EPIGENETICS JIGSAW

Dutch Hunger Winter/Holocaust

In September 1944, after Dutch railway workers attempted to aid Allied forces against Nazi troops, Nazis punished the Netherlands by blocking food shipments to the country. The country was not freed until May 1945 and by that time over 20,000 citizens starved to death due to the Nazis' actions. Years later, scientists wanted to see what the impacts of this starvation had on following generations. Women who were pregnant during this time, gave birth to children that had some interesting health outcomes. As adults, these children displayed higher levels of triglycerides (a type of fat) and LDL (bad) cholesterol. Additionally, they were more likely to be obese or diabetic. These children also had a higher death rate after 68 years than that of citizens whose parents had not been starved. Researchers, recently, found genes that seemed likely to be a part of this. They compared the genes of children who were in the womb when their mother was starved to that of their siblings who were in the womb when the mother was well fed, years later. They found that the epigenetic marks of the two groups were significantly different. One of the most interesting genes is the PIM3 gene (involved in the body's ability to use fuel) which is silenced in famine exposed children.

As amazing as these results are, many scientists around the world are still skeptical about inheritance of epigenetic marks. Is it possible that gaining weight changes the PIM3 gene's mark and not the other way around? Many women died or had miscarriages during this time so the number of children to study is quite small.

Similar findings have been found in the offspring of Holocaust survivors. Survivors produce lower amounts of cortisol (a stress hormone) and all displayed a unique epigenetic pattern. In addition to low levels of cortisol, they also had low levels of the protein that breaks down cortisol. This allowed cortisol to stay in the body and maximize the process that controls fat and glucose storage. This would have been helpful to those experiencing starvation. Their children also produce low levels of cortisol but normal amounts of cortisol destroying enzyme. This meant that children had even less cortisol than their parents, causing survivors' children to be more at risk for PTSD (Post-traumatic stress disorder) like symptoms, other mental health issues and a multitude of other syndromes (obesity, insulin resistance, high blood pressure, etc.).

Answer the questions for this article in your lab notebook.

Epigenetics of Maternal Care & Stress Management

In 1957, a psychiatrist found that baby rats removed from their mother for 15 minutes a day made lower amounts of stress hormones later in life. When we think of stress hormones, we may associate it with something negative. Stress hormones are important for how our body manages and deals with adverse situations. However, too much of anything can create negative consequences later on in life.

Michael Meaney, PhD, and his lab wanted to find out why the rat pups showed low levels of stress hormones. Upon watching hours of videos of new mother rats with her pups, they chose two groups of rats, one which naturally displayed twice as much licking, grooming and nursing than the other. When the newborn rats were grown, they were tested for their reactions to different stressful situations (i.e. being put into a small box). The team saw that rats who grew up with more nurturing from their mother, tended to be more relaxed in the stressful situation. Additionally, the nurtured rats produced about half as much of two different hormones produced during stressful situations as the neglected group.

Researchers went on to show that the nurtured rats had more receptors for the stress hormones. These receptors are able to shut down the production of stress hormones when there is too much in the body. In other words, the rats who were nurtured more had a biological way to manage stress hormones better than the neglected rats. Meaney also found that rats raised by under-nurtured mothers carried a methyl group on genes that shut off stress response. Methyl groups were also found on genes that increase the production of receptors for a hormone involved with maternal care and nurturing. Rats who were not licked by their mothers responded less to the needs of their own rat pups. Interestingly, when rat pups born to a high nuturing mother were given to a low nurturing mother, they later grew to display low nurturing when having pups of her own and vice versa. They displayed epigenetics similar to those displayed by the rat mother they were raised by, not born to.

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Critiques & Questions About Inheritance

A reason why many scientists still doubt that epigenetic changes are heritable is that studies have shown that during fertilization (when egg and sperm fuse), there is a “reset” of the epigenetic marks in order to have cells return to their stem cell state (a state in which the cells do not have any specific differences i.e heart cell, brain cell, skin cell...). There are many questions that remain to show that traits can be inherited via the epigenome. The biggest obstacle to solving these questions is how to show that these epigenetic marks are what actually cause the characteristic.

To explain, correlation is the extent to which two (or more) variables change at the same time. For example, as the rate of ice cream sales increases, so does the rate of beach towel sales. Does the increased rate of ice cream sales cause people to buy beach towels? Probably not, a more likely thought would be that the sun shining increased the sale of both items. Therefore the relationship of beach towel sales and ice cream sales is correlational while the relationship of the sun shining and the sales of both items increasing is causal. To show a causal relationship between an inherited trait and epigenetic inheritance, would go against the beliefs of many scientists.

There are many steps that are involved in proving causality in science. The following measures would need to be taken to prove causality:

1. Genetic causes would need to be ruled out for a specific trait. Any ecological or cultural differences, behaviors that are acquired due to societal pressures, must be taken out.
2. Several generations must be studied in order to truly identify if characteristics are passed down by epigenetic changes.
3. After other causes have been ruled out, an epigenetic mark or pattern would need to be chosen that was common among the people being studied. In other words, is there a common epigenetic difference in those who display the characteristic being studied compared to those who do not?
4. It would then need to be shown that the change is in both normal bodily cells and cells that pass information on to babies (egg and sperm).
5. Finally, it would need to be proven that the epigenetic change is causing the characteristic and not the other way around. If the epigenetic mark in question was removed, would the characteristic being studied be lost?

To date, many studies that have hinted inheritance of traits and characteristics by epigenetics have dealt with small amounts of people and have had to largely dismiss extra factors. For something to be considered strong evidence, the number of people being studied needs to be large.

Answer the questions for this article in your lab notebook.