Surprise discovery shows you may inherit more from your mom than you think

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Credit: leah hetteberg/unsplash

What if we could inherit more than our parents' genes? What if we could inherit the ability to turn genes on and off?

These possibilities have come to light after our recent study, published in *Nature Communications*. We found information, in addition to our genes, was passed down from mom to offspring to affect how their skeleton develops. That's the "epigenetic" information that's normally reset between generations.

Our research was in mice, the first case of its kind in mammals where a long-lasting epigenetic effect from the mother's egg is carried down to the next generation. This has lifelong consequences for that generation's health.

However, we cannot be certain the equivalent epigenetic changes are also inherited in humans, including the implications for how our skeleton develops and potential impact on diseases.

Hold up, what's epigenetics again?

Our genes (packages of DNA) tell our body to make certain proteins. But our cells also need instructions to know whether a gene should be used (switched on) or not (switched off).

These instructions come in the form of chemical or "epigenetic" tags (small molecules) that sit on top of the DNA. You accumulate these tags throughout your life.

Think of how punctuation marks help a reader understand a sentence. Epigenetic tags allow the cell to understand a DNA sequence.

Without these epigenetic tags, the cell might make a protein at the wrong time or not at all.

Timing is crucial in how embryos develop. If certain genes are expressed (switched on to produce a protein) too early or too late, an embryo will not develop properly.

What did we find?

We were interested in understanding the function of a protein in mouse eggs (ova) called SMCHD1.

By removing SMCHD1 from mouse eggs, we found mice that developed from eggs lacking SMCHD1 had an altered skeleton, with some vertebrae in the spine being disrupted.

This could only be explained by an epigenetic change due to the loss of SMCHD1 in the egg.

In particular, we looked at a set of genes known as *Hox* genes. These encode a series of proteins known to control how mammals' skeletons develop.

Hox genes are found in all animals, from flies to humans, and are crucial for setting up our spine. Evolution has finely tuned the timing of the expression of *Hox* genes during embryonic development to ensure the skeleton is assembled correctly.

> Happy to share that my first first author paper is out in @NatureComms showing that maternal SMCHD1 regulates Hox genes in the mouse embryo! Thanks to my Ph.D. supervisors @BlewittMarnie @Eddy_McGlinn #Epigenetics #InHoxWeTrust https://t.co/taYQmt1NAU 1/n
>
> — Natalia Benetti (@nataliabenetti_) July 25, 2022

Our study showed that epigenetic tags established by the mother's SMCHD1 in her egg can impact how these *Hox* genes are expressed in her offspring.

The findings are a big surprise because almost all epigenetic tags in the egg are erased shortly after conception. Think of this a bit like a factory reset.

This means it's unusual to have epigenetic information from the mother's egg carried on to her offspring to shape how they grow.

What does this mean for us?

Our findings suggest even the genes you don't inherit from your mother can still influence your development.

This may have implications for the children of women with variants in their SMCHD1 gene. Variations in SMCHD1 cause human diseases such as a form of muscular dystrophy.

In the future, SMCHD1 might be a target for new medicines to alter how the protein functions and help patients with diseases caused by variations in SMCHD1. So it's important to understand what consequences the disruption of SMCHD1 in the egg might have on future generations.

How about other diseases?

Scientists are now beginning to understand that the epigenetic tags added to our genes are sensitive to changes in the environment. This can mean environmental variations, such as our diet or level of physical activity, can affect how our genes are expressed. However, these changes do not alter the DNA itself.

The epigenetic state undergoes the most changes when the egg is developing and during very early embryonic development, due to the "factory reset" between generations. This means the embryo is more vulnerable to epigenetic, including environmental, changes during this developmental window.

As we discover more cases where epigenetic information is inherited from the mother, there may be instances where the diet or other environmental changes the mother experiences could impact the next generation.

Given that scientists can now study what happens in a single egg, we are well placed to determine how that might happen and work out what exactly we could be inheriting.

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