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Life span of human cells defined: most cells are younger than the individual

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Until now, defining the life span of specific human cell populations was limited by an inability to mark the exact time when cells were born in a way that can be detected over many years. However, a team of Swedish researchers from the Karolinska Institute (<https://www.timeshighereducation.com/world-university-rankings/karolinska-institute>) in Stockholm, lead by Jonas Frisén, has announced that cells can be dated by applying carbon-14 techniques to DNA, a method commonly used in archaeology and palaeontology to pinpoint the age of fossils.

Using this method, Dr Frisén has shown that most cells in the body are less than 10 years old. Moreover, the team has also discovered why people behave their birth age, rather than the physical age of their cells: This is because a few of the body's cell types endure from birth to death without renewal, and this special minority includes some or all of the cells of the cerebral cortex.

The new dating approach relies on a peak in the atmospheric levels of C14 as a result of aboveground nuclear arms testing during the Cold War. C14 dating looks at the ratio of radioactive carbon, naturally present at low levels in the atmosphere and food, to normal carbon within an organism. While a creature lives, eats and breathes, its ratio of radioactive to normal carbon will equal the ratio in its environment. But when it dies, this ratio will fall, as the carbon-14 decays.

Until now, the main obstacle to applying this technique was that radioactive carbon decays slowly, such that a given amount of carbon-14 halves every 6,000 years. Detecting the subtle change in the ratio of normal to naturally occurring radioactive carbon over just a few years proved too difficult. But Dr Frisén maintains that it can be done if one takes advantage of the signal left by nuclear testing, which vastly increased the levels of carbon-14 in the atmosphere during the Cold War.

According to Dr Frisén, by the time aboveground nuclear testing ended in 1963, the levels of atmospheric C14 had doubled beyond natural background levels. Since the halt, this has halved every 11 years. By taking this into account, one can see detectable changes in levels of C14 in modern DNA.

'Most molecules of the cell will turn over all the time. But DNA is a material that does not exchange carbon after cell division, so it serves as a time capsule for carbon,' he says. All the C14 in a cell's DNA is acquired on the cell's birth date, the day its parent cell divided. By measuring C14 levels in their DNA, it would be possible to pinpoint individual cells' birth dates to within two years.

In practice, the method has to be performed on tissue samples, not individual cells, because not enough C14 gets into any single cell to reveal its age. Dr Frisén worked out a scale for converting carbon 14 enrichment into calendar dates by measuring the carbon 14 incorporated

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into individual tree rings in Swedish pine trees. Having validated the method with various tests, the team reported the results of their first tests using body tissues in the July 15 issue of the journal Cell.

Dr Fris and his team looked at tissue samples from more than a dozen deceased subjects, about half of whom were born after the mid-1960s.

Each kind of tissue has its own turnover time, related at least partially to the workload endured by its cells. Epidermic cells, forming the easily damaged skin of the body, are recycled every two weeks or so. Red blood cells, in constant motion on their journey through the circulatory system, last only 4 months. As for the liver, the human body's detoxifier, its cells' lives are quite short - an adult human liver cell has a turnover time of 300 to 500 days.

Cells lining the surface of the gut, known by other methods to last for only five days, are among the shortest-lived in the whole body. Ignoring them, the average age of intestinal cells is 15.9 years, Dr Fris found. Skeletal cells are a bit older than a decade and cells from the muscles of the ribs have an average age of 15.1 years. When looking into the brain cells, all of the samples taken from the visual cortex, the region responsible for processing sight, were as old as the subjects themselves, supporting the idea that these cells do not regenerate. 'The reason these cells live so long is probably that they need to be wired in a very stable way,' Fris speculates. Other brain cells are more short-lived. Dr Fris found that the heart, as a whole, does generate new cells, but he has not yet measured the turnover rate of the heart's muscle cells. And the average age of all the cells in an adult's body may turn out to be as young as 7 to 10 years, according to him.

Why then, if the body remains so eminently capable of renewing its tissues, doesn't the regeneration continue forever? Some scientists believe this is explained by the accumulation of mutations in the DNA, which gradually degrades its information. Another theory blames mitochondrial DNA, which lack the repair mechanisms available for the chromosomes, whilst a third theory postulates that stem cells, which are the source of new cells in each tissue, eventually grow feeble with age.

'The notion that stem cells themselves age and become less capable of generating progeny is gaining increasing support,' Dr Fris said. He hopes to see if the rate of a tissue's regeneration slows as a person ages, which could point to stem cells being the impediment to immortality. To download the abstract of the Cell Journal paper, please: click here Remarks: Reference document: Retrospective Birth Dating of Cells in Humans. Kirsty L. Spalding, Ratan D. Bhardwaj, Bruce A. Buchholz, Henrik Druid, and Jonas Fris. Cell, Vol 122, 133-143, 15 July 2005.

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