

Genome ID Method Extended to Humans

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A mathematical discovery has extended the reach of a novel genome mapping method to humans, potentially giving cancer biology a faster and more cost-effective tool than traditional DNA sequencing.

A student-led group from the laboratory of Michael Waterman, University Professor in molecular and computational biology in USC College, has developed an algorithm to handle the massive amounts of data created by a restriction mapping technology known as “optical mapping.”

Restriction maps provide coordinates on chromosomes analogous to mile markers on freeways.

Lead author Anton Valouev, a recent graduate of Waterman’s lab and now a postdoctoral fellow at Stanford University, said the algorithm makes it possible to optically map the human genome.

“It carries tremendous benefits for medical applications, specifically for finding genomic abnormalities,” he said.

The algorithm appears in this week’s PNAS Early Edition.

Optical mapping was developed at New York University in the late 1990s by David Schwartz, now a professor of chemistry and genetics at the University of Wisconsin-Madison. Schwartz and a collaborator at Wisconsin, Shiguo Zhou, co-authored the PNAS paper.

The power of optical mapping lies in its ability to reveal the size and large-scale structure of a genome. The method uses fluorescence microscopy to image individual DNA molecules that have been divided into orderly fragments by so-called restriction enzymes.

By imaging large numbers of an organism's DNA molecules, optical mapping can produce a map of its genome at a relatively low cost.

An optical map lacks the minute detail of a genetic sequence, but it makes up for that shortcoming in other ways, said Philip Green, a professor of genome sciences at the University of Washington who edited the PNAS paper.

Geneticists often say that humans have 99.9 percent of their DNA in common. But, Green said, "individuals occasionally have big differences in their chromosome structure. You sometimes find regions where there are larger changes."

Such changes could include wholesale deletions of chunks of the genome or additions of extra copies. Cancer genomes, in particular, mutate rapidly and contain frequent abnormalities.

"That's something that's very hard to detect" by conventional sequencing, Green said, adding that sequencing can simply miss part of a genome.

Optical mapping, by contrast, can estimate the absolute length of a genome and quickly detect differences in length and structure between two genomes. Comparing optical maps of healthy and diseased genomes can guide researchers to crucial mutations.

Though he called optical mapping "potentially very powerful," Green added that it requires such a high level of expertise that only a couple of laboratories in the world use the method.

The Waterman group's algorithm may encourage others to take a second look.

Source: USC College

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