Evolution of cytogenetic techniques

20,000 genes

46 chromosomes

# 23 pairs

Karyotyping | FISH | Microarrays | NGS

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# What is cytogenetics?

The study of chromosomal changes in cells.

## Glossary of genetic terms

**Chromosome**
A combination of nucleic acids and protein that contains genetic information

**Nucleotide**
A basic building block of nucleic acids, found in DNA and RNA

**Genome**
A complete set of DNA found in cells with nuclei, including all genes

**Mutation**
A change to one's DNA sequence as a result of cell division, mutagens, or infection

**Congenital defect**
An abnormality present at birth that can be a result of genetic or chromosomal mutations

# 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 research. |
| **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 1980s
- 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
- Cannot detect balanced translocations

### 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

# An evolving field

The field of cytogenetics is important for scientific research and medical diagnoses, and it can help us understand reproductive health, cancer, and other diseases. To date, technological advances have helped detect gene alterations, SNPs, numerical chromosome alterations, and more.

Using aniline dyes, Flemming first observed thread-like structures in the nucleus. During the 1870s, he also witnessed the behavior of chromosomes during mitosis. Flemming called the structures chromatin, but the name was later changed based on observations by Waldeyer-Hartz.

Between 1960 and 1970, techniques like quinacrine fluorescence staining (Q-banding), centromeric banding (C-banding), and Giemsa banding (G-banding) were established. At this point, an international standard of quality, accuracy, and consistency across laboratories was needed. This led to the development of the ISCN in 1978.

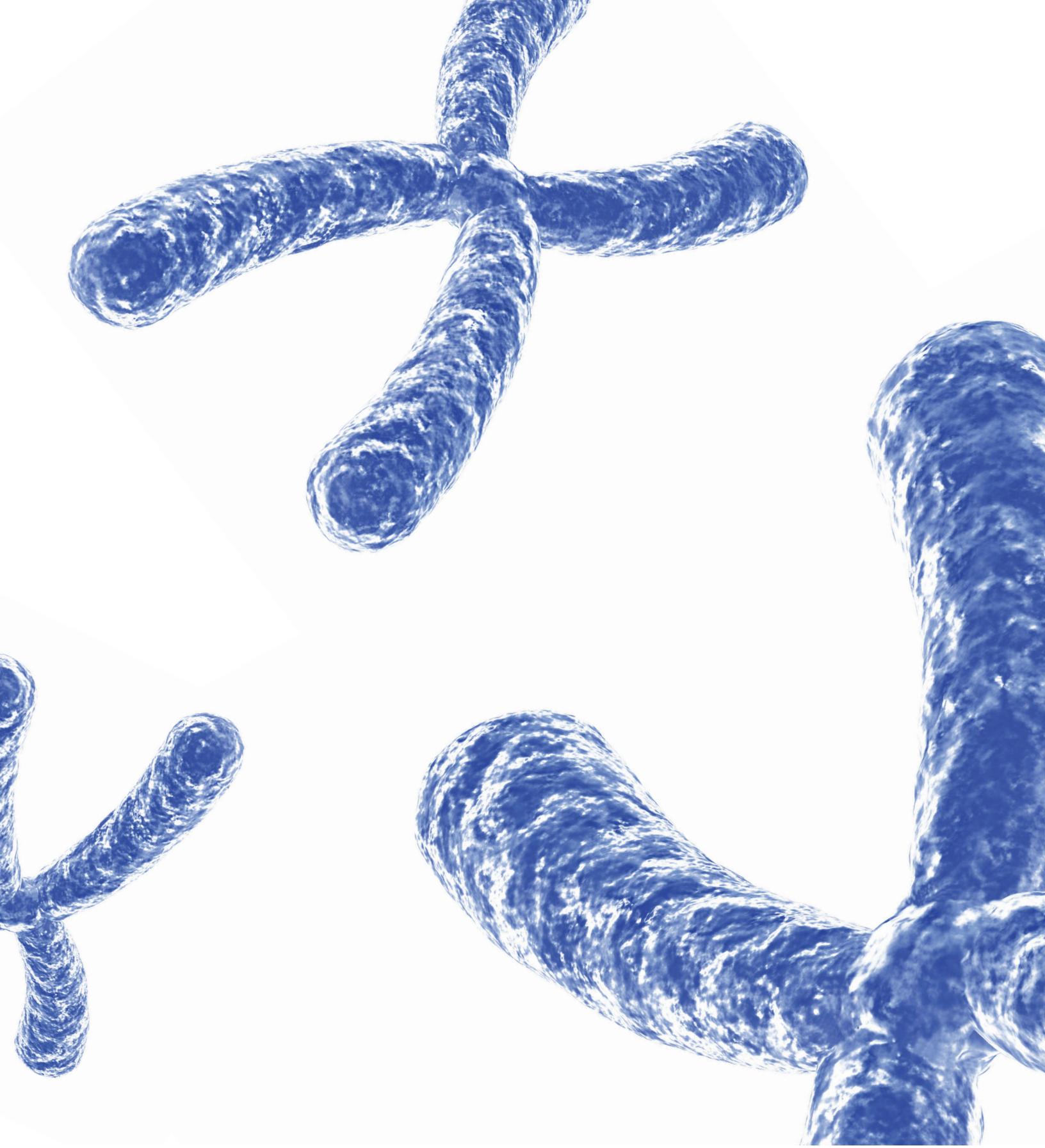
Since the early 1970s, FISH has become a popular molecular cytogenetic technique. First described in the late 1960s, it moved from using radioactive isotopes to fluorescence and achieved widespread use. It is currently used in a variety of biology-related disciplines to help detect single genes, specific regions, and whole chromosomes.

The rise of comparative genomic hybridization (CGH) can be attributed to its resolution; the results are better than G-banding or FISH. CGH is used to detect chromosomal CNVs and can help find abnormalities in prenatal and neonatal genomes.

With the help of genome-wide microarrays, medical genetics researchers were able to identify SNPs. Combining CGH with microarrays let researchers catalog and assess variations in human genetics.

Additional FISH techniques, including spectral karyotyping and multicolor FISH (mFISH), have also helped revolutionized the field, and they have many applications in pre- and post-natal diagnostics.

With that said, technological advances like these will continue to lead to new discoveries in cytogenetics research.



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