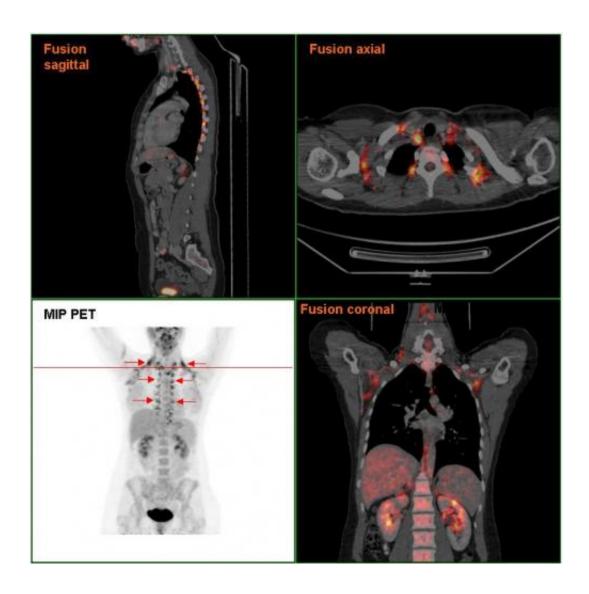


Environmental impact passed on to offspring

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Brown adipose tissue in a woman shown in a PET/CT exam. Credit: Public Domain



Anyone with lots of brown adipose tissue, or brown fat, can count themselves lucky: this tissue—which is found in some people under the tongue, around the collarbone and along the spine—helps them to use up excess energy. The more brown fat someone has and the more active it is, the lower their risk seems to be of becoming overweight or developing metabolic disorders.

An international research team led by ETH Professor Christian Wolfrum has now shown that one key variable in the formation of brown adipose tissue is set before conception: males who spend time in low temperatures prior to mating will produce offspring with more active brown adipose tissue. This quite literally means that the environmental impact a father experiences is passed on to his offspring.

Analysing computed tomography images

The researchers reached this conclusion by studying mice, but in humans, too, there is a correlation between the ambient temperature before conception and the prevalence of brown fat. Together with colleagues at the University Hospital Zurich, the ETH scientists analysed computed tomography images of 8,400 adult patients. They noted that people born between July and November (meaning they were conceived in the colder half of the year) have significantly more active brown adipose tissue than people born between January and June (who were conceived in the hotter half of the year).

To follow up on this correlation, the researchers conducted studies in mice. They kept the animals at either a moderate (23° Celsius) or a cool (8° Celsius) temperature and allowed them to mate. An analysis of the offspring showed that the temperature females were kept at before and after mating had no impact on levels of brown adipose tissue in their offspring, but this was not the case for males: the offspring of males kept in a cool environment for several days prior to mating had more



active brown adipose tissue than those of males kept in a temperate environment. In addition, the offspring of males kept in cool conditions were better protected against excess weight—they gained less weight on a high-fat diet—and against metabolic disorders.

Epigenetic changes in sperm

Using in vitro fertilisation and studies on sperm, the researchers were ultimately able to demonstrate that the information about the ambient temperature a father was kept at is passed on to his offspring via his sperm's epigenetic programming. This refers to changes made in the particular pattern of chemical markings (methylations) on the DNA.

It has been known for several years that certain environmental factors can modify the epigenetic pattern of sperm. What the scientists have now shown for the first time is that ambient temperature can also lead to epigenetic changes.

Brown fat cells burn energy to produce body heat, so mice with more brown adipose tissue are better at regulating their body temperature in low ambient temperatures. "Perhaps this protects them from icy cold, which might explain why this epigenetic mechanism has been selected for, in the course of evolution," says ETH Professor Wolfrum.

Temperatures at home and excess weight

The results that the ETH scientists obtained from their studies of mice and men agree with earlier observations that people in cold regions have particularly high levels of <u>brown adipose tissue</u>. "Until now, the assumption was that this had something to do with the temperatures people experienced during their lifetime," Wolfrum says, "but our observations suggest that temperatures prior to conception might also



affect later levels of brown fat."

Wolfrum points out another correlation: Average indoor temperatures have increased in recent decades, at least in the United States, where research has been done on this topic. What's more, studies have shown that the <u>temperature</u> people experience at home correlates with how overweight they are. "Our work highlights a possible mechanism for this," Wolfrum says.

Does this mean couples trying for children should be advised to have the man go for a swim in a cold lake or even play about in the snow before having relations? "Before we can give that kind of advice, we need to study the correlation in people more closely," Wolfrum says, "but it is likely that the exposure to cold needs to persist over a longer period for it to have an effect on epigenetic programming. Taking a plunge in cold water or spending a short time lying on a block of ice probably won't be enough." The scientists are now planning a study that will compare the epigenetic programming of human sperm in summer and winter.

More information: Wenfei Sun et al, Cold-induced epigenetic programming of the sperm enhances brown adipose tissue activity in the offspring, *Nature Medicine* (2018). DOI: 10.1038/s41591-018-0102-y

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