Skin cells reveal DNA's genetic mosaic

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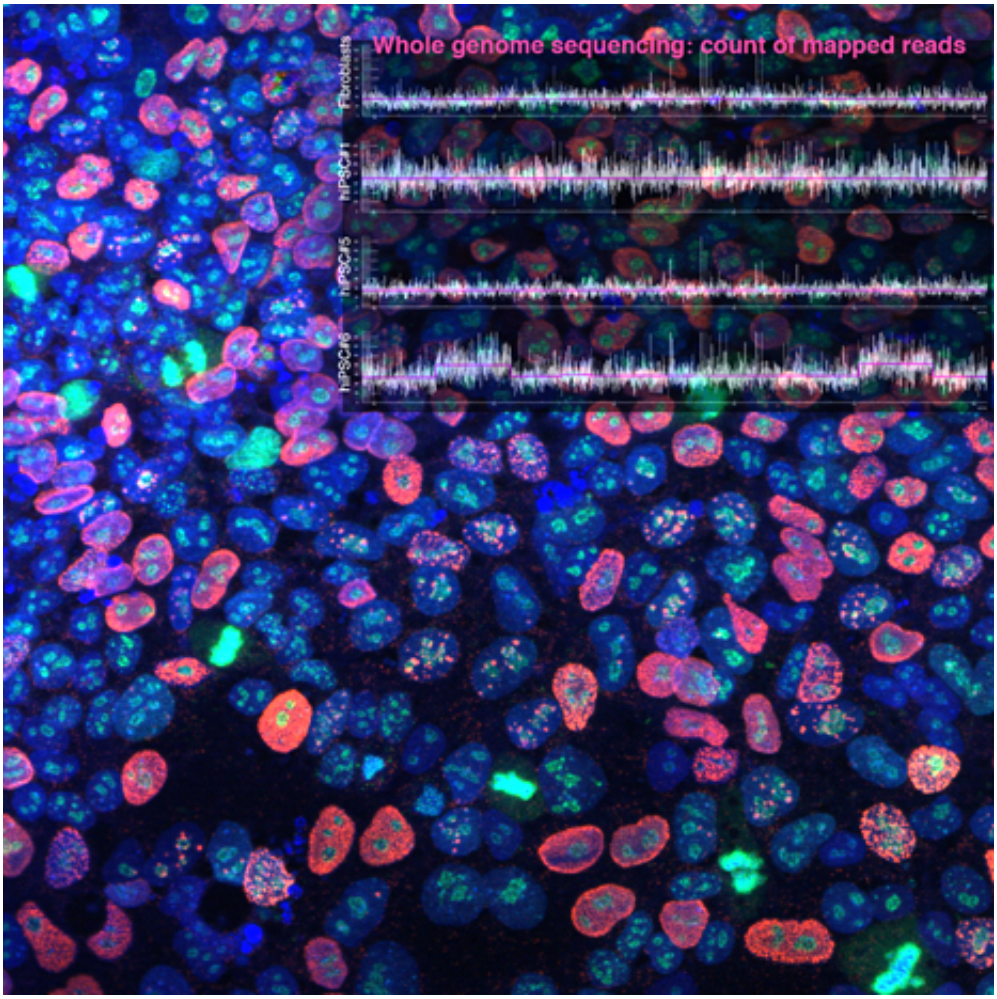
Credit: Michael Helfenbein

(Medical Xpress)—The prevailing wisdom has been that every cell in the body contains identical DNA. However, a new study of stem cells derived from the skin has found that genetic variations are widespread in the body's tissues, a finding with profound implications for genetic screening, according to Yale School of Medicine researchers.

Published in the Nov. 18 issue of *Nature*, the study paves the way for assessing the extent of gene variation, and for better understanding human development and disease.

"We found that humans are made up of a mosaic of cells with different genomes," said lead author Dr. Flora Vaccarino, the Harris Professor of Child Psychiatry at the Yale Child Study Center. "We saw that 30 percent of skin cells harbor copy number variations (CNV), which are segments of DNA that are deleted or duplicated. Previously it was assumed that these variations only occurred in cases of disease, such as cancer. The mosaic that we've seen in the skin could also be found in the blood, in the brain, and in other parts of the human body."



iPS cells stained for proteins expressed during the cell cycle. Credit: Vaccarino lab

The longstanding belief has been that our cells have the same DNA sequence and this blueprint governs the body's functions. The Yale team's research challenges this dogma. Some scientists have hypothesized that during development, when DNA is copied from mother to daughter cells, there could be deletions, duplications and changes in the sequence of the DNA, and an entire group of genes could be affected. This premise has been incredibly difficult to test, but Vaccarino and colleagues have done so in this new study.

The team used whole genome sequencing to study induced pluripotent stem cells lines (iPS), which are stem cells developed from a mature-differentiated cell. The team grew cells taken from the inner upper arms of two families. The team spent two years characterizing these iPS cell lines and comparing them to the original skin cells.

While observing that the genome of iPS cells closely resembles the genome of skin cells from which they originated, the team could identify several deletions or duplications involving thousands of base pairs of DNA. The team then performed additional experiments to understand the origin of those differences, and showed that at least half of them pre-existed in small fractions of skin cells. These differences were revealed in iPS cells because each iPS line is derived from one, or very few, skin cells. Vaccarino said these iPS lines could act as a magnifying glass to see the mosaic of genomic differences in the body's cells.

"In the skin, this mosaicism is extensive and at least 30 percent of skin cells harbor different deletion or duplication of DNA, each found in a small percentage of cells," said Vaccarino. "The observation of somatic mosaicism has far-reaching consequences for genetic analyses, which currently use only blood samples. When we look at the blood DNA, it's not exactly reflecting the DNA of other tissues such as the brain. There could be mutations that we're missing."

"These findings are shaping our future studies, and we're doing more studies of the developing brains of animals and humans to see if this variation exists there as well," Vaccarino added.

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