Four studies devoted to understanding how mutations accumulate in human cells over time

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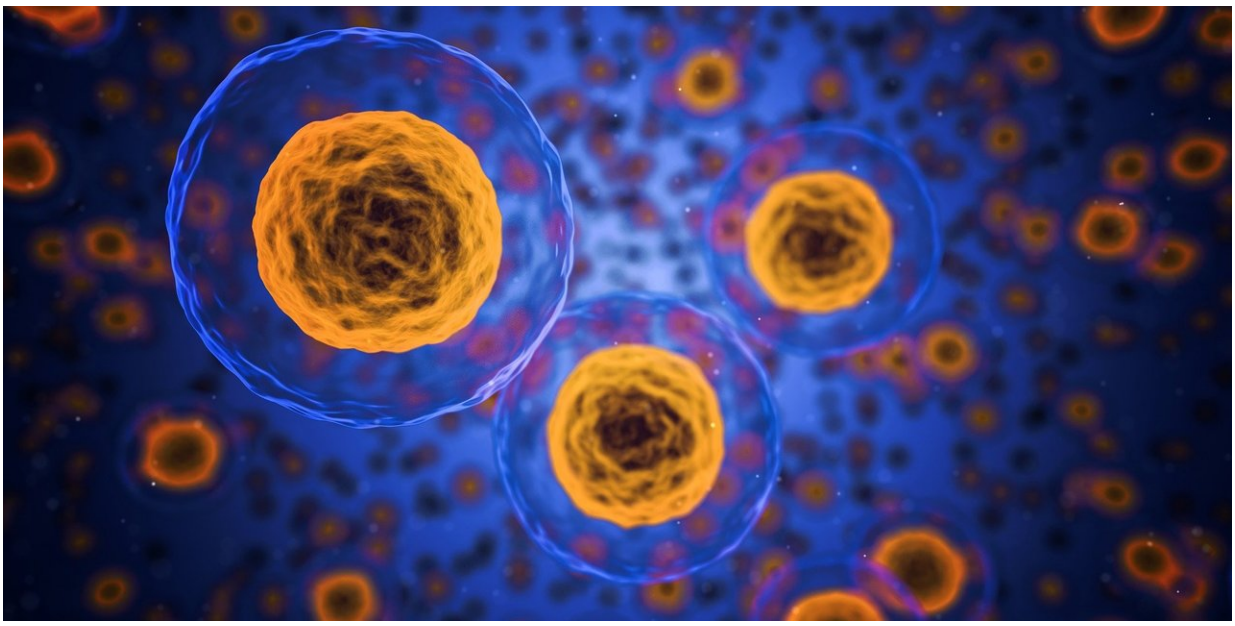

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Four teams of researchers from multiple institutions in South Korea, the U.K. and China, working independently of one another, have made progress in understanding how mutations accumulate in human cells over time. All four have published outlines of their work in the journal *Nature*.

All four of the teams began with the notion of cell lineage in a single organism, such as a person. When a cell divides, any mutations will be passed on to its progeny. And because the human body starts out as single fertilized eggs, researchers can trace the lineage of every cell in the body by tracking all of the mutations that have been passed on as a person ages from birth to death. Thus, every single cell in the human body has its own individual profile. To learn more about the process, the researchers all conducted sequencing of the genomes of cells obtained from tissues samples in different parts of the body.

The team from Korea and the first team from the U.K. focused their efforts on learning more about what happens during the earliest stages of human development, creating cell lineage trees from samples taken from adults who had recently passed away—all the way back to their embryonic stages. Both teams found that it was likely that the first lineage cells resulted from the first division of two cells from the egg—another six cells were found to develop into other tissue such as embryonic. The Korean team also found that cells located physically close to other cells are not always closely related.

The other two teams focused on cell division and mutations that occur later on in life. The second team from the U.K. found differences in lineages between those that reside in self-renewing tissue such as stem cells, versus those that do not renew, such as muscle tissue. Also, the team from China found that a large percentage of tissue samples from different body parts had three or more mutations that are known to lead to cancer. And both teams found differences in lineage in cells that are more prone to mutations from external factors, such as exposure to toxins.

Taken together, the work by the four teams represents a new approach to understanding not only human development, but in figuring out what happens when things go wrong, such as the development of cancerous

tumors—it could be that the lineage of the cells involved play a role.

More information: Tim H. H. Coorens et al, Extensive phylogenies of human development inferred from somatic mutations, *Nature* (2021). DOI: 10.1038/s41586-021-03790-y

Ruoyan Li et al, A body map of somatic mutagenesis in morphologically normal human tissues, *Nature* (2021). DOI: 10.1038/s41586-021-03836-1

Luiza Moore et al, The mutational landscape of human somatic and germline cells, *Nature* (2021). DOI: 10.1038/s41586-021-03822-7

Seongyeol Park et al, Clonal dynamics in early human embryogenesis inferred from somatic mutation, *Nature* (2021). DOI: 10.1038/s41586-021-03786-8