Cetaceans' Genomes Unmasking the Secrets Behind Peto's Paradox, Aging and the Evolution of the SWI/SNF Chromatin Remodeling Complex

Stangel, Emily (School: Byram Hills High School)

Despite decades of research, scientists have yet to understand the molecular mechanisms behind aging. Currently, scientists have utilized the thoroughly annotated genomes of model organisms to search for molecular variants in genes related to the prevention of certain diseases closely associated with aging, such as cancer and neurodegenerative disorders (NDDs). Cetaceans, specifically whales, have sparked interest due to their ability to live up to 200 years, with little to no age-related disease incidence. More specifically, mutations in their genes encoding the Switch/Sucrose Non-Fermentable (SWI/SNF) complexes, which aid in chromatin remodeling, are hypothesized to be responsible for the low occurrence of NDDs. In order to determine whether there are evolutionarily beneficial cetacean-specific variants within these genes, a positive selection analysis was conducted. This study is the first to find that the gene SMARCA4 is positively selected within the ancestor of Odontoceti (toothed-whales) (LRT p-value = 0.008879). Further, this mutation occurred millions of years ago in the branch of toothed-whales, thus remaining in the clade’s gene pool and potentially conferring advantages against age-related diseases. Hence, our finding is promising. Since Odontoceti have large and complex mammalian brains, and SMARCA4 is associated with the early development of neurons, our study lays the groundwork for future research on the functionality of this gene and whether it can be used in various gene therapies with regard to human aging and age-related disease suppression.

Awards Won:

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