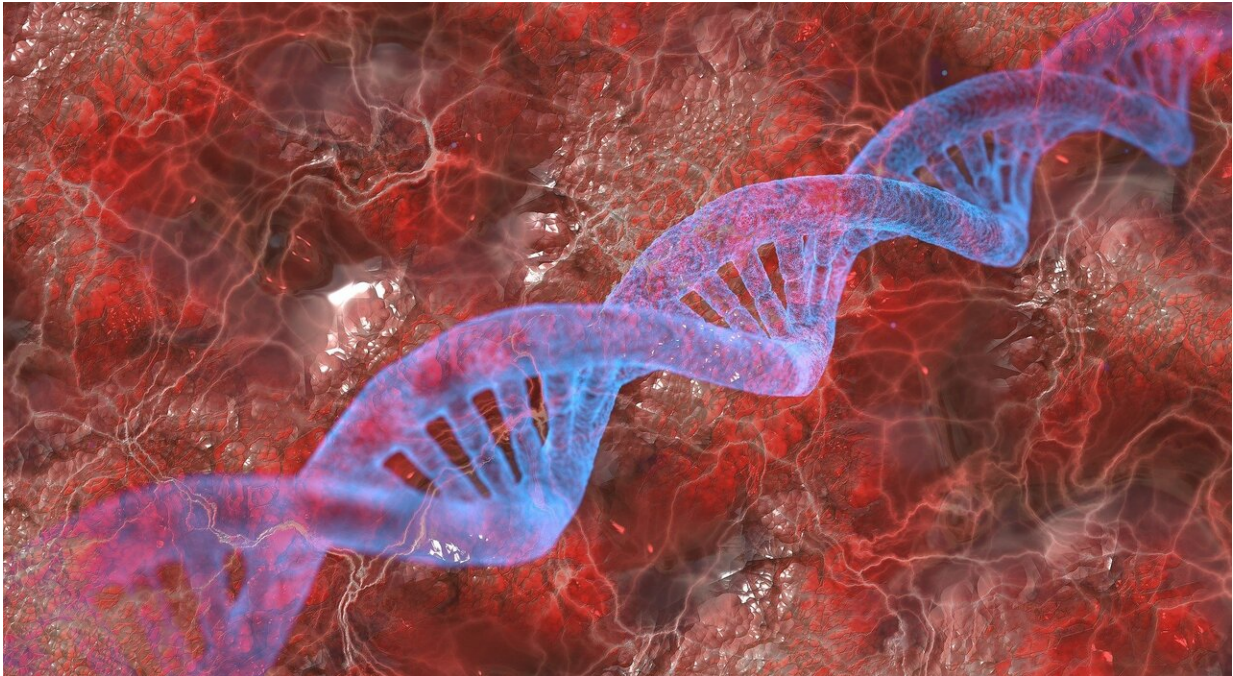


Next generation cytogenetics is on its way

July 7 2021



Credit: Pixabay/CC0 Public Domain

Dutch-French research shows that Optical Genome Mapping (OGM) detects abnormalities in chromosomes and DNA very quickly, effectively and accurately. Sometimes even better than all existing techniques together, as they describe in two proof-of-concept studies published in the *American Journal of Human Genetics*. This new technique could radically change the existing workflow within cytogenetic laboratories.

Human hereditary material is stored in 46 chromosomes (23 pairs). Although those chromosomes are quite stable, changes in number or structure can still occur. A well-known example is Down syndrome, which is caused by an extra chromosome 21 (trisomy 21). An extra chromosome makes a big difference and is quite easy to visualize. But all kinds of other, smaller changes can occur as well in chromosomes. Sometimes pieces of DNA are lost (deletions), sometimes a piece is just repeated (duplication) or it is moved to another place (translocation). An existing piece can also be turned over (inversion) and sometimes new pieces are inserted (insertions). All these structural abnormalities in the chromosomes can cause disease, either congenital genetic diseases, which are present from birth, similar to Down syndrome, or acquired disorders, when the change occurs in a few cells during life which can lead to cancer, such as in leukemia.

Optical mapping

Cytogenetics is the genetic discipline that examines [chromosomes](#) for such abnormalities. To visualize both the large and small changes, several complementary techniques are needed, such as FISH, karyotyping and Copy Number Variant (CNV) microarrays. These are often laborious techniques that individually can only visualize a part of the above-mentioned abnormalities. Recently a new technique has become available—Optical Genome Mapping—which more or less brings together the previous techniques. But new techniques must prove themselves in practice. At Radboud University Medical Center (Radboudumc), Alexander Hoischen, associate professor of Genomics Technologies and Immuno-Genomics, researches new techniques for usability in clinical research and possibly later in patient care. It requires close cooperation between Radboudumc and the industry involved in building latest genomic technologies, in this case the America-based company Bionano Genomics.

Two advantages

Hoischen immediately mentions two major advantages of OGM: "We can now look at extremely long stretches of DNA, so there's fewer pieces needed to map the entire chromosome. It's faster and produces fewer errors. Furthermore, unlike the other techniques, we do not have to pre-process or manipulate the DNA, so we look at the real, 'natural' DNA. In short: what you see is what you get."

Automatic, objective, digital

Bionano has created a label that attaches to a specific piece of DNA that occurs very often, but irregularly. The ever-changing distances between the labels create a unique barcode so researchers always know exactly where they are situated in the DNA. This labeled DNA is pulled through thin long nanochannels, while a camera continuously takes pictures. Hoischen: "In this way we can automatically, objectively and digitally record DNA at a rapid pace, and at a resolution that is 10,000 times higher than in karyotyping. It's a kind of 'cytogenetics on steroids' because of its power and speed."

Hereditary disorders

But how well does the technology work? Two papers in the *American Journal of Human Genetics* give a positive answer. Dr. Laïla El Khattabi of the Université de Paris, Hoischen, and their colleagues, tested OGM on 85 samples from patients with a hereditary disorder that had previously been examined with the standard tests (karyotyping, FISH, CNV microarray). Remarkable and exceptional: OGM found them all. El Khattabi: "OGM can really revolutionize the detection of chromosomal aberrations. I think it could be the most significant technological breakthrough in the history of cytogenetics since the CNV

microarray."

Early adapters

In the second paper, the team of Nijmegen researchers again compared the technique to the standard tests. This time they looked at the DNA of leukemia cells of 52 patients with leukemia, a hematological malignancy. Here too, OGM performed optimally by detecting all clinically known deviations. And even more than that. In a number of cases, the technique provided better and more accurate analyzes of chromosomal abnormalities. This is rather important, because the right treatment often depends on this. Hoischen: "We are early adapters of different genome technologies, often with the aim of quickly applying them routinely in the clinic. The very convincing data in these two proof-of-concept studies again place Radboudumc at the forefront of technical innovation for healthcare in human genetics. This 'Next Generation Cytogenetics' could replace decade old routine testing, vastly improving workflow and patient care." This is echoed by Dr. Marian Stevens-Kroef, Clinical Laboratory Geneticist for hematological malignancies: "OGM promises to greatly improve cytogenetic testing in patients with hematological malignancies."

Further roll out

Radboudumc researchers Dr. Kornelia Neveling and Dr. Tuomo Mantere, first authors in both studies, are also positive about the technique. Neveling: "It is a rather simple technology, for both the wet lab and data analysis, and we foresee great advantages for a use in a clinical setting. In addition, OGM has already helped to solve several medical mysteries, some of which have been waiting for answers for more than 20 years."

Tuomo Mantere, former postdoc in Hoischen's laboratory and now affiliated with Oulu University in Finland: "The easy implementation of this technique and the convincing concordance with the standard cytogenetic methods as presented in these two studies convinced me to set up OGM now in Finland as well."

More information: Tuomo Mantere et al, Optical genome mapping enables constitutional chromosomal aberration detection, *American Journal of Human Genetics* (2021). [DOI: 10.1016/j.ajhg.2021.05.012](https://doi.org/10.1016/j.ajhg.2021.05.012)

Provided by Radboud University

Citation: Next generation cytogenetics is on its way (2021, July 7) retrieved 27 April 2024 from <https://phys.org/news/2021-07-cytogenetics.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.