

New clues from fruit flies about the critical role of sex hormones in stem cell control

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In one of the first studies addressing the role of sex hormones' impact on stem cells in the gut, scientists outline new insights showing how a steroidal sex hormone, that is structurally and functionally similar to human steroid hormones, drastically alters the way intestinal stem cells behave, ultimately affecting the overarching structure and function of this critical organ. The authors found that ecdysone, a steroid hormone produced by fruit flies, stimulates intestinal stem cell growth and causes the gut of the female fruit fly to grow in size, and induces other critical changes. The study also provides a mechanism to account for sex-specific roles for intestinal stem cells in normal gut function. Moreover, the research presents evidence that gut hormones may accelerate tumor development. The findings, reported jointly by Huntsman Cancer Institute (HCI) at the University of Utah (U of U) and the German Cancer Research Center (DKFZ), are published today in the journal *Nature*.

Bruce Edgar, Ph.D., a stem cell biologist at HCI and professor of oncological sciences at the U of

U, together with Aurelio Teleman, Ph.D., division head at DKFZ and professor at Heidelberg University jointly led the work. They asked whether sex hormones affect [intestinal stem cells](#)' ability to multiply and contribute to gut growth. "My lab and many others around the world have studied the *Drosophila* gut for some time to better understand how stem [cells](#) are regulated," says Edgar. "We knew that male and female [fruit flies](#) exhibited differences in their intestine—for example, the female's intestine is larger than the male's, and females develop intestinal tumors much more readily than males—but we didn't know why." This study adds significant insights into these differences, and how they arise.

The Edgar and Teleman teams found that ecdysone, a sex-specific [hormone](#), can drastically alter the growth properties of stem cells in an organ that, remarkably, is not directly involved in reproduction. They found that these changes affect the structure and function of the entire organ. They discovered that subjecting male flies to ecdysone caused their otherwise slow dividing stem cells to divide as fast as in females, leading to intestinal growth in males as well. This suggests that the limiting difference between the division of [stem cells](#) in male and female flies is the circulating levels of the hormone.

This process confers both advantages and disadvantages to the female fruit fly during the course of its life. Initially, more ecdysone in females helps with the evolutionarily critical processes of reproduction. It promotes gut enlargement, facilitating nutrient absorption, which helps the fly lay more eggs. But later in life, the ecdysone hormone, produced by the ovaries, eventually causes gut dysfunction that can shorten the lifespan in female fruit flies by creating an environment that favors tumor growth. While humans don't produce ecdysone, they do have related steroid hormones such as estrogen, progesterone and testosterone, which have similar mechanisms of action.

The [experimental work](#) on this study was performed primarily by Sara Ahmed, a joint Ph.D. student between the Edgar and Teleman labs at the Zentrum für Molekulare Biologie der Universität Heidelberg (ZMBH) and the DKFZ. Ahmed designed experiments utilizing various genetic tools to switch genes on and off in different cell types in the fly's intestine and in its ovaries, which produce ecdysone. "Our study provides conclusive evidence that sex hormones alter the behavior of non-sex organs like the intestine," says Ahmed. She further speculates that long-term implications of this research may include exploration of new paths to treating human cancers.

According to the researchers, understanding whether a similar stem cell-hormone relationship operates in human organs will require further studies. They plan to explore this in the future. In addition to the critical role played by sex hormones in intestinal stem cell behavior, the authors believe this study in *Drosophila* potentially unveils a new mechanism that may play out in human physiology and pathology. Insights from this study add to a growing body of work showing that the incidence cancers of non-reproductive organs, including colon and gastric cancers, are different in males and females.

More information: Sara Mahmoud H. Ahmed et al. Fitness trade-offs incurred by ovary-to-gut steroid signaling in *Drosophila*, *Nature* (2020). [DOI: 10.1038/s41586-020-2462-y](https://doi.org/10.1038/s41586-020-2462-y)

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