Evolution of cytogenetic techniques

20,000 genes

46 chromosomes

23 pairs

Karyotyping | FISH | Microarrays | NGS

What is **cytogenetics**?

The study of chromosomal changes in cells for diagnosis or treatment.

Key contributors

Karl Nägeli
(1817–1891)
Swiss Botanist

Published a paper on the development of pollen and the "transitory cytoblasts" that were later identified as chromosomes.

Walther Flemming
(1843–1905)
German Anatomist

Observed and described the behavior of chromosomes during cell division.

Joe Hin Tjio, PhD
(1919–2001)
American Geneticist

Found that human cells contain 46 chromosomes arranged as 23 pairs.

Joe W. Gray, PhD & Daniel Pinkel, PhD

Applied FISH in a clinical setting to visualize chromosomes.

Edwin Southern, PhD

Filed the first patent application for *in situ* synthesized, oligonucleotide microarrays in the United Kingdom.

Innovation and **discovery**

- **1842** Nägeli identifies chromosomes for the first time.
- **1870** Flemming uses aniline dye to observe chromosomes.
- **1888** Waleyer-Hartz coins the term "chromosomes."
- **1956** Tjio and Levan determine that humans have 46 chromosomes.
- **1959** Lejeune discovers that people with Down syndrome (trisomy 21) have an extra chromosome.
- **1960** The first International System for Chromosome Nomenclature (ISCN) conference is held.
- **1971** Scientists develop G-banding, C-banding, and reverse banding.
- **1980** Bauman, Wiegant, Borst, and van Dujin use FISH (fluorescence *in situ* hybridization).
- **1986-88** Pinkel and Gray add interphase and metaphase FISH for clinical diagnostics.
- **1988** Southern files a UK patent application for *in situ* synthesized, oligonucleotide microarrays.
- **1991** Fodor and colleagues publish the photolithographic array fabrication method.
- **1995** Schena publishes the first use of microarrays for gene expression analysis.
- **1996** Schrock and Ried describe multicolor spectral karyotyping.
- **2010** The American College of Medical Genetics (ACMG) recommends replacing karyotyping with chromosomal microarrays as a first-line postnatal test.
- **2012** Microarray technology is applied to prenatal diagnostics.
- **2013** ACMG recommends the use of prenatal chromosomal microarray analysis to monitor a fetus with one or more major structural abnormalities.

Current and future applications

Building on history and forging new paths

Technologies have been applied and advanced for more than a century, helping scientists understand chromosome defects and rearrangements. Their ability to examine genetic material at the nucleotide level has opened a world of exciting possibilities.

Genetic diseases

- Birth defects
- Fetal loss
- Developmental delays

Genetic diseases = mutation in chromosomal structure

Common genetic disorders

- Down syndrome
- Turner syndrome
- Cystic fibrosis
- Huntington's disease

Chromosome research

- White blood cells
- Bone marrow cells
- Fetal cells

Chromosomes are often extracted from live cells.

Early visualization: karyotyping

- Aniline dyes were used to witness chromosome behavior during mitosis
- Techniques like G-banding, C-banding, and Q-banding were established
- Spectral karyotyping and multicolor FISH (mFISH) revolutionized the field in the 1970s and 80s
- Limitations: Karyotyping cannot detect small SNV abnormalities and it requires cell culture

FISH

- First described in the late 1960s and later achieved widespread use
- Helps detect single genes, specific regions, and whole chromosomes
- Offers speed, sensitivity, stability, and convenience
- Does not allow for efficient break point mapping for chromosome translocations

Comparative genomic hybridization

- Has better resolution than G-banding or FISH
- Used to detect chromosomal copy number variations (CNVs)
- Can help find abnormalities in prenatal and neonatal genomes
- Cannot be used to identify structural chromosome aberrations

Microarrays

- Medical genetics researchers identified single nucleotide polymorphisms (SNPs)
- Combined CGH with microarrays to catalog and assess variations in human genetics
- Modern CNV and SNP probe arrays offer greater insight across the whole genome

Next-generation sequencing

- Short- and long-read sequencing continue to drive variant discovery in cytogenetic research
- Custom testing options like focused exome and whole exome sequencing
- High levels of data complexity

ThermoFisher SCIENTIFIC