WHAT'S THE BIOBUZZ?
A journal for students by students

# Protein Adventures: How Do Neurons Get Calcium

## Key Terms

**Organelle** - structure inside a cell that has a specific function

**Calcium** - element that is an essential nutrient for our bodies

**Mitochondria** - organelle that is responsible for making energy

**Endoplasmic reticulum (ER)** - organelle that stores calcium, makes proteins, and breaks down fats

**PDZD8**- protein found at ER-Mitochondia contact sites in animals

**Neuron** - cells that work in our brains

**Dendrites**- parts of nerve cells that receive signals from other brain cells

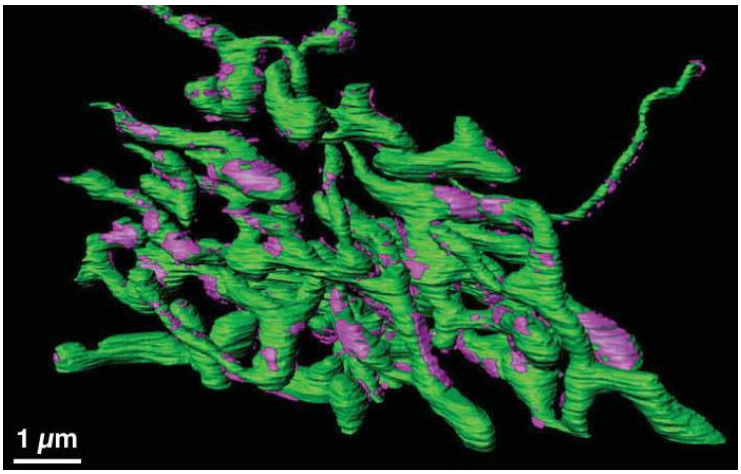


**Figure 1:** 3D reconstruction of mitochondria (green), with purple showing where it contacts the endoplasmic reticulum (ER) in HeLa cells

## ABSTRACT

We take in calcium from drinking lots of milk, but how does that help our bodies work? Let's start with the first step in the process: **organelles**. Organelles in the cell work together to carry out different jobs. These jobs require lots of help from neighboring proteins and other organelles. Proteins are building blocks that do most of the work in cells. One of these proteins is **PDZD8**, which is seen in the **endoplasmic reticulum** (**ER**). The ER and the **mitochondria** join together at many contact sites. At these contact sites the organelles communicate with each other to help control different processes that happen throughout the body.

The study focuses on what PDZD8 does at these contact sites and in the movement of calcium within the cell. Calcium detectors are used to track calcium movement between the ER and mitochondria. The detectors light up when they bind to calcium, which is known as fluorescence. By studying how calcium travels inside neurons we can better understand how neurons work and what can make them and our brains stop working.

# INTRODUCTION

The endoplasmic reticulum (ER) and the mitochondria are two cell structures that perform essential functions in our bodies. The ER is a network of tubes that produce, package, and transport important molecules such as proteins and fats. The mitochondria is responsible for producing the energy that helps fuel our cells and bodies. The ER and mitochondria can also interact inside our cells at special locations known as ER-mitochondrial contact sites. These contact sites are small junctions where the ER and mitochondria are linked together by specific proteins and they allow for exchange of small molecules such as **calcium**. Calcium is an important element that helps our **neurons**, the cells inside our brain, communicate.

Researchers have found that a certain protein PDZD8 has special structural features that help the ER and mitochondria exchange molecules at their contact sites. This study discovered that PDZD8 is the specific protein that is responsible for linking the ER and mitochondria at these sites. A second goal of the study was to show that PDZD8 is critical for the movement of calcium in our neurons, specifically in the **dendrites**.

# METHODS

- Researchers used **HeLa cells** as the standard cell line because these cells are commonly used in scientific research since they are immortal!

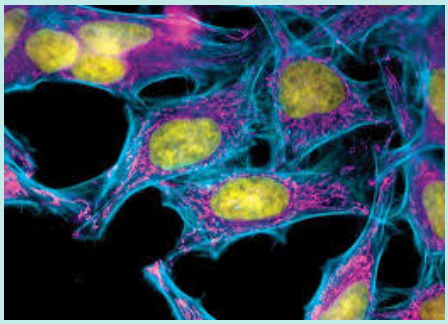

**FIGURE 2:** Visual representation of HeLa cells.

## Who is Henrietta Lacks?

Henrietta Lacks is the young African-American mother of five whom HeLa cells are named for. She went to Johns Hopkins Hospital complaining of vaginal bleeding, after being diagnosed with cervical cancer. She died at 31 years old after extensive treatment.

When she was at Johns Hopkins, Lacks' tumor cells were taken without her permission and sent to Dr. George Gey, a cancer researcher, who found that her cells never died, but instead grew indefinitely. Her cells went on to become the most widely used cells in biology, all without her family's informed consent. Her own family only found out through the friend of Lacks's daughter-in-law. The world didn't know about her contribution until an article was published with Lacks' name in it.

So next time you read about HeLa cells, think about Henrietta Lacks, without whom we wouldn't have been able to make so many amazing scientific discoveries!

# METHODS CONTINUED

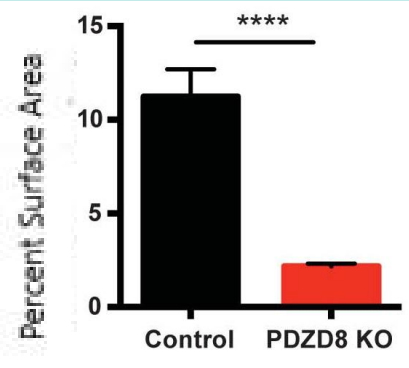


**FIGURE 3:** This shows the difference between surface areas in the mitochondria between the control and PDZD8 knockout.

- The study was designed with two groups: a control group and a PDZD8 knockout (PDZD8-KO) group as the experimental group. The HeLa cells in the control group were normal and contained the PDZD8 protein, while the HeLa cells in the PDZD8-KO group did not contain the PDZD8 protein.
- Scientists made 3D images of the cell organelles using a special type of electron microscope. They measured surface area of the ER and mitochondria using these images.
- In order to measure the movement of calcium in the dendrites, researchers used calcium indicators which emit light when they bind to calcium.

# RESULTS

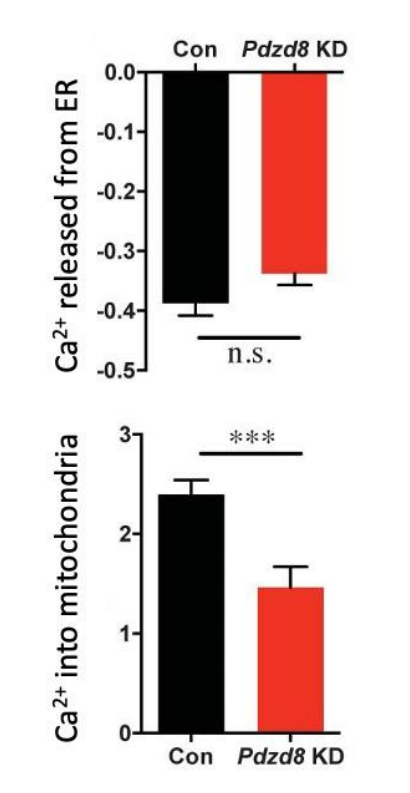


**FIGURE 4:** This shows the levels of calcium release from the ER (top) and uptake from the mitochondria (bottom).

- The PDZD8-KO group, in red, has a smaller percentage of mitochondrial surface area in contact with the ER compared to the control **[Figure 3]**.
- Both the control and the PDZD8-KO groups release the same amount of calcium from the ER **[Figure 4]**.
- Without PDZD8 (in red) much less calcium goes into to the mitochondria **[Figure 4]**.

# DISCUSSION

- The study highlighted the importance of the protein PDZD8 in the formation of ER-mitochondrial contacts in mammalian neurons. The contact sites in cells without PDZD8 had smaller percentages of ER and mitochondrial surface area in contact.

- The study also showed the importance of PDZD8 for calcium movement in our neurons. Figure 5 below is an excellent summary that shows how, in control neurons with PDZD8, the mitochondria receives most of the calcium leaving the ER. But in neurons without PDZD8, a majority of the calcium from the ER enters the surrounding cytoplasm, suggesting PDZD8 is a key protein involved in calcium entry into the mitochondria at these contact sites.

- Calcium is important for people because it helps the body in many different ways. These include helping our neurons send messages to each other, allowing our muscles to move and helping us strengthen our bones. This study helps us think about the role PDZD8 could play in our lives.

- The discovery of PDZD8's role and location in the ER sparks ideas for future experiments to find the identity of PDZD8's mystery friend located in the mitochondria that allows for ER-mitochondrial interactions. Scientists can then see how these two parts help drive the calcium transfer.

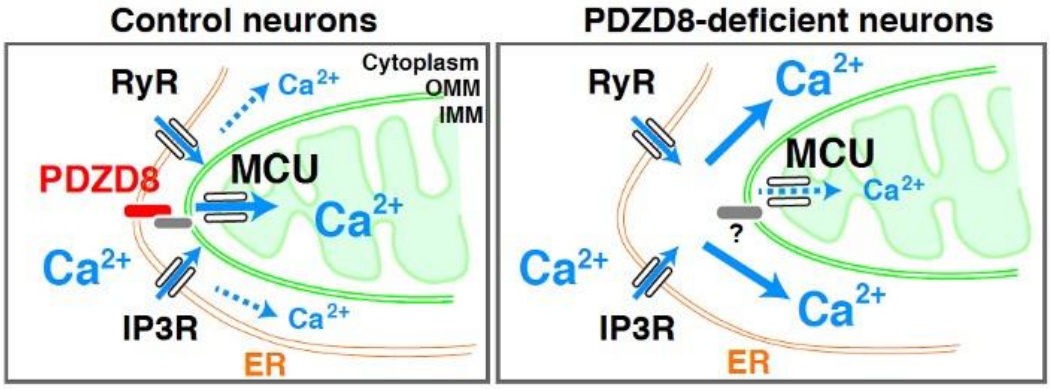


**Figure 5:** In control neurons with PDZD8, calcium from the endoplasmic reticulum (ER) moves into the mitochondria through a special calcium channel called MCU, without PDZD8, calcium from the ER primarily moves into the cytoplasm.

Adapted by Deena Haque, Amy Ngo, and Dhara Salazar from *ER-mitochondria tethering by PDZD8 regulates Ca2+ dynamics in mammalian neurons,* by Hirabayashi, Kwon *et al.*, Science, 2017 with assistance from Victoria Hewitt