

Senescence, the process of organismic decay with ageing, is a public health challenge and a fascinating evolutionary problem. We have studied ageing mechanisms and discovered ageing-related genes using two different approaches. First, I will present tests of the evolutionary explanations of senescence which postulate that genetic variants with harmful effects in old ages can be tolerated by natural selection, or even favoured by it, provided they foster health at early ages. Second, I will show the results a phylogenetic-based genome-phenome analysis, tracking genes of the primate lineage that have evolved in parallel with changes in the lifespan of different species.

We first studied human genomic diversity linked to disease. Based on data from Genome-Wide Association Studies and focusing on the effects of genetic variants associated with diseases appearing at different periods in life and found that data fit expectations. Namely, we observed higher risk allele frequencies combined with large effect sizes for late-onset diseases; we also detect a significant excess of early-late antagonistically pleiotropic variants which, strikingly, tend to be harboured by ageing-related genes.

We then studied 17 complete genomes in the primate lineage (including humans) to ascertain if there are any genetic changes that can be linked to increases in the lifespan of primate species. We found 25 genes that contain parallel mutations in the primate lineage that might have increased longevity in at least three species. Additionally, we show that some genes present strong correlations between their rates of protein evolutions and longevity-associated traits.