

# New study reveals important role of insulin in making breast milk

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Image: Wikipedia.

Why do so many mothers have difficulty making enough milk to breastfeed? A new study by scientists at Cincinnati Children's Hospital Medical Center and the University of California Davis adds to their previous research implicating insulin's role in lactation success.

The study is the first to describe how the human mammary gland becomes highly sensitive to insulin during lactation. It is also the first study to get an accurate picture of how specific genes are switched on in the human mammary gland during lactation.

The researchers used next generation sequencing technology, RNA sequencing, to reveal "in exquisite detail" the blueprint for making milk in the human mammary gland, according to Laurie Nommsen-Rivers, PhD, a scientist at Cincinnati Children's and corresponding author of the study, published online in *PLOS ONE*, a journal of the Public Library of Science.

Nommsen-Rivers' previous research had shown that for mothers with markers of sub-optimal [glucose metabolism](#), such as being overweight, being at an [advanced maternal age](#), or having a large birth-weight baby, it takes longer for their milk to come in, suggesting a role for insulin in the mammary gland. The new research shows how the mammary gland becomes sensitive to insulin during lactation.

For a long time, insulin was not thought to play a direct role in regulating the milk-making cells of the human breast, because insulin is not needed for these cells to take in sugars, such as glucose. Scientists now, however, appreciate that insulin does more than facilitate uptake of sugars.

"This new study shows a dramatic switching on of the [insulin receptor](#) and its downstream signals during the breast's transition to a biofactory that manufactures massive amounts of proteins, fats and carbohydrates for nourishing the [newborn baby](#)," says Dr. Nommsen-Rivers.

"Considering that 20 percent of women between 20 and 44 are prediabetic, it's conceivable that up to 20 percent of [new mothers](#) in the United States are at risk for low milk supply due to insulin dysregulation."

Dr. Nommsen-Rivers and her colleagues were able to use a non-invasive method to capture mammary gland RNA – a chain of molecules that are blueprints for making specified proteins – in samples of human breast milk. They then created the first publicly accessible library of genes

expressed in the mammary gland based on RNA-sequencing technology.

This approach revealed a highly sensitive portrait of the genes being expressed in human milk-making cells. They discovered an orchestrated switching on and off of various genes as the mammary gland transitions from secreting small amounts of immunity-boosting colostrum in the first days after giving birth to the copious production of milk in mature lactation.

In particular, the PTPRF gene, which is known to suppress intracellular signals that are usually triggered by insulin binding to its receptor on the cell surface, may serve as a biomarker linking insulin resistance with insufficient milk supply. These results lay the foundation for future research focused on the physiological contributors to mothers' milk supply difficulties.

Now that they've demonstrated the significance of insulin signaling in the human mammary gland, they are planning a phase I/II clinical trial with a drug used to control blood sugar in type 2 diabetes to determine whether it improves [insulin](#) action in the [mammary gland](#), thus improving milk supply. While a drug is not an ideal way to solve the problem of sub-optimal glucose metabolism impairing breastfeeding, according to Dr. Nommsen-Rivers, it is excellent for establishing proof-of-concept through the use of a placebo controlled randomized clinical trial.

"The ideal approach is a preventive one," she says. "Modifications in diet and exercise are more powerful than any drug. After this clinical trial, we hope to study those interventions."

Dr. Nommsen-Rivers began her quest to understand why so many U.S. mothers today struggle with low milk supply when she was a doctoral student at the University of California Davis.

Provided by Cincinnati Children's Hospital Medical Center

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