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Gene expression changes in the glucocorticoid receptor of the female reproductive tract in rabbits: a new role in the reproductive physiology?

Glucocorticoids modulate essential animal functions, including reproduction. A new study on their signaling mechanisms, specifically on the changes in gene expression of the NR3C1/GR receptor in rabbits in response to different stimuli, could have potential applications in the use of assisted reproduction techniques in this species and also in other mammals.

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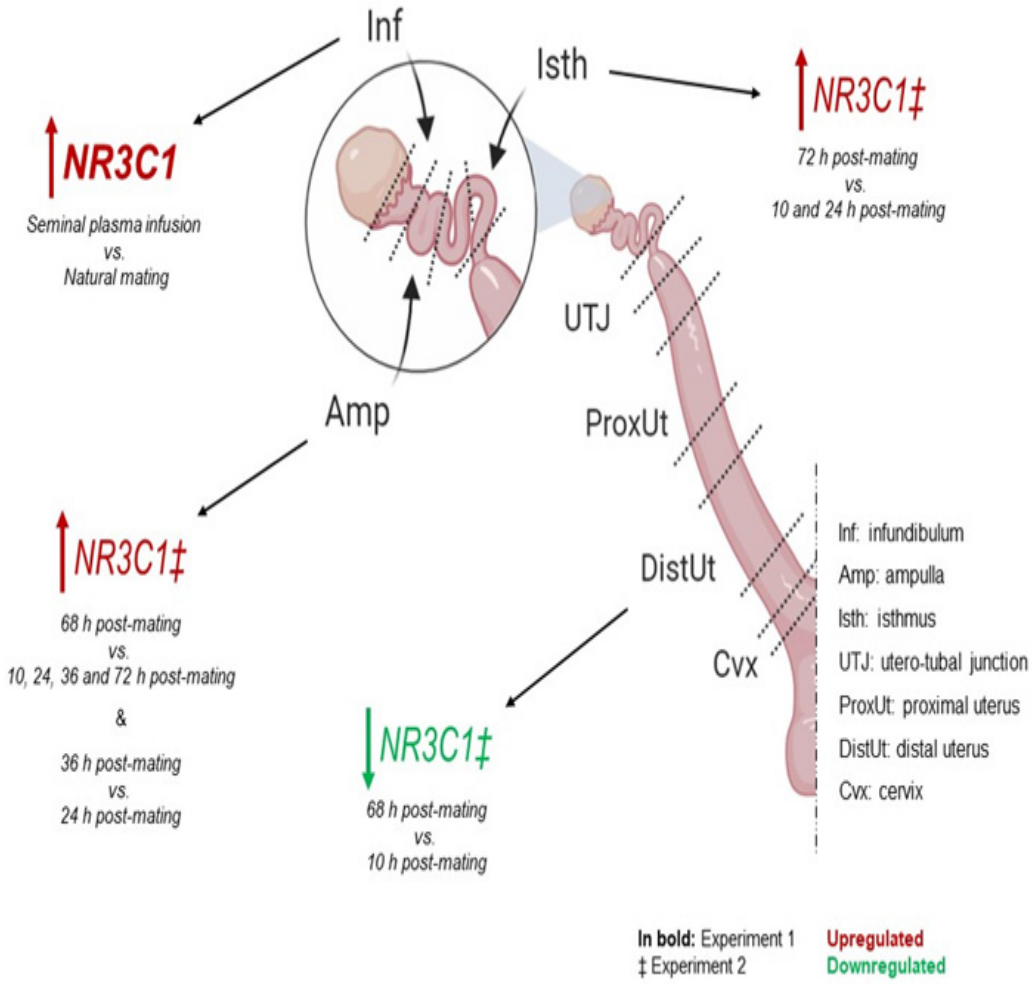
Glucocorticoids are steroid hormones that modulate essential functions for life, such as the response to stressful situations, metabolism, the immune system, and also, reproduction. The actions of these hormones at the cellular level are carried out mainly through the glucocorticoid receptor, also called NR3C1.

Currently, there is a growing interest to better understand the glucocorticoid signaling mechanisms, and their influence on the different stages of reproduction and development in animals, including humans. The rabbit is a suited animal model to study these processes due to its chronological similarity with human embryonic development, and also for being a species of induced ovulation; that is, the female ovulates in response to the stimulus that occurs during intercourse, or during artificial insemination, so the age of the embryo and gestational changes can be easily tracked.

In this study, gene expression changes of the glucocorticoid receptor are described, by means of qPCR mRNA analysis, in seven anatomical regions along the female reproductive tract in rabbits (cervix, distal uterus, proximal uterus, utero-tubal junction, isthmus, ampulla and infundibulum), in response to different stimuli. In the first experiment, the changes produced in the reproductive tract were recorded at 20 hours after the induction of ovulation with gonadotropin-releasing hormone (GnRH) and 1) natural mating, 2) infusion with seminal plasma (sperm-free), or 3) control without any of these stimuli. Our results showed that the NR3C1 gene is overexpressed in the infundibulum compared to other regions, especially after insemination with seminal plasma. These results suggest that, although seminal plasma does not reach the infundibulum, anatomically close to the ovary, it could activate signaling cascades relevant to the immune response and ovulation, among others.

In the second experiment, changes were recorded at 10, 24, 36, 68 and 72 h after mating, time periods corresponding to the phenomena of ovulation, fertilization, and different moments of the embryonic development prior to the implantation in the uterus. We found that the expression of NR3C1 increased in the anatomical regions of the tract that matched with the theoretical location of the rabbit embryos, which could suggest an active participation of the receptor in these reproductive processes. This increased expression is especially pronounced in the isthmus at 72 h, where the embryos are retained and continue their maturation towards the blastula stage to reach the uterus.



Representative diagram of the main changes in the gene expression of NR3C1 throughout

the different tissues of the female reproductive tract in rabbits. Increased expression is depicted in red, while decreased expression is depicted in green.

Being the first time that the gene expression of NR3C1 has been reported in the reproduction of this species, in this study we describe changes during the journey that the embryos make through the maternal tract from the place of fertilization - the ampulla, until they reach the uterus, where the implantation will be established. Taking these results into account, glucocorticoids could play a relevant role in reproduction and early embryonic development through their receptor. Although the molecular mechanisms behind this signaling are complex, and in part still unknown, a greater understanding of reproductive physiology in this topic could have potential applications in the use of assisted reproductive techniques in this species and other mammals.

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