Scientists identify DNA that may contribute to each person's uniqueness

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Building on a tool that they developed in yeast four years ago, researchers at the Johns Hopkins University School of Medicine scanned the human genome and discovered what they believe is the reason people have such a variety of physical traits and disease risks.

In a report published in the June 25 issue of *Cell*, the team identified a near complete catalog of the DNA segments that copy themselves, move around in, and insert themselves here and there in our genome. The insertion locations of these moveable segments — transposons — in each individual's genome helps determine why some are short or tall, blond or brunette, and more likely or less likely to have cancer or heart disease. The Johns Hopkins researchers say that tracking the locations of transposons in people with specific diseases might lead to the discovery of new disease genes or mutations.

Using their specialized "chip" with DNA spots that contain all of the DNA sequences that appear in the genome, researchers applied human DNA from 15 unrelated people. The research team compared transposon sites first identified in the original published human "index" genome and found approximately 100 new transposon sites in each person screened.

"We were surprised by how many novel insertions we were able to find," says Jef Boeke, Ph.D., Sc.D., an author on the article, a professor of molecular biology and genetics, and co-director of the High Throughput Biology Center of the Institute for Basic Biomedical Sciences at Johns Hopkins. "A single microarray experiment was able to reveal such a

large number of new insertions that no one had ever reported before. The discovery taught us that these transposons are much more active than we had guessed."

Each of the 15 different DNA samples used in the study was purified from blood cells before it was applied to a DNA chip. Transposons stick to spots on the DNA chip corresponding to where they're normally found in the genome, letting the researchers locate new ones.

Boeke's group first invented the transposon chip in 2006 for use in yeast. But, it was Kathleen Burns, M.D., Ph.D., now an assistant professor of pathology at Johns Hopkins, who first got the chip to work with human DNA. "The human genome is much larger and more complex, and there are lots of look-a-like DNAs that are not actively moving but are similar to the transposons that we were interested in," says Burns. The trick was to modify how they copied the DNA before it was applied over the chip. The team was able to copy DNA from the transposons of interest, which have just three different genetic code letters than other look-alike DNA segments.

"We've known that genomes aren't static places, but we didn't know how many transposons there are in each one of us; we didn't know how often a child is born with a new one that isn't found in either parent and we didn't know if these DNAs were moving around in diseases like cancer," says Burns. "Now we have a tool for answering these questions. This adds a whole dimension to how we look at our DNA."

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