High-sugar diet in fathers can lead to obese offspring

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Juan Carreño de Miranda's "La monstrua desnuda" (The Nude Monster) painting.

A new study shows that increasing sugar in the diet of male fruit flies for just 1 or 2 days before mating can cause obesity in their offspring through alterations that affect gene expression in the embryo. There is also evidence that a similar system regulates obesity susceptibility in mice and humans. The research, which is published online December 4 in the Cell Press journal *Cell*, provides insights into how certain metabolic traits are inherited and may help investigators determine

whether they can be altered.

Research has shown that various factors that are passed on by parents or are present in the uterine environment can affect offspring's metabolism and body type. Investigators led by Dr. J. Andrew Pospisilik, of the Max Planck Institute of Immunobiology and Epigenetics in Germany, and team member Dr. Anita Öst, now at Linkoping University in Sweden, sought to understand whether normal fluctuations in a parent's diet might have such an impact on the next generation.

Through mating experiments in Drosophila melanogaster, or fruit flies, the scientists found that dietary interventions in males could change the body composition of offspring, with increased sugar leading to obesity in the next generation. High dietary sugar increased gene expression through epigenetic changes, which affect gene activity without changing the DNA's underlying sequence. "To use computer terms, if our genes are the hardware, our epigenetics is the software that decides how the hardware is used," explains Dr. Öst. "It turns out that the father's diet reprograms the epigenetic 'software' so that genes needed for fat production are turned on in their sons."

Because epigenetic programs are somewhat plastic, the investigators suspect that it might be possible to reprogram obese epigenetic programs to lean epigenetic programs. "At the moment, we and other researchers are manipulating the epigenetics in early life, but we don't know if it is possible to rewrite an adult program," says Dr. Öst.

The fruit fly models and experiments that the team designed will be valuable resources for the scientific community. Because the flies reproduce quickly, they can allow investigators to quickly map out the details of how nutrition and other environmental stimuli affect epigenetics and whether or not they can be modulated, both early and later in life.

"It's very early days for our understanding of how parental experiences can stably reprogram offspring physiology, lifelong. The mechanisms mapped here, which seem in some way to be conserved in mouse and man, provide a seed for research that has the potential to profoundly change views and practices in medicine," says Dr. Pospisilik.

More information: *Cell*, Öst et al.: "Paternal diet defines offspring chromatin state and intergenerational obesity" www.cell.com/cell/abstract/S0092-8674(14)01436-6

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