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Grant to Extend Research into Obesity and Reproduction

A researcher at UC Santa Barbara has received a three-year, \$228,000 grant from the National Science Foundation to explore further the possible link between obesity and reproductive disorders in Zucker rats. The research could yield new clues as to how obesity influences human reproduction.

"The focus has usually been on reproductive difficulties in women who are underweight or undernourished. But the fact is, women who are seriously obese tend to have menstrual cycle irregularities and other reproductive problems. Obese Zucker rats could be a good model for understanding these and other problems related to obesity," said Deborah Olster, a neuroendocrinologist and an associate professor of psychology at UCSB.

Overweight and prone to inactivity, obese Zucker rats are not only unable to reproduce, they suffer from a variety of hormonal and metabolic abnormalities. Olster and her research team want to know if these abnormalities are responsible, at least in part, for the Zuckers' obesity and reproductive dysfunction.

Specifically, the researchers are examining the connection between the reproductive behavior of obese Zuckers and leptin, a hormone produced in fat tissue that, among other things, helps regulate metabolism, food intake, and body weight. While Zucker rats---so named for the researcher who discovered them---produce more than enough leptin, also known as OB protein, they are less able or incapable of

responding to it due to a genetic defect in their leptin "receptors," proteins whose function it is to mediate the hormone's effects on bodily processes.

"The hormone exerts its effects by binding to receptors in target tissues. But the Zuckers' receptors are not fully functional because they've been altered as a result of genetic mutation," said Olster.

"If the primary defect of these animals is that they don't respond normally to leptin, there might be something down the line from what leptin ordinarily does that is essential for normal reproduction. The fact that Zuckers don't respond normally to leptin may trigger a lot of other abnormalities. For instance, they make too much insulin and they're insulin-resistant, similar to humans with adult onset diabetes."

Conclusively identifying leptin-receptor dysfunction as the culprit in Zucker reproductive problems would bring researchers a step closer to firmly establishing such a link in humans---and perhaps to understanding a primary cause of obesity in the world's mammals.

"Most obese humans have been found to produce plenty of leptin, so now the focus is on whether they respond to it. It could be that these people have mutations in their leptin-receptor gene like the Zucker rats," said Olster.

Begun three years ago, Olster's research was originally funded by the National Institutes of Health. Her new National Science Foundation grant will be allocated in yearly sums of \$75,000, \$76,000, and \$77,000.

About UC Santa Barbara

The University of California, Santa Barbara is a leading research institution that also provides a comprehensive liberal arts learning experience. Our academic community of faculty, students, and staff is characterized by a culture of interdisciplinary collaboration that is responsive to the needs of our multicultural and global society. All of this takes place within a living and learning environment like no other, as we draw inspiration from the beauty and resources of our extraordinary location at the edge of the Pacific Ocean.