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WSU epigeneticist posits that obesity may be caused by ancestors' exposure to toxic chemicals

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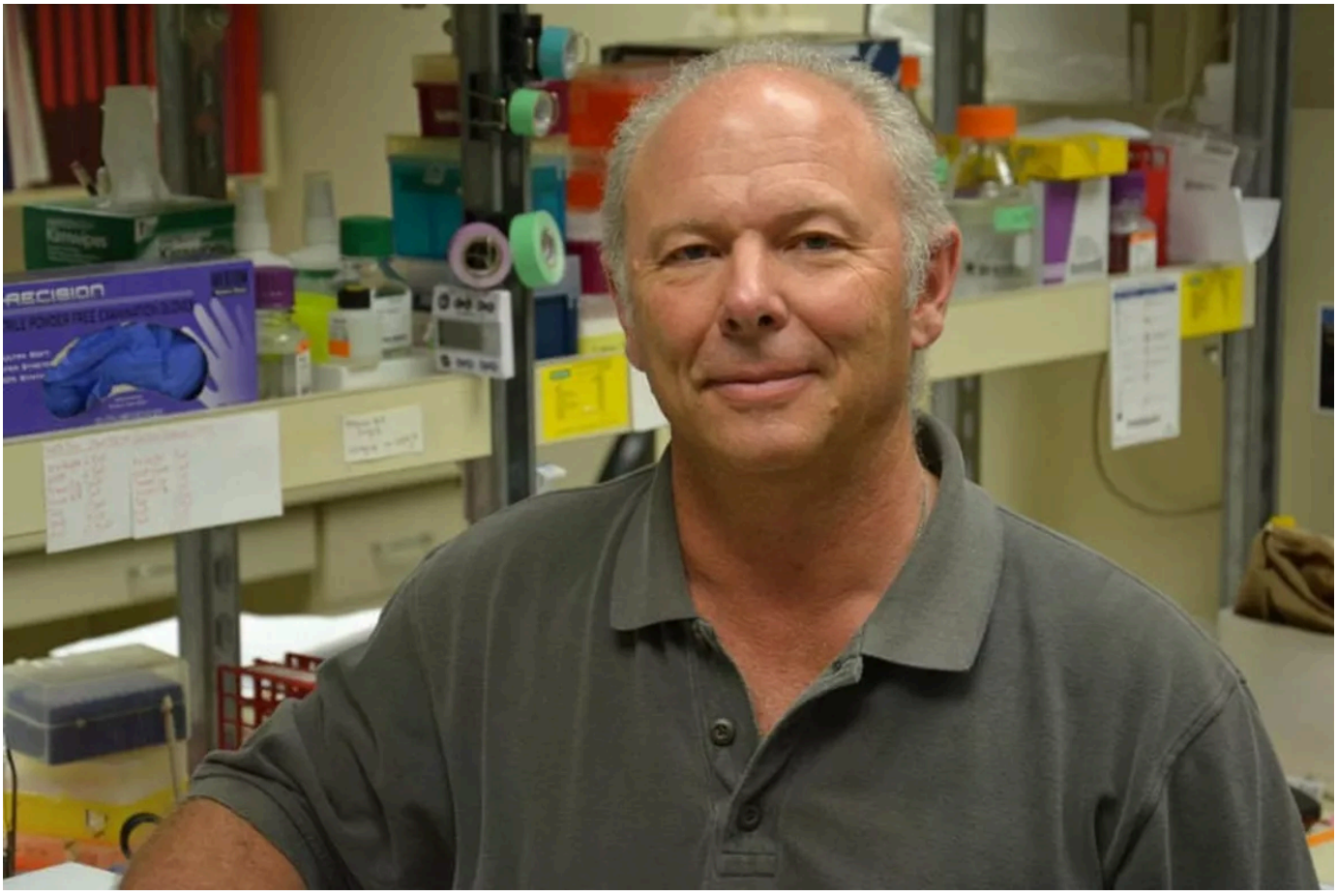

Professor Michael Skinner in his laboratory at WSU (Provided by Washington State University)

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Decades ago, someone's grandmother was exposed to a toxic pesticide that was later banned. A Washington State University professor's research suggests that person's grandchild may be suffering the consequences of that environmental exposure.

The inheritance that WSU's Michael Skinner studies does not come from genes – those are set in stone after birth. But epigenetics, the way those genes express themselves, do change throughout a person's life and can also be passed down through the generations.

Skinner suggests that today's high rates of obesity could be linked to epigenetics rather than just diet and exercise.

Though each cell in the body has an identical DNA sequence, the form and function of cells are often quite different. That is because different epigenetic processes can "turn on and turn off" different cells, according to Skinner.

"Disease we now know primarily comes from an abnormal epigenetics, which is causing an abnormal set of genes to turn on or off and gives genes an abnormal function," he said.

Unlike DNA, the body's epigenetics can change throughout their life – largely based on environmental factors. That's how exposure to a chemical can cause disease decades later.

Over his decades of research, Skinner's contribution to the field of epigenetics has been the discovery that epigenetics is inherited just like the genes themselves.

"An environmental exposure of a chemical or some sort of trauma event can change the epigenetics in the parent," he said. "That will lead to epigenetic change in the sperm or the egg, which will carry epigenetics to the next generation."

While that child's epigenetics can be changed again throughout their life, the impacts of environmental exposures of their parents and grandparents can still be seen in the child.

Skinner first made his discovery during 2005 at his lab on the WSU campus in Pullman. He exposed rats to a chemical known to stunt the growth of a fetus and continued to see the changes induced by the chemical several generations of rats later – even though those rats had not been exposed to the chemical itself.

Years later, Skinner is still studying genetics – now studying how epigenetic disposition for disease can improve health care in humans.

Are epigenetic changes causing obesity?

In a proof-of-concept study released in November, Skinner found an "epigenetic signature" correlated to obesity – meaning a doctor could theoretically test early in life whether an individual has a predisposition toward obesity.

Through his and similar research, Skinner hopes medicine can move toward "predicting illness," rather than just reacting after the disease is already present.

"We can find the biomarker before the obesity onset early in life and there are preventative treatments we can do if we could detect that susceptibility," Skinner said.

He took cheek swab samples from a set of 22 identical twins. Despite these twins having identical genetics, one twin in each set was obese and the other was not.

Skinner discovered an epigenetic biomarker 90-95% of the time specifically among the obese sibling. Whether the biomarker impacts the obesity itself or is merely correlated with it, a simple test for the biomarker could diagnose someone with the predisposition toward obesity.

"It turns out for many diseases, if you knew that you were going to develop the disease later in life, there are clinical procedures or management conditions or preventative sort of therapeutics that can be taken for a short period of time early in life, and it would delay or prevent the onset of the disease later in life," Skinner said.

The use of twins is common in Skinner's research. In each case, he sourced study participants through the Washington State Twin Registry, which is also based at WSU.

Director of the registry and study co-author Glen Duncan said the use of twins in epigenetic research is vital because it removes the possibility that any difference could

be caused by the genes themselves.

“Twins become a very useful model to study epigenetic phenomenon because you have the same genetic material,” Duncan said. “It’s just that those genes may work a little bit different, and so that’s one of the beauties of the twin model.”

Why is obesity on the rise?

The results of Skinner’s small study need to be confirmed in larger sample sizes. But they point to the idea there is much more going on below the surface of obesity than personal decisions such as diet or exercise.

“The general public has thought that the primary cause for obesity was primarily food intake,” Skinner said. “We just assume everybody that is obese is eating large amounts of food. There are many individuals who don’t do that and yet everything they eat goes to fat and they develop obesity. Two people on the same diet, one can develop obesity and one may not.”

An early life exposure to some environmental factor or an environmental exposure in a previous generation could have a larger impact over whether someone is obese.

The United States has seen a sharp uptick of obesity. According to the Centers for Disease Control and Prevention, 30.5% of Americans were obese at the turn of the millennium, compared to 41.7% of Americans as of 2020.

“It’s not a minor thing,” Skinner said of obesity. “Literally half of the U.S. has metabolic disease and obesity.”

Though it is just a hypothesis, Skinner believes that increase may have less to do with personal choices than a specific pesticide ubiquitously used in America during the mid-20th century.

Called DDT, that compound was banned in the United States in 1972 after it was determined that high exposures could cause cancer, seizures and other conditions. In the years since, the CDC has found levels of DDT have fallen by five to 10 times compared to rates in the 1970s.

Skinner believes high levels of exposure to DDT may have also caused an epigenetic change that promotes obesity when passed down several generations.

In previous research, Skinner exposed rats to the compound and found 50% of the rat population three or four generations later reliably had obesity – even though those rats had no DDT exposure.

Skinner speculates the United States may be seeing the same impact in humans.

“What we see today three generations from the 1950s is that 50% of the human population has obesity,” he said. “My suspicion is the pesticide certainly has a role in what we see today.”

Skinner emphasized that diet and exercise have a large impact on whether a person is obese, but they may not be a solution for the public health crisis of obesity.

“Choice is an important factor,” he said. “If the wrong choices are taken by the individual in terms of diet and the lack of exercise, that will help promote obesity. But I think the general public needs to realize that there’s more to this disease than just how much you eat.

“Whether it was your great-grandparents or whether it was early in your own life – what you did, or what your parents did, needs to be taken into consideration.”