What makes You, You: A Stem Cell Journey into Cri Du Chat Syndrome

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What makes you, you?

From the shape of your nose to the sound of our voice, the answer lies deep within your chromosomes. Almost every cell in your body contains 46 chromosomes, arranged in a in 23 pairs. You inherit half from your mother and half from your father. The first 22 pairs are called autosomes, and the 23rd pair determines your biological sex. Together, these chromosomes carry the genetic instructions that influence everything about you—from your complexion and hair texture to your overall physique.

But what happens if one of these chromosomes is missing, duplicated or altered? That's called a **chromosomal abnormality**. These abnormalities are typically grouped into two main categories: numerical and structural.

Numerical Abnormalities

Numerical abnormalities occur when there's an error in the number of chromosomes in a person's cells. Instead of 46 chromosomes arranged in 23 pairs, someone may have one missing or an extra copy.

- If a person is missing a chromosome from a pair, it's called **monosomy** (1).
- If there are three copies of a chromosome instead of two, it's known as a **trisomy**.

These imbalances can significantly affect development. For example, Trisomy 21, more commonly known as Down syndrome, results from three copies of chromosome 21. This extra genetic material disrupts typical development, leading to characteristic physical features, developmental delays and varying degrees of intellectual disability (2–4).

Structural Abnormalities

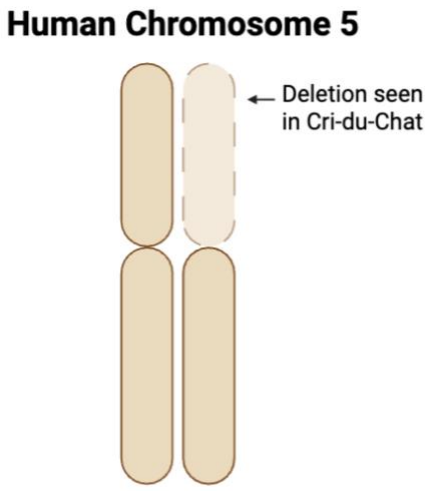
Structural abnormalities occur when the physical shape or internal arrangement of a chromosome is altered. These changes include:

- **Deletions**: a segment of a chromosome is missing
- **Duplications**: a segment is repeated
- **Translocations**: segments are exchanged between chromosomes
- **Inversions**: a segment is flipped in orientation
- **Ring chromosomes:** ends of a chromosome fuse into a loop (3,4).

These structural changes can disrupt how genes are regulated, often leading to various health and developmental issues.

Cri du Chat Syndrome: A Case Study in Chromosomal Deletion

One well-known structural abnormality is **Cri du Chat syndrome (CdCS)**, caused by a deletion on the short arm of chromosome 5. Even though it's considered rare, CdCS occurs in about 1 in every 15,000 to 50,000 births (5,8). French for "cry of the cat," the syndrome gets its name from the distinctive, high-pitched cry many affected newborns produce (5–7).



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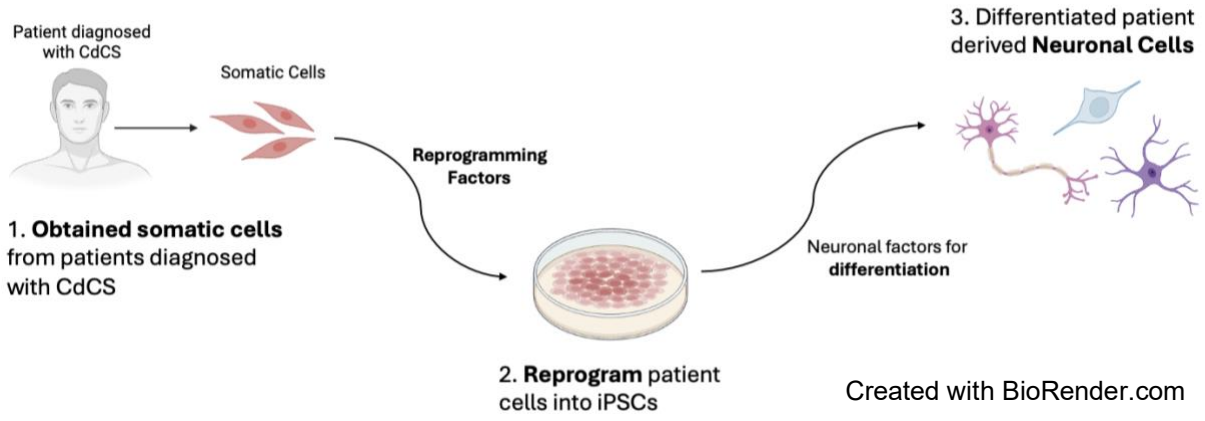
CdCS is often caused by a random, or *de novo*, deletion on chromosome 5.

The deletion affects multiple genes that are important for brain and body development. People with CdCS often face serious challenges with learning and movement. Though there is currently no cure for CdCS, supportive care can make a big difference. Early intervention programs—such as speech, occupational, physical, and feeding therapies—can improve communication, motor coordination, and daily functioning. Customized education plans also help address specific learning needs.

New Hope Through Stem Cell Research

Thanks to advances in stem cell research, scientists are making exciting progress toward understanding—and possibly treating CdCS.



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One powerful tool is the use of **induced pluripotent stem cells, or iPSCs.** These are adult cells (like skin or blood cells), that scientists reprogram into a stem-cell-like state iPSCs can then be guided to become nearly any cell type in the body, including neurons.

As shown in the figure above, here is how scientists are using iPSCs to study CdCS:

Step 1: Collect cells from individuals with CdCS.

Step 2: Reprogram them into iPSCs using specific reprogramming factors.

Step 3: Differentiate the iPSCs into neurons using specialized signals.

These lab-grown neurons carry the same chromosome 5 deletion as the original patient cells, allowing researchers to study how the deletion impacts neural development. By examining which genes are missing, scientists can better understand the syndrome and identify potential therapeutic targets.

Using this method, scientists can recreate disease-specific brain cells in the lab and study how the deletion disrupts development. This could pave the way for creating targeted therapeutic strategies to manage symptoms—or potentially, to a cure for CdCS.

As CdCS illustrates, even small structural changes in our chromosomes can profoundly influence how we grow, communicate, and interact with the world. After all, your chromosomes help define what makes you, *you*.

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