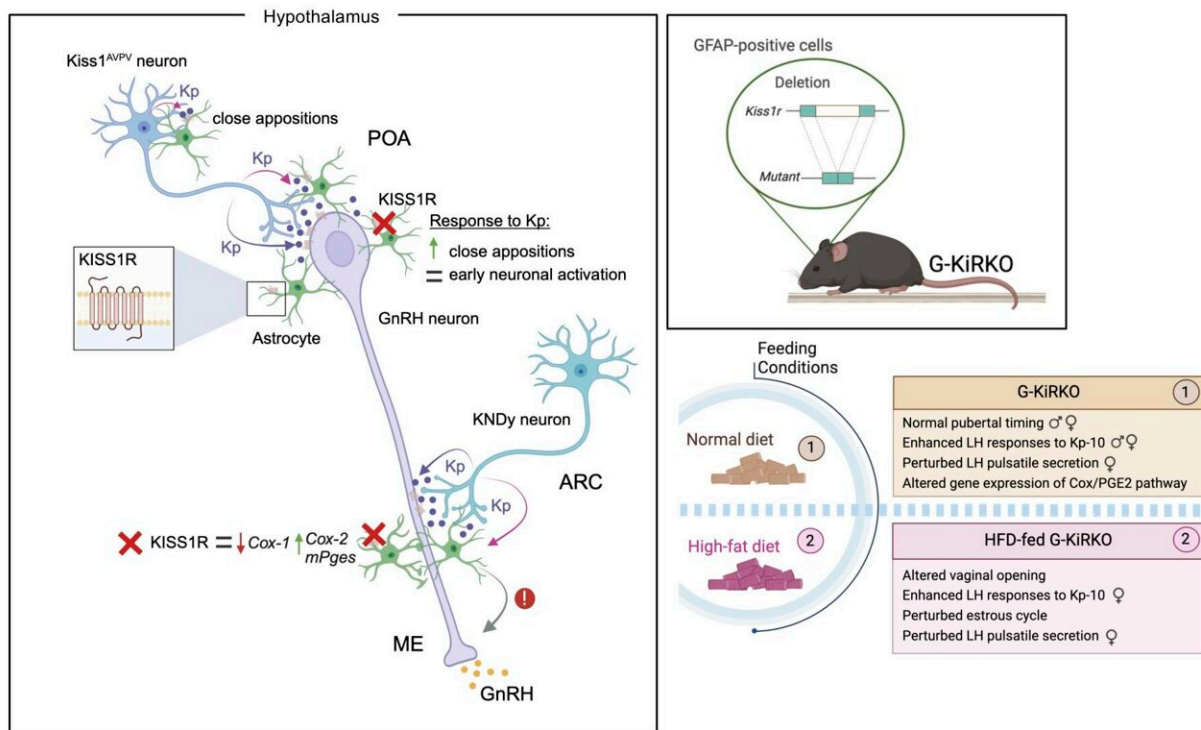


Study describes a new molecular pathway involved in the control of reproduction

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Graphical abstract. Credit: *Journal of Clinical Investigation* (2024). DOI: 10.1172/JCI1172908

Sexual reproduction is protected by a sophisticated network of regulatory systems functioning in a coordinated manner. Within this framework, some of the most important molecules are kisspeptins, proteins produced mostly in the hypothalamus and that play a crucial

role in the regulation of the reproductive system. Recent research coordinated by the University of Cordoba and the IMIBIC has managed to describe, for the first time, a new molecular pathway involved in the control of reproduction and that involves, precisely, these proteins.

The results of the study, in which the researcher Encarnación Torres is the first author, indicate that these molecules, called kisspeptins, modulate the activity of astrocytes, a type of non-neuronal cell that plays key functions in the central nervous system. It was previously believed that all these kisspeptins' interactions occurred with neurons.

This study provided the first evidence that these proteins also act on other cellular elements of the brain. The work is [published](#) in the *Journal of Clinical Investigation*.

A parallel pathway for 'self-regulation'

The study, mainly carried out in [preclinical models](#) using mice, and in collaboration with other institutions, such as the Spanish Biomedical Research Centre in the Physiopathology of Obesity and Nutrition (CIBEROBN) and the Universities of Cambridge (England) and Lille (France), also managed to shed some light on the utility of this new molecular route.

As Manuel Tena-Sempere, co-director of the work, together with researcher Antonio Romero, indicates, the results suggest that this interaction acts as a kind of parallel route supporting the [self-regulation](#) of the brain's reproductive circuits.

It has been known for several decades that kisspeptins stimulate a series of brain neurons, known as GnRH, which control the reproductive axis. According to what was discovered in this new study, kisspeptins also interact with astrocytes, precisely to avert the over-activation of these

neurons present in the brain, thus preventing excessive stimulation, which could generate failures in the reproductive system. In short, it is a control mechanism that allows balance to be maintained.

"As often happens with physiological circuits, more is not always better, and overexpression can produce the opposite of what is sought," Tena stresses.

The role of diet

The Tena-Sempere team has spent years studying the hypothalamus to understand in [greater depth](#) how this region of the brain controls obesity and puberty, and, above all, how these two factors are interrelated.

In this regard, the results of the work have also shown how certain reproductive alterations associated with obesity are also modulated by the action of kisspeptins on astrocytes, something that has been verified by analyzing changes in the reproductive responses of rodents subjected to high-fat diets.

The work, thus, represents a step forward in understanding the complex regulation of the reproductive system. And, although it is classifiable as basic to translational science, it aims to better understand how metabolic and reproductive states interact in order to eventually be able to diagnose alterations, investigate new therapeutic targets, and develop pharmacological treatments.

More information: Encarnacion Torres et al, Kisspeptin signaling in astrocytes modulates the reproductive axis, *Journal of Clinical Investigation* (2024). [DOI: 10.1172/JCI172908](https://doi.org/10.1172/JCI172908)

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