MUTATION RATE AND LIFESPAN

The relationship between DNA mutations and repair on the one hand and aging and lifespan on the other may seem somewhat intuitive but is nevertheless complex, as expressed, for example, by the Peto paradox (1977). Tumors are mainly due to DNA mutations occurring during DNA replication. If this is true, Peto reasoned, large animals like elephants should be much more prone to cancer and aging than small animals like mice, which are home to far fewer cells, i.e. they undergo fewer cell doublings. But this is not the case. Some recent papers have added important pieces to the puzzle.

Kolora et al. (2021)[1] (see post dated 9 December 21) suggested that the large difference in lifespan between closely related rockfish species could be explained by the difference in DNA repair efficiency; in other words, better repair efficiency, fewer mutations, longer life.

Vincze et al. (2022)[2] reported a zoo survey showing that animals with larger and smaller bodies have a similar risk of dying from cancer.

Now, Cagan et al. (2022)[3] have filled an additional hole in this puzzle. They devised a clever way to measure the mutation rate in different animals. They then tried to correlate their results with different biological indicators. As Gorelick and Naxerova (2022)[4] comment in the related News and Views, "The most striking correlation was with lifespan. Longer-lived animals acquired few mutations every year and shorter-lived animals acquired many mutations, which meant that the total number of mutations at the end of an animal's life was roughly similar across species".

The puzzle isn't solved yet (for example, what about telomere shortening?), but the holes to fill are getting fewer.

1- https://www.science.org/doi/10.1126/science.abg5332
2- https://www.nature.com/articles/s41586-021-04224-5
3- https://www.nature.com/articles/s41586-022-04618-z
4- https://www.nature.com/articles/d41586-022-00976-w