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Study takes novel approach to understanding pituitary function

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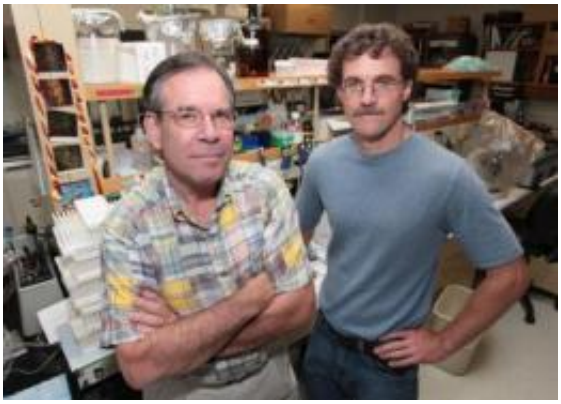

Marc Freeman and Richard Bertram are researchers at Florida State University. Credit: Michele Edmunds/FSU Photo Lab

A Florida State University biologist and mathematician have joined forces to find out exactly how the brain oversees the secretion of the hormone prolactin from the pituitary gland, research that could lead to new ways to treat hundreds of disorders, including infertility.

Marc Freeman, the Lloyd M. Beidler Professor of Biological Science and Distinguished Research Professor Emeritus, and mathematics Professor Richard Bertram have received a $2.64 million, five-year renewal grant from the National Institutes of Health to continue their work. Arturo E. Gonzalez-Iglesias and Joel Tabak-Sznajder, both assistant scholar/scientists in biology at FSU, are working on

experimental and mathematical aspects of the project as co-principal investigators.

"We're taking a mathematical approach to answer a biological question," Freeman said, explaining that he and his colleagues have developed a mathematical model to help them find out more about how an important area of the brain, the hypothalamus, oversees the secretion of prolactin. Primarily known for its role in stimulating the mammary gland to produce milk, prolactin actually plays a role in more than 300 functions in addition to those involving reproduction.

The researchers are testing their theory that secretion of prolactin is inhibited by dopamine and stimulated by oxytocin. In addition, the researchers hypothesize that the activities of these neurons are regulated by the hypothalamus and prolactin itself.

"There are two-way interactions here, with the hypothalamus releasing neurohormones like dopamine and oxytocin that act on pituitary cells and the pituitary cells releasing hormones that act on neurons of the hypothalamus," Bertram said. "These hormones and neurohormones are carried by the blood in contrast to communication by the brain itself, which is primarily carried by neurotransmitters released by synapses."

Freeman, who has received continuous NIH funding since 1974 for his research into how the hypothalamus regulates the pituitary gland in the control of reproduction, said it has long been known that dopamine produced by the hypothalamus inhibits prolactin secretion. However, in the case of breastfeeding, a nursing baby will provide enough prolactin-releasing stimuli to inhibit the mother's dopamine so that she can produce prolactin and subsequently breast milk. About 20 years ago, Freeman found that oxytocin could also stimulate prolactin secretion.

Clarifying the role and mechanisms through which oxytocin interacts

with dopamine to regulate prolactin secretion has important ramifications for the treatment of disorders, including infertility, related to prolactin's hundreds of biological actions, Freeman said.

For example, the findings could lead to the development of a new way to suppress elevated levels of prolactin that are produced by prolactinomas, which are noncancerous pitituary tumors. Women who have prolactinomas have such high levels of prolactin that it inhibits ovulation and they are unable to conceive. Drugs currently used to treat these tumors have serious negative side effects, Freeman said.

Adding a mathematician to the research team has allowed Freeman to look at his ongoing work from a new angle. He began collaborating with Bertram in 2003, with Bertram writing mathematical equations that simulated Freeman's biological data.

Traditionally, biologists develop a conceptual model of how things interact and use this conceptual model to design and interpret experiments, Bertram explained. Typically, this is a verbal model, complemented with a "box-and-arrows" diagram showing the biological players and their interactions. A mathematical model converts the diagram into differential equations, which describe how things affect each other and change over time.

"With a mathematical model, it is much easier to see if hypotheses can possibly work, and to make predictions that can be tested in the lab," Bertram said. "Another benefit of the mathematical model is that it points out missing information — things that are required for the equations but are often overlooked in box-and-arrows diagrams."

Provided by Florida State University