



Genetics, genomics, gene expression and epigenetics in health and disease

Enhanced DNA Damage Response in a Clade of Long-Lived Bats Resolved Using Chromosome-Length Genome Assemblies

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Abstract

Lifespan is one of the most variable traits across the entire tree of life, and especially in mammals. Differences in lifespans between closely-related species provides a promising avenue for discovering novel pro-longevity pathways using evolutionary techniques. Previous studies focused on the evolution of longevity-associated traits, such as DNA damage response, have been hampered by a combination of low-quality genomes, low-phylogenetic coverage, or long evolutionary times, all of which can negatively affect their power to detect genes associated with longevity. In order to comprehensively study the evolution of aging and aging-associated traits in bats, we generated chromosome-level reference genomes and primary cell line libraries from a 10-million-year-old clade of 9 California Myotis species spanning a 3-fold range of lifespans. Increases and decreases in longevity independent of body size have evolved multiple times in this clade, providing a dynamic range which can be studied through functional genomics. Leveraging both genomes and cell lines, we identify several pathways specifically associated with longevity, in addition to other longevity-associated traits such as DNA repair and immunity; and show that these changes are associated with cellular resistance to various forms of chemically-induced DNA damage. These pathways represent new targets for exploration using primary cell cultures, and contribute to our understanding of how both agonistic and antagonistic pleiotropy play a role in the evolution of longevity.

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