bristol.