What our research team has discovered about CASK

Thanks to funding from the CASK Coalition, the Fink and Halmai labs at UC Davis have showed that **reactivating CASK in brain cells is possible**, paving the way for a new curative therapeutic for CASK disorders.

To do this, scientists used stem cells that can be turned into brain cells and created versions that with a mutation in the CASK gene, to mimic the heterozygote (female) presentation of MICPCH.

They successfully created several types of human cells from these stem cells, including:

- early stem cells (iPSCs)
- neural stem cells
- mature neurones (brain cells)
- small “mini-brain” structures called organoids

Studying these cells allowed the team to look closely at how the CASK gene is switched on or off in different cell types.

A completely new discovery

The team discovered something never reported before:

In the iPSCs, **the healthy copy of the CASK gene was found to “escape” being switched off**. This seemed to be driven by fewer chemical tags on the DNA, called methylation. These tags sit near the gene and influence whether the gene is active or silent.

This means the activity of CASK isn’t fixed — it can potentially be controlled.

Why this matters for treatment

This finding strengthens an important therapeutic idea:
if scientists can safely adjust these methylation tags, they may be able to switch the healthy CASK gene back on in humans.

Using a gene-editing technology called CRISPR, our researchers have already identified molecular “guides” that can target the CASK gene and change how active it is.

Most importantly, they showed that **reactivating CASK in human neurones is possible**.

What this means for the future

This work provides an important step toward treatments that could:

- reactivate the healthy copy of CASK
- restore the missing protein in brain cells
- This would address the underlying cause of CASK disorders rather than just symptoms

In other words, this research provides real evidence that switching CASK back on in human neurons may be achievable, bringing the field closer to therapies that could one day change the course of these conditions.