# Understanding the effect of aging on the genome

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Time may be our worst enemy, and aging its most powerful weapon. Our hair turns gray, our strength wanes, and a slew of age-related diseases represent what is happening at the cellular and molecular levels. Aging

affects all the cells in our body's different tissues, and understanding its impact would be of great value in fighting this eternal enemy of all ephemeral life forms.

The key is to first observe and measure. In a paper published in *Cell Reports*, scientists led by Johan Auwerx at EPFL started by asking a simple question: how do the tissues of aging mice differ from those of mice that are mere adults?

To answer the question, the researchers used the multiple techniques to measure the expression of everyone one of the thousands of mouse's genes, and to identify any underlying epigenetic differences. The researchers not only measured different layers of information, but they did it across three different tissues: liver, heart, and muscle.

The data collectively allowed them to define an aging 'footprint' that can serve as a field for investigation. But while many of the known aging manifestations were recovered, different tissues behaved differently.

"We will never have a thorough understanding of aging by studying a single tissue, and this applies to many other processes and diseases," says lead author Maroun Bou Sleiman. "Data, whether freshly produced or reused, is the key to understanding complex systems, and we are just scratching the surface."

Through multiple bioinformatics analyses, the scientists identified certain genes and proteins that may be controlling the complex aging process. By including human population data, they also showed that many of the "players" they identified in the mouse genome may be also relevant in human aging.

Finally, the researchers used human genetic data to show that some of the 'players' may also explain why some humans live longer than others.

"Our final goal is not to stop aging, but to age better and disease-free, and to do that, we will need to characterize this system," says Johan Auwerx. "This is a perfect example of cross-species integration starting from the laboratory mouse and ending in human population data that takes us one step closer to understanding one of the most complex processes in biology."

**More information:** Maroun Bou Sleiman et al, The Gene-Regulatory Footprint of Aging Highlights Conserved Central Regulators, *Cell Reports* (2020). DOI: 10.1016/j.celrep.2020.108203

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