Maternal protein deficiency during pregnancy 'memorized' by fetal muscle cells

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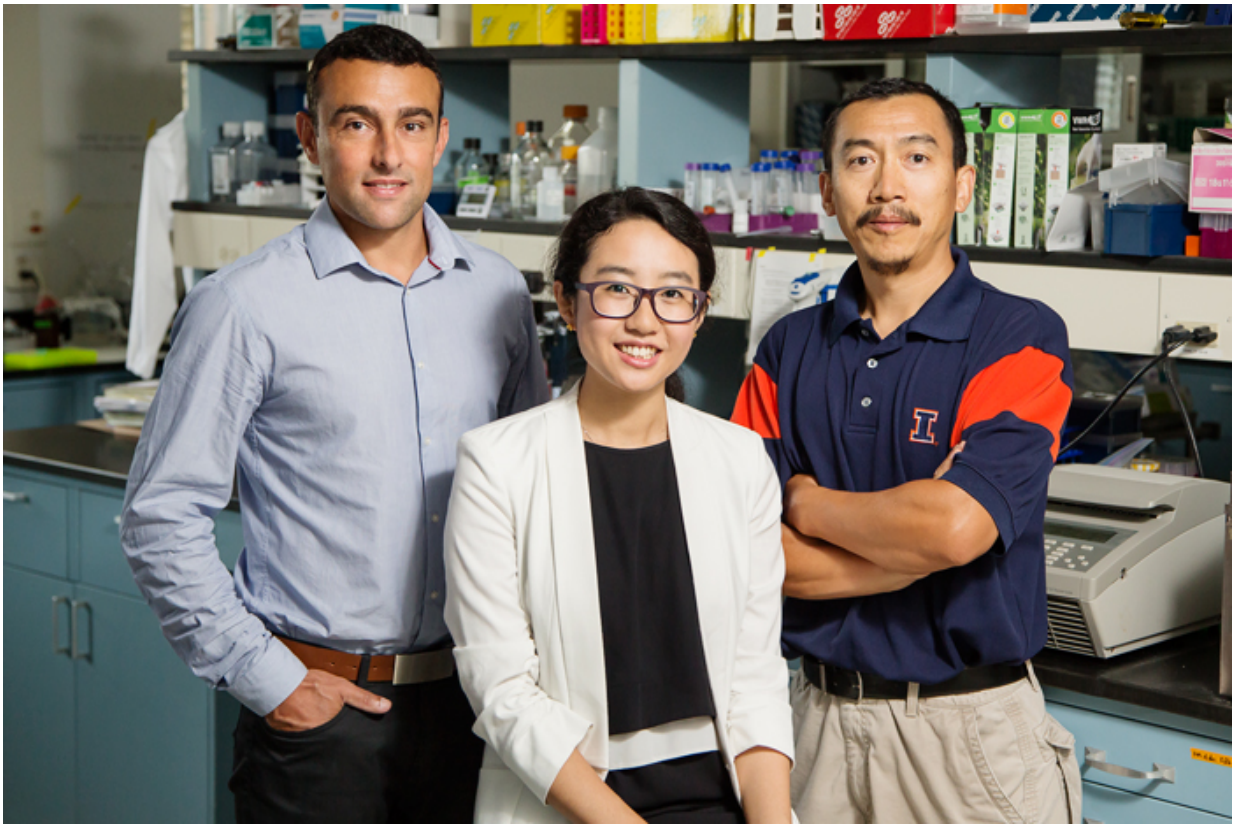

New research by doctoral researcher Huan Wang and food science professor Yuan-Xiang Pan, both at the University of Illinois, found the long-sought link between maternal protein deficiency during pregnancy and problems such as stunted growth and metabolic diseases in offspring. Credit: L. Brian Stauffer

A new study has uncovered the genetic processes that link insufficient

protein consumption during pregnancy with the development of muscle problems in mothers and their male offspring.

The findings also shed light on the metabolic pathway through which these genetic changes are transferred to the fetus, potentially triggering the development of chronic health problems in adulthood such as cardiovascular disease, obesity and Type 2 diabetes, according to researchers at the University of Illinois.

Detecting biomarkers of protein insufficiency during the early stages of pregnancy could enable clinicians to treat it through dietary changes or other strategies, possibly averting many serious health conditions in the next generation, said Huan Wang, the principal investigator on the study, published in the *British Journal of Nutrition*.

Although Wang's study involved rats, prior research has shown that the implications are similar for humans. During pregnancy, women require at least an additional 25 grams of protein per day. Inadequate protein consumption by pregnant women has been linked to their children developing various chronic health problems as adults.

Wang found that inadequate protein intake during pregnancy activates the amino acid response (AAR) pathway, triggering cell destruction - a process called autophagy - as well as atrophy, or wasting, of the mother's skeletal muscles.

Autophagy is a survival mechanism whereby cells under stress conditions degrade unnecessary or dysfunctional components to maintain homeostasis in the body.

These genetic changes may be transferred through the placenta and "memorized" in the skeletal muscles of the fetus, causing low birth weight and stunted growth in male offspring, the research team reported

in the study.

"This is the link we've been seeking for years, which shows transduction from the mom through the placenta to the child," said Wang, who conducted the research while completing her doctorate in food science and human nutrition at Illinois. "However, the cell autophagy is activated in the skeletal muscles of the male offspring only, so there is gender specificity. Apparently the female offspring have more resistance to low-protein exposure during gestation and to cell autophagy."

In Wang's study, pregnant rats in the low-protein group consumed food that contained 8 or 9 percent protein, while those in the control group consumed about twice as much - 18 to 20 percent protein. After giving birth, all of the rats consumed the control diet during lactation, as did all of their pups after weaning. The rats' body weights and food intake were recorded every other day.

The mother rats on the low-protein diet gained significantly less weight during pregnancy, and their pups were smaller at birth, Wang found.

The low-protein diet also changed the levels of key amino acids in the mothers' blood plasma. At the end of pregnancy, mothers in the low-protein group had lower levels of threonine and histidine, and higher levels of alanine, lysine and serine, suggesting potential disturbances in their protein metabolism, according to the study.

Examining the mothers' skeletal muscle fibers after delivery, Wang found evidence of muscle atrophy, including smaller fiber size, greater variation in fiber diameter and split fibers.

Insufficient protein intake also increased the activation of several AAR pathway downstream genes in both the mothers' and their male pups' skeletal muscles. However, their other tissues - and those of the female

pups - were unaffected.

Wang also found that mothers on the low-protein diet showed higher expression of the ATF4 gene, a key regulatory protein within the AAR pathway that recently was found to play a critical role in muscle dystrophy caused by fasting.

ATF4 also has been associated with cell autophagy.

The expression of several autophagy-related genes and the binding of these genes with ATF4 were significantly increased among mothers on the low-protein diet - confirming a molecular link between the activation of the AAR signal and the autophagy pathway, Wang said.

Follow-up data indicated that the AAR- and autophagy-related genes remained activated in the skeletal muscles of the male pups, suggesting that the amino acid limitation signal within the pregnant mothers' skeletal muscles was transferred to the placenta and then to their offspring, according to the study.

The findings underscore the importance of women consuming healthy diets with adequate amounts of protein during pregnancy to protect the health of their children, from birth through adulthood, said Wang, currently a postdoctoral researcher in human genetics at the University of California at Los Angeles.

More information: "Induction of autophagy through the activating transcription factor 4 (ATF4)-dependent amino acid response pathway in maternal skeletal muscle may function as the molecular memory in response to gestational protein restriction to alert offspring to maternal nutrition" journals.cambridge.org/action/ … Id=S0007114515002172