MATING EFFECTS ON FEMALE REPRODUCTIVE ORGANS: THE PARADIGM OF ESTROGEN SIGNALING PATHWAYS IN THE OVIDUCT

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ABSTRACT

Mating induces several physiological changes in the female reproductive tract independently of oocyte fertilization, which are potentially required for a successful pregnancy. These effects include modifications in the cellular and molecular mechanisms by which some steroidal hormones exert their actions in the oviduct and uterus, changes in the expression of some key molecules inside the uterus and modulation of the steroidogenic functions in the ovary.

Mating impinges on the female reproductive tract with sensory stimulation, seminal fluid and sperm cells, so these effects may involve a direct interaction between the cells of the female reproductive tract and the different components of the seminal plasma and/or spermatozoa to modulate the immune system or neuroendocrine changes elucidated by the mechanical stimulation of the cervix, which indirectly affect the functioning of the cells that compose the female reproductive tract.

In this chapter we will review the available literature on the effects of mating in the physiology of oviduct, ovary and uterus highlighting a hitherto unsuspected early, strong and broad influence of mating on the physiology of female
reproductive organs. We will be specially centered into review of the well-defined effect of mating on the rat oviduct, where it changes the mechanism by which estradiol accelerates oviductal egg transport, from a nongenomic to a genomic pathway. This change has been named intracellular pathway shifting (IPS) and reflects a novel example of functional plasticity in well-differentiated cells induced by mating. We will describe that IPS involves inhibition of the conversion of estradiol to 2-methoxyestradiol, which probably protects the embryos from the deleterious effect that methoxyestradiols exert during the embryo development. IPS seems to involve changes in intraoviductal signaling mediated by cytokines TNF-α and TGFβ and is independently induced either by cervico-vaginal stimulation with a rod glass or by intrauterine insemination. Such redundancy of triggering factors suggest that IPS is an important element in the reproductive strategy.

**Keywords:** Mating, female reproductive organs, estradiol, reproductive strategy, and cytokines

**INTRODUCTION**

Mating components include sensory stimulation, seminal plasma and spermatozoa. Either individually or collectively, these constituents impact the female physiology through their interaction with cells composing the female reproductive tract. It is now widely accepted that, independently of its fertilizing role, mating has physiological relevance since it affects at molecular and cellular level the functioning of reproductive organs near or beyond to the site of insemination.

The relevance of mating-associated factors on the molecular and cellular changes occurring in the female reproductive organs is clearly illustrated by the fact that both cervico-vaginal stimulation and the presence of spermatozoa can itself changes the mechanism by which estradiol (E2) regulates oviductal egg transport, from a nongenomic mode to a genomic mode. We have denominated this shunt in E2 pathways *intracellular path shifting (IPS)*. The biological basis of IPS involves silencing of the intraoviductal E2 non-genomic pathway at least at two levels: 1) Inhibiting the expression and activity of Catechol-O-Methyl-Transferase (COMT) therefore decreasing production of 2-Methoxyestradiol (2ME) in the oviductal cells and 2) silencing the signaling cascades downstream of 2ME in the oviductal cells.

In this chapter we review the effects of mating and associated components on ovarian and uterine physiology of some mammals and discuss the