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Hibernation Slows Aging

A (preprint) study in yellow-bellied marmots suggests that hibernation slows epigenetic aging





(Pixabay, Bru-nO)

To slow the hands of time

At first glance, it seems that we're in a golden 'age' for aging research.

We hear about new lifespan-extending interventions almost every day: <u>drugs</u> (such as <u>metformin</u> or <u>rapamycin</u>), <u>supplements</u> (such as <u>resveratrol</u>), blood exchange and/or <u>dilution</u>, custom-made <u>molecules</u>, <u>stem cells</u>,.... Or why not try some <u>fasting</u> or <u>calorie</u> <u>restriction</u> (which may not work as well as you think)? Or have some <u>red wine</u>.

For all these things, the extent of their influence — if any — is quite variable among individuals. After all, some hundred-year-olds <u>have eggs and bacon for breakfast</u>. Your body will respond differently to certain interventions than someone else's.

If there are human longevity-promoting intervention studies, these are mostly short-term and assessed via proxies such as certain blood markers, which may or may not truly reflect various aspects of the aging process. (Finding truly accurate markers of aging is still a work in progress, see for example the recent work on 'aging clocks'.)

We can study healthy <u>centenarians</u>, people who reach the age of 100 in relatively good health. If we find certain characteristics — genes, lifestyle factors, etc. — that centenarians share (for example, their <u>methionine metabolism</u>), that's at least a good starting point for our investigations into the aging process.

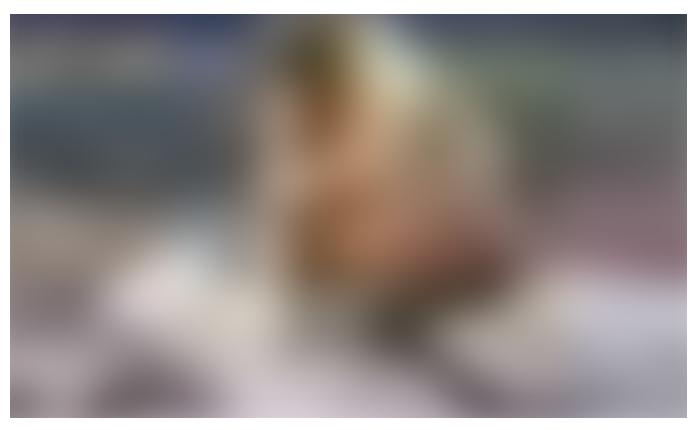
What we can also do is study animals who live longer than we might expect from their body size (which, on average, across species, <u>tends to correlate with lifespan</u>).

Sleep away aging

For example, animals that hibernate live longer than their body size seems to warrant.

Since metabolic rate correlates with the rate of aging, this makes intuitive sense. Your metabolism is not firing when you're hibernating. Also, hibernation tends to activate certain stress responses in the body, such as improved antioxidant defenses.

A <u>new study</u> now looks at whether hibernation actually slows aging by investigating <u>epigenetic</u> markers. These markers are molecules (often methyl groups) that bind to DNA and alter the activity of genes.



Yellow-bellied marmot (Wikimedia commons, Inklein)

The scientists did so in a group of 73 female <u>yellow-bellied marmots</u>, a group of medium-sized rodents that hibernate for up to eight months per year. They used only females because the precise age of males is hard to ascertain as they tend to immigrate from elsewhere. The researchers collected samples every two weeks, for a total of 149 workable samples that were analyzed.

Then, the researchers used two measured of epigenetic aging: an epigenetic clock, which takes a 'snapshot' of the marmot's epigenetic status, and an epigenetic pacemaker, which tracks the epigenetic changes over time.

Compute away, and...

The epigenetic pacemaker (EPM) results showed a rapid change in epigenetic age until marmots reached 2-years old, their age of sexual maturity. After reaching adulthood, epigenetic age change was more linear and slower, which is similar to the pattern observed in humans older than 20 years.

Growing up coincides with plenty of physiological changes and associated epigenetic tweaks. As expected.

What we're interested in here is this:

According to the model that used EPM-estimated epigenetic age, biological aging slows during hibernation.

What changed during sleepy time?

Our enrichment analysis of age-related CpG sites revealed pathways related to development and cell differentiation, while the season-related CpGs enriched pathways related to central carbon metabolism, immune system, and circadian clock.

Overall:

Taken together, our results are consistent with the hibernation-aging hypothesis and may explain the enhanced longevity in hibernators.

Caveat time:

- This study is, at the moment of writing, a preprint. It hasn't gone through peer review yet.
- Marmots are not people. And we generally don't hibernate.
- Due to the algorithm they used: "seasonality probably influences many more CpGs in common with aging than we were able to detect."

Sleep tight.

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