MedicalXpress

Unexpected turn in diabetes research

January 20 2015

Years of diabetes research carried out on mice whose DNA had been altered with a human growth hormone gene is now ripe for reinterpretation after a new study by researchers at KU Leuven confirms that the gene had an unintended effect on the mice's insulin production, a key variable in diabetes research.

Genetically modified mice have been used in medical research for over thirty years. To expedite the cutting-and-pasting of fragments of DNA, the pioneers of the method inserted a human growth hormone gene alongside other modified DNA. Researchers assumed that the DNA of the human growth hormone would remain tightly encapsulated in the modified DNA of the mouse.

They did not expect the mice to begin producing their own human growth hormone - but that appears to be exactly what happened.

KU Leuven professors Frans Schuit and John Creemers used the genetically modified mice regularly in their lab. To their surprise, they observed that the mice showed pregnancy-like symptoms despite not being pregnant at all.

Digging deeper, the researchers discovered that this pregnancy-like state was being caused by the human growth hormone, explains Professor Schuit: "In mice, the human growth hormone has the same effect as hormones that are produced by the placenta in pregnant mice. Just as in pregnancy, the cells in the pancreas that are responsible for the production of insulin change. They increase in number and begin to

produce more insulin. And that happens to be exactly what we study in diabetes research."

Roughly 250 published studies about diabetes were conducted using these tainted mice, continues Professor Creemers: "In many of them, researchers were looking to see if a given gene played a role in insulin production. The genetically modified mice distort the results because of the human growth hormone, so in many cases the effect of that gene was either overvalued or undervalued. Those results now need to be reinterpreted."

"Meanwhile, there are genetically modified mice available today that do not include human growth hormone. These mice can be used to reinterpret previous results," adds Professor Creemers.

Stepping back and correcting false assumptions is part and parcel of the scientific method, concludes Professor Schuit: "We have to continue verifying our methods with a critical eye, even if it means that research advances at a slower pace. For diabetes research, this unexpected turn is an important step forward. Now that the haze around the artificial growth hormone has been cleared, scientists can plan future research with a clear vision."

More information: Impaired Islet Function in Commonly Used Transgenic Mouse Lines Due to Human Growth Hormone Minigene Expression, *Cell Metabolism*, www.cell.com/cell-metabolism/abstract/S1550-4131%2814%2900501-4

Provided by KU Leuven