Researchers identify new functional roles on cell surfaces for estrogen

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A discovery by UC Irvine endocrinologists about the importance of cell surface receptors for estrogen has the potential to change how researchers view the hormone's role in normal organ development and function.

To date, scientists in the field focused on receptors in the cell's nucleus as the primary site for estrogen's effect on gene activity and organ development and function. There has been acknowledgement of similar estrogen receptors outside of the nucleus but much debate as to whether they are important.

To investigate this, Dr. Ellis Levin, professor of medicine at UC Irvine, employed a knock-in mouse that prevented the main estrogen receptor, ER-alpha, from trafficking to the cell membrane.

As a result, Levin found that many organs in the female mice were extremely abnormal, including the mammary gland, uterus, and ovaries. Additionally, pituitary hormone production and fat development were also severely impacted, and the mice were completely infertile.

"Until now, research has taken a narrow view on the importance of estrogen signaling outside the nucleus during development," Levin said. "What this study shows is that both nuclear and cell membrane estrogen receptors are required to collaborate for normal organ development and function."

The implications of this discover move beyond development, Levin added, and can include estrogen's role in causing cancers, or preventing cardiovascular diseases and bone diseases. Current therapeutic efforts propose to target estrogen's ability in the nucleus to turn genes on and off, but Levin notes new approaches should also explore irregularities of functions at cell membrane receptors that affect disease.

"The cell membrane receptor is very sophisticated, impacting the nuclear receptor action and modifying certain proteins and their functions throughout the cells of many organs," Levin said. "By studying how to regulate the partnership between these two receptor sets, and modulate membrane receptor signaling, we can understand how to better treat estrogen-linked diseases and gain benefits in other aspects."

Provided by University of California, Irvine