

Researchers define molecular basis to explain link between a pregnant mother's nutrition and infant growth

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A new study, led by OHSU researcher Jae W. Lee, Ph.D., demonstrates that two neurons which are key to growth and metabolism are developmentally interconnected. Credit: OHSU

For years, pregnant mothers have questioned their nutritional habits: "Will eating more cause my baby to be overweight?" Or, "I'm eating for two, so it won't hurt to have an extra serving, right?"

While many factors, such as the age of the mother, overall health and genetics ultimately play a role, the correlation between a mother's nutrition habits and metabolism has been proved to directly impact the growth of her child. And researchers at OHSU in Portland, Oregon, believe they may be one step closer to knowing why.

In a study published online in *Nature Communications*, the research team, led by Jae W. Lee, Ph.D., has demonstrated that two <u>neurons</u> key to growth and metabolism—GHRH and AgRP—are developmentally interconnected.

Located in the hypothalamus region of the brain, within a grouping of neurons known as the arcuate nucleus, GHRH, or growth hormonerelease hormone, neurons orchestrate body growth and maturation. Meanwhile, AgRP, or Agouti-related peptide, neurons stimulate feeding and suppress energy usage.

To understand how these neurons are developed, the research team cataloged various proteins expressed in the arcuate nucleus of mice and analyzed their overall function.

"We found that one specific protein called DLX1 is critical for GHRH neuron development. However, it also suppresses the development of the AgRP neuron," said Lee, a professor of pediatrics in the OHSU School of Medicine and OHSU Doernbecher Children's Hospital. "When DLX1 was removed, the mouse's growth was stunted, yet it appears obese."

Additionally, DLX1 was found to suppress the development of OTPlabeled cells that become AgRP neurons. This would suggest normal

growth development, but limited blockage of energy use, resulting in a trim figure.

"For the first time, these findings prove the intimate relationship between GHRH and AgRP neurons in developmental lineage. Further, the <u>development</u> of both neurons can be artificially preset in controlling postnatal <u>growth</u>," Lee said.

The researchers now are working to determine if DLX1 may be controlled by diet. By testing both high-fat and low-protein—or malnourished—diets in mice, Lee hopes to identify how food impacts a baby's genetic makeup in the womb. This could scientifically support the idea that 'you are what your mother eats.'

More information: Bora Lee et al, Dlx1/2 and Otp coordinate the production of hypothalamic GHRH- and AgRP-neurons, *Nature Communications* (2018). DOI: 10.1038/s41467-018-04377-4

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