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The Role of Mating in Oviduct Biology

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SUMMARY

The oviduct connects the ovary to the uterus, and is subject to changes that influence gamete transport, fertilization, and early embryo development. The ovarian steroids estradiol and progesterone are largely responsible for regulating oviduct function, although mating signals also affect the female reproductive tract, both indirectly, through sensory stimulation, and directly, through contact with seminal plasma or spermatozoa. The resulting alterations in gene and protein expression help establish a microenvironment that is appropriate for sperm storage and selection, embryo development, and gamete transport. Mating may also induce the switch from a non-genomic to a genomic pathway of estradiol-accelerated oviduct egg transport, reflecting a novel example of the functional plasticity in well-differentiated cells. This review highlights the physiological relevance of various aspects of mating to oviduct biology and reproductive success. Expanding our knowledge of the mating-associated molecular and cellular events in oviduct cells would undoubtedly facilitate new therapeutic strategies to treat infertility attributable to oviduct pathologies.

[M]ating-associated signals exert a profound influence on the oviduct environment and affect the odds of a successful pregnancy.

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INTRODUCTION

The oviduct is subject to dynamic changes that modulate complex events including gamete transport, fertilization, and embryo development (Hunter, 2012). Assisted reproductive techniques may be sufficient to bypass oviduct function in some species, whereas adding oviduct fluid to the gamete or embryo culture may be beneficial or even essential for increasing the number or viability of embryos in other species (Bavister, 2000). These findings indicate that

Abbreviations: 2ME, 2-methoxyestradiol; COMT, catechol-o-methyltransferase; E_2, estradiol; PTGS2, prostaglandin-endoperoxide synthase 2; TGFβ1, transforming growth factor-beta 1; TNFα, tumor necrosis factor alpha

oviduct secretions play a key role in establishing a favorable microenvironment for embryo development (Ménézo et al., 2012). Changes in embryo transport rate can also lead to infertility or ectopic (tubal) pregnancy, a common and potentially life-threatening health problem (Shao et al., 2009; Ezzati et al., 2014); consequently, a focus of recent work is the role of oviduct function in reproductive success. Fluctuations in the levels of the ovarian steroids estradiol (E_2) and progesterone are the primary regulators of oviduct function, although the act of mating also influences oviduct physiology in a variety of species (Orihuela et al., 2001; Shafik et al., 2005, 2006; Kapelnikov et al., 2008; Apichela et al., 2013).

Mating affects the female reproductive tract through sensory stimulation and contact with seminal plasma and sperm cells (Fig. 1). Although mating primarily provides spermatozoa for fertilization, the behavior also affects the molecular and cellular function of reproductive organs proximal and distal to the insemination site (Erskine, 1995; Robertson, 2005). In the oviduct, mating influences gene and protein expression (Fazeli et al., 2004; Kapelnikov et al., 2008; Artemenko et al., 2015), modulating processes such as angiogenesis (Krawczynski and Kaczmarek, 2012), sperm storage and selection (Apichela et al., 2013; Almiñana et al., 2014), preimplantation embryonic development (Chan et al., 2001), and oviduct motility and egg transport (Orihuela et al., 2001; Shafik et al., 2006). Mating also affects E_2-accelerated egg transport in the rat oviduct, inducing the shift from a non-genomic to a genomic mechanism (Orihuela et al., 2001, 2006).

Here we assess the known cellular and molecular mechanisms underlying mating-associated signals that influence oviduct biology. First, we review the global effects of mating on oviduct gene expression, as reported for invertebrate and vertebrate models. We then analyze the individual contribution of various aspects of mating to oviduct function. Finally, we provide a detailed discussion of the mechanism by which mating switches the mode of action of E_2 in the oviduct, including the role of the cytokines tumor necrosis factor alpha (TNFα) and transforming growth factor beta (TGFβ).

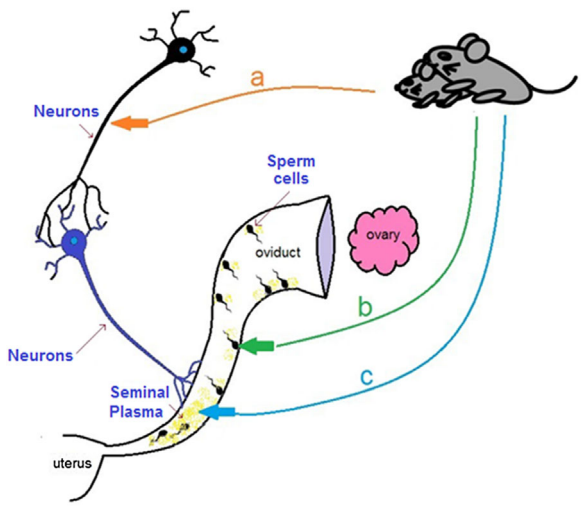

Figure 1. Mating-associated factors that may influence oviduct function. **a**: Sensory stimulation. **b**: Interaction of spermatozoa with oviduct cells. **c**: Molecular components of seminal plasma.

INFLUENCE OF MATING ON OVIDUCT GENE EXPRESSION

Various studies analyzing gene expression in oviduct cells have helped elucidate the role of mating in oviduct function. Among vertebrates, studies by Fazeli et al. (2004) reported changes in the transcriptome of the mouse oviduct shortly after coitus: A microarray analysis using whole oviducts from female mice 0 to 6 hr after mating showed that 58 and 156 transcripts, out of a total of 11,263, were respectively up- and down-regulated after mating; these changes were enriched for the signaling pathways of adrenomedullin (*Adm*), integrin-α4 (*Itga4*), cadherin 15 (*Cdh15*), and prostaglandin-endoperoxide synthase 2 (*Ptgs2*), and for transcription regulators, such as activating transcription factor-3 (*Atf3*) and basic helix-loop-helix domain containing class B2 (*Bhlhe40*). Using a similar paradigm in the rat, Parada-Bustamante et al. (2007) found that only 17 out of 31,100 transcripts (12 up-regulated and 5 down-regulated) were significantly altered 6 hr after mating. The rat genes regulated by mating include enzymes such as phospholipase B (*Phlpb*), *Ptgs2*, or catechol-O-methyltransferase (*Comt*); ion channels such as calcium channel voltage-dependent gamma subunit 4 (*Cacng4*) or potassium inwardly-rectifying channel subfamily J member 16 (*Kcnj16*); and neurotransmitter receptors as glutamate ionotropic receptor AMPA type subunit 4 (*Gria4*). López-Úbeda et al. (2015) recently compared oviduct gene expression between inseminated and non-inseminated pigs, reporting that, out of a total of 43,263 transcripts, 17 were up-regulated and 9 were down-regulated 24 or 48 hr after insemination. Bioinformatics analysis of the differential transcriptome revealed gene clusters associated with immune response—including complement component 3 (*C3*), MHC class I antigen 3 (*SLA-3*), immunoglobulin G gamma 1 heavy chain (*IGHG1*), or tumor necrosis factor (*TNF*); molecular transport, protein trafficking, and developmental disorders—including torsin family 3, member A (*TOR3A*) or RAB1B, member RAS oncogene family (*RAB1B*); and cell–cell signaling and interaction—including cytochrome P450, family 51, subfamily A, polypeptide 1 (*CYP51*), parathyroid hormone 1 receptor (*PTH1R*), and tropomodulin 3 (*TMOD3*).

Similar comparative approaches were performed for invertebrates, specifically using the fruit fly *Drosophila melanogaster*. Kapelnikov et al. (2008) performed a comparative microarray study in unmated and mated oviducts, and found 53 out of a total of 5,615 transcripts were present only in unmated oviducts and 198 transcripts were only in mated oviducts; 155 genes were

also differentially expressed 3 hr post-mating—33 were up-regulated and 122 were down-regulated. Analysis of the genetic network identified a cluster of immune-responsive genes, such as the cationic peptides Cecropin A1 (*CecA1*) and A2 (*CecA2*) and glycine-rich peptides attacin *A* (*AttA*) and *B* (*AttB*), while another cluster included genes related to cell growth and differentiation, such as Reptor-binding partner (*Reptor-bp*), Thor (*Thor*), and a positive regulator of homeotic genes Homeotic discs-2 (*Ash2*) (Giot et al., 2003; Stanyon et al., 2004). McGraw et al. (2004) used a different approach, analyzing the effect of mating on gene expression in the whole female. The authors mated Drosophila females to normal males, males lacking spermatozoa, or males lacking both spermatozoa and seminal plasma proteins. At 1–3 hr post-mating, 549 genes showed altered expression in response to sperm cells, 160 in response to seminal proteins, and 1,074 in response to other aspects of mating—likely sensory stimulation. Despite evaluating the whole body, these results clearly demonstrate that sperm, seminal proteins, and sensory stimulation robustly and differentially affect the female reproductive tract. Furthermore, a comparison between the Kapelnikov et al. (2008) and McGraw et al. (2004) studies revealed that 66 genes were induced by mating in both the whole-body and the oviduct analyses; of these genes, 11 were mediated by seminal proteins, 28 by spermatozoa, and 27 by another signal, presumably vaginal stimulation.

A comparison of the affected genes reported among all species suggests that multiple oviduct functions are regulated in response to mating. Genes associated with changes in the growth and differentiation of oviduct cells, for example, could affect remodeling of the epithelium layer, allowing for efficient egg activation and fertilization as well as preimplantation embryo development (Abe et al., 1999; Kapelnikov et al., 2008; Chen et al., 2013). Another cluster of genes relates to modulation of the immune system, which may play a role in maintaining a microbe-free environment in the oviduct (Kylsten et al., 1990; Cardenas et al., 1998; Jeoung and Bridges, 2011) or providing maternal immune tolerance to paternal antigens from sperm cells, as occurs in the uterus (Hancock and Faruki, 1986). Genes associated with smooth muscle contraction, such as *Ptgs2* and *Gria4*, could help regulate oviduct motility; in this context, oviduct contraction in Drosophila is modulated by glutamatergic neurons (Rodríguez-Valentín et al., 2006) while prostanoids metabolized by cyclooxygenases are essential for oviductal egg and embryo transport (Rodríguez-Martínez and Einarsson, 1985; Ortega-Moreno, 1995; Wijayagunawardane et al., 2001). Expression changes in genes that code for cell-signaling or interaction proteins, on the other hand, may participate in the establishment of a sperm reservoir in the oviduct (Cortés et al., 2004; Suarez, 2016). Thus, these gene expression analyses clearly highlight the profound influence of mating on oviduct cells, while identifying the specific genes that change following mating help decipher the molecular signals underlying mating-associated signaling.

ROLE OF MATING-ASSOCIATED SIGNALS IN OVIDUCT FUNCTION

Sensory Stimulation

Vaginal stimulation induced by penile buffeting initiates neuroendocrine or neural reflexes in vertebrates that trigger the release of a variety of molecules, such as prolactin, progesterone, opioids, nitric oxide, oxytocin, and neuromodulators that can induce changes in the oviduct (Erskine, 1995; Guevara-Guzman et al., 2001). The afferent neural pathways associated with vaginal stimulation travel through the hypogastric, pelvic, and pudendal nerves, via somata localized in the dorsal root ganglia of spinal regions T13–L3 and L6–S1 (Jobling et al., 2010). The efferent pathway is mainly associated with adrenergic and cholinergic innervation from the T14–L5 sympathetic chain ganglia and prevertebral ganglia, such as the celiac-superior mesenteric ganglion complex; the adrenal, aortic-renal, and ovarian ganglia; and the inferior mesenteric ganglia (Czaja et al., 2001). A variety of neuropeptide and gamma-aminobutyric acid (GABA) innervation patterns have also been detected in the extrinsic innervation of the oviduct (Erdö and Amenta, 1986; Sedra et al., 2015), confirming the presence of afferent and efferent innervation that supply the oviduct vasculature, smooth muscle, and epithelial cells as well as providing a plausible means for regulating oviduct motility and secretory activity by mating-induced sensory stimuli (Fig. 1).

Several studies have shown that vaginal stimulation exerts a direct effect on the brain and pituitary gland (Erskine, 1995), whereas few studies have explored the relationship between vaginal stimulation and oviduct function. Shafik et al. (2005, 2006) provided unequivocal evidence that sensory stimulation can directly influence oviduct motility by recording changes in oviduct pressure following electrical and mechanical cervical-uterine stimulation in 16 women with regular menstrual cycles. These authors observed a rise in pressure in the ampullary and isthmic regions of the oviduct and a drop in pressure within the intramural segment of the oviduct, which are consistent with a cervico/utero/tubal-reflex loop induced by cervical sensory stimulation that may be involved in gamete transport and fertilization (Shafik et al., 2005, 2006).

Seminal Plasma

Seminal plasma provides a survival medium for sperm transported along the female reproductive tract. This fluid is an abundant source of active molecules, including lipids, glycans, steroids, prostaglandins, cytokines, inorganic ions, peptides and proteins, cell-free DNA, RNA, and oligosaccharides (Agarwal et al., 2004; Assumpção et al., 2005; Bergeron et al., 2005; Kareskoski and Katila, 2008; Drabovich et al., 2014). The biochemical composition of seminal plasma is complex and species-dependent (Chandonnet et al., 1990; Killian et al., 1993; Aurich et al., 1996), suggesting that its role in the oviduct may vary among species. The contents of seminal plasma

derive from secretions of the testes, epididymis, and accessory sex glands (seminal vesicle, prostate, and bulbo-urethral glands), with species-dependent variations in which organs contribute specific components (Metafora et al., 2008). Although the utero-tubal junction filters the seminal plasma, small amounts of plasma may enter the oviduct along with the spermatozoa due to sustained uterine peristaltic contractions—which is especially likely in species in which spermatozoa are deposited directly into the uterus (mice, rats, hamster, pig, dog, llama) rather than the cervix/vagina (human, rabbit, rabbits, sheep, cows) (Kunz et al., 2006).

The importance of seminal plasma in oviduct function was tested in proestrus female hamsters and mice that were hand-mated to males with ablated accessory sex glands or seminal vesicles, followed by recovery of the preimplantation embryos from the oviduct 26–72 hr post-mating (Chan et al., 2001; Bromfield et al., 2014). Abnormally low numbers of early embryos were observed in these hamsters and mice, suggesting that seminal plasma components are required for adequate preimplantation embryo development, independent of species. Elegant studies by Kaczmarek et al. (2010), in the pig, and by Bromfield et al. (2014), in the mouse, elucidated the molecular mechanisms potentially underlying the influence of seminal plasma on embryo development in the oviduct. Kaczmarek et al. (2010) injected 100 ml of seminal plasma into uterine horns of pre-ovulatory gilt pigs, and then surveyed the mRNA and protein content for a variety of enzymes involved in prostaglandin synthesis 24 hr after insemination. These authors reported the down-regulation of prostaglandin F2-alpha ($PGF_{2\alpha}$) synthase and prostaglandin 9-ketoreductase, which mediate conversion of PGE_2 to $PGF_{2\alpha}$. PGE_2 secretion also increased in primary cultures of oviduct epithelial cells isolated from gilt pigs 12 hr after treatment with 2.5–20% seminal plasma (Kaczmarek et al., 2010). Follow-up studies by Krawczynski and Kaczmarek (2012) found increased mRNA encoding the angiogenic factors fibroblast growth factor-2 (*FGF2*) and von Willebrand factor (*VWF*) in the gilt oviduct 1 day after insemination with seminal plasma. Seminal plasma components may therefore interact with oviduct cells, favoring PGE_2 production in the oviduct fluid (Rodríguez-Martínez and Einarsson, 1985; Gabler et al., 2008), which could stimulates angiogenesis by activating the fibroblast growth factor system that supports vascular remodeling to provide embryotrophic factors in the oviduct milieu (Finetti et al., 2012). Studies by Bromfield et al. (2014) support the latter notion that seminal plasma induces embryotrophic cytokines in the oviduct: They reported decreased mRNA abundance for the cytokines colony-stimulating factor (*Csf2*), leukemia inhibitory factor (*Lif*), and inteleukin-6 (*Il6*) in the oviducts of female mice mated to males with ablated seminal vesicles, indicating that seminal plasma components modulate the embryotrophic response in the oviduct.

Seminal plasma proteins can also modulate adhesion of spermatozoa onto specialized oviduct cells in a region termed the oviductal sperm reservoir. Gwathmey et al. (2003, 2006) incubated bull epididymal spermatozoa with oviduct epithelium explants for 20–35 min in the presence of the seminal proteins PDC-109, BSP-A3, or BSP-30-KDa, and reported increased spermatozoa binding to oviduct cells in the tissues exposed to these proteins as compared to controls incubated without the proteins. Recently, Henry et al. (2015) reported that motile epididymal spermatozoa from domestic cats preincubated for 30 min with seminal plasma could increase its bind to oviduct epithelial cell explants from preovulatoy females. These findings are supported by an elegant study by Apichela et al. (2013), who mated female llamas to males with ablated bulbourethral glands, excised the oviducts 24 hr after mating, and used scanning electron microscopy to visualize the number of adherent spermatozoa in the various oviduct regions. In contrast to oviducts from females mated to normal males, no spermatozoa were bound to epithelial cells in the uterine-tube junction explants from the experimental animals. Biochemical analysis of seminal plasma proteins extracted from normal males and males with ablated bulbourethral glands revealed that a $>$300 kDa proteoglycan of keratin sulphate is absent in the semen of males without bulbourethral glands; this protein could be the dominant factor in seminal plasma responsible for the formation of an oviductal sperm reservoir in the llama. The anatomical origins of the seminal plasma proteins differ greatly between the bull versus the llama: Seminal vesicle secretions account for all of the major plasma proteins in the bull (Bergeron et al., 2005), whereas seminal plasma arises from the bulbourethral glands and prostate in the llama (Tibary and Vaughan, 2006). Yet, the fact that seminal plasma secretions enhance sperm binding to the oviduct independent of anatomical origin suggests that their effect plays a crucial role in reproduction.

Spermatozoa

Sperm bind to epithelial cells in the oviduct (Cortés et al., 2004; Suarez, 2016), so these gametes likely exert a direct effect on oviduct function. Pioneering work performed in the equine by Ellington et al. (1993a) showed that binding of spermatozoa to oviduct epithelial cell monolayers increases intracellular calcium in the epithelial cells. Further studies by Ellington et al. (1993b) and Thomas et al. (1995), using co-cultures of bull or stallion spermatozoa with oviduct epithelial cells, revealed that sperm binding may induce or inhibit de novo protein synthesis in the oviduct epithelium; however, the specific molecules synthesized were not identified, complicating biological interpretation. Valuable studies by Fazeli et al. (2004) elucidated the molecules involved in oviduct epithelial response to the presence of spermatozoa. Microarray plus quantitative PCR analysis of the oviducts from female mice mated with fertile or T145H-mutant males, which produce seminal plasma but no spermatozoa, identified two transcripts, *Adm* and *Ptgs2*, that increase in abundance after mating with fertile males, indicating that spermatozoa induce their expression in the oviduct. ADM (adrenomedullin) is a hypertensive peptide hormone involved in the

control of ciliary beating frequency, smooth muscle contraction, and inflammatory response in the oviduct (Liao et al., 2013; O et al., 2013; Li et al., 2015); decreased ADM expression correlates with the pathogenesis of tubal pregnancy (Li et al., 2015). PTGS2 is also associated with oviduct motility and inflammatory responses that facilitate gamete and embryo transport and allogenic spermatozoa recognition (Wijayagunawardane et al., 2005; Holt and Fazeli, 2015). A proteomic approach was used by Georgiou et al. (2005) and Artemenko et al. (2015) to identify proteins in the rabbit and porcine oviduct epithelial cells that are regulated by spermatozoa at various times after insemination, revealing various clusters of activity that are mainly associated with antioxidant activity and free radical scavenging, protein folding and stability, and cell metabolism; how these components contribute to oviduct biology remains unknown.

An astonishing role for the interaction between spermatozoa and oviduct cells was recently revealed by Almiñana et al. (2014) after inseminating X- or Y-sperm cells into each oviduct of a single gilt, and analyzing oviduct gene expression by microarray 24 hr after insemination: 501 transcripts showed differential expression in oviducts exposed to Y versus X spermatozoa. In addition, more genes involved in signal transduction and immune system function were expressed after insemination with Y spermatozoa, suggesting that oviduct cells can discriminate between X and Y content and potentially modulate gender selection of the offspring. Further studies are needed to determine how oviduct cells distinguish between X and Y spermatozoa since no differences in morphology, metabolic activity, or functionality between X and Y spermatozoa have been reported (Hossain et al., 2001).

MATING SWITCHES THE MECHANISM BY WHICH E_2 ACCELERATES OVIDUCTAL EGG TRANSPORT FROM A NON-GENOMIC TO A GENOMIC PATHWAY

Injecting E_2 on the first day of the rat estrous cycle or pregnancy reduces oviduct transport of eggs, from the typical 72–96 hr to less than 24 hr (Orihuela et al., 2001). This phenomenon is known as E_2-induced acceleration of oviduct transport. In cycling rats, accelerated egg transport induced by E_2 is blocked by the broad-spectrum protein kinase inhibitor H-89, but still occurs under conditions in which mRNA transcription and translation are totally suppressed by actinomycin D and cycloheximide, respectively; in pregnant females, however, accelerated egg transport induced by E_2 is blocked by actinomycin D but not by H-89 (Orihuela et al., 2001; Orihuela and Croxatto, 2001). Mating therefore induces a switch in the mechanism by which E_2 accelerates oviductal egg transport, from a non-genomic to a genomic pathway.

The non-genomic E_2 pathway requires prior conversion of E_2 to its metabolite 2-methoxyestradiol (2ME), which is mediated by COMT activation and involves sequential activation of cyclic adenosine monophosphate (cAMP)/protein kinase A (PKA)/phospholipase C (PLC)/inositol triphosphate (IP3) signaling in oviduct cells of unmated rats (Orihuela et al., 2006; Parada-Bustamante et al., 2007). Conversely, the E_2 genomic pathway involves changes in oviductal protein synthesis associated with signaling through endothelin-1 (Parada-Bustamante et al., 2012) and S100G (Ríos et al., 2011). Both E_2 pathways require participation of estrogen receptors (ER), albeit the non-genomic pathway operates through both ESR1 and ESR2 whereas the genomic only requires ESR1 (Orihuela et al., 2009). Our current model is that the E_2 non-genomic intra-oviductal pathway is blocked at two levels after mating: First by inhibiting *Comt* expression and enzyme activity, thereby decreasing 2ME production in the oviduct cells, and second by silencing signaling cascades downstream of 2ME in the oviduct cells (Parada-Bustamante et al., 2007).

Vaginal stimulation of proestrus rats, induced with a glass rod or intrauterine administration of spermatozoa, can shut down the non-genomic E_2 pathway in the oviduct (Peñarroja-Matutano et al., 2007; Parada-Bustamante et al., 2003). Thus, vaginal stimulation or sperm acting directly on the female genital tract can independently mimic the effect of mating on E_2 signaling in the oviduct, suggesting that redundancy in E_2 activation of oviduct function is a reproductive strategy by which mating can consistently result in pregnancy in rats. The mating-associated inhibition of *Comt* expression and enzyme activity, as well as inhibition of downstream 2ME signaling, likely protects early embryos from the deleterious effects of 2ME (Lattanzi et al., 2003). On other hand, the effect of seminal plasma alone on the non-genomic E_2 pathway was not studied in the rat oviduct.

MATING INHIBITS THE NON-GENOMIC E_2 PATHWAY IN THE OVIDUCT THROUGH TNFα

Cytokines modulate COMT activity in many organs, including the brain, placenta, and uterus (Wentz et al., 2006; Tchivileva et al., 2000; Das, 2015). Oróstica et al. (2013) showed that mating increases TNFα abundance in the oviduct fluid, and that administering this cytokine into the oviduct of cycling rats mimicked the effect of mating, accelerating E_2-induced egg transport. Mating decreased TGFβ1 concentration in the plasma but not the oviduct fluid; however, neutralization of circulating TGFβ1 did not prevent the effect of E_2 on egg transport (Oróstica et al., 2014). Taken together, these results indicate that TNFα is a mating-induced signal that can switch how E_2 accelerates oviductal egg transport from a non-genomic to a genomic pathway. The role of TGFβ remains to be determined (Fig. 2).

Although few studies evaluated the role of TNFα in the oviduct—other than findings related to inflammatory processes—evidence does support an association between TNFα and cell and tissue damage, observed in

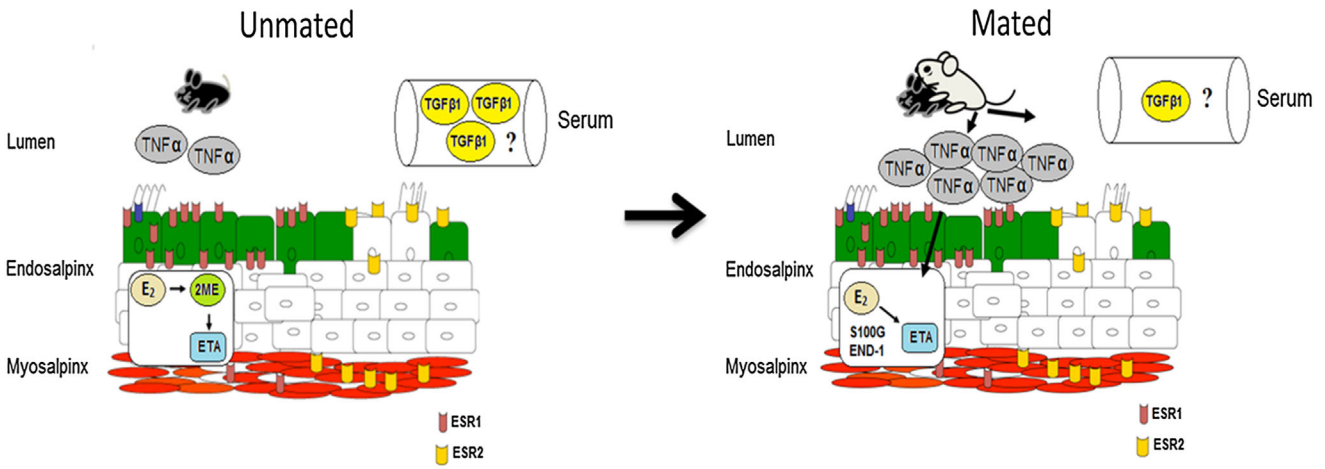

Figure 2. Proposed model describing how mating-induced release of the cytokine TNFα into the oviduct lumen switches the mechanism by which E_2 accelerates egg transport (ETA) in the rat. END1, endothelin 1; S100G, calcium-binding protein S100G; ESR1, estrogen receptor-alpha; ESR2, estrogen receptor-beta.

gonococcal salpingitis (Morales et al., 2006), as well as regulation of the oviduct motility necessary for transporting the embryo into the uterus at the optimal time for implantation (Wijayagunawardane et al., 2003). These findings thus suggest a new physiological function for TNFα in the mammalian oviduct that is specifically associated with a change in mating-induced E_2 signaling.

CONCLUDING REMARKS

The oviduct is responsive to cellular and molecular signals induced by mating. Sensory stimulation and contact with seminal plasma and sperm cells, either alone or in combination, can alter gene and protein expression; modulate sperm selection and storage; provide embryotrophic cytokines; regulate motility; or shut down the non-genomic E_2 pathway in the oviduct. These findings unequivocally demonstrate that mating-associated signals exert a profound influence on the oviduct environment and affect the odds of a successful pregnancy. Yet gaps in our understanding of the molecular mechanisms underlying the effects of mating on oviduct biology still remain: The role of sensory stimulation, in particular, is under-explored. Despite extensive evaluation of various genes and proteins induced by sperm cells and seminal plasma in the oviduct, the functional roles and signaling pathways associated with most of these proteins remain unknown. Seminal plasma also clearly modulates sperm storage and selection, and regulates secretion of embryotrophic factors in the oviduct —yet a paucity of studies have successfully identified specific molecules in the seminal plasma that are responsible for this effect.

Although the role of mating in oviduct function has been demonstrated in a variety of species, the number of species studied is too small to formulate a phylogenetic-based algorithm that predicts species-specificity for the effects of mating on the oviduct. A better understanding of the effects of mating on the oviduct microenvironment surrounding the gamete and embryo will nevertheless improve assisted reproductive techniques, which are usually implemented in the absence of mating. Clarifying how mating and its consequences influence the oviduct may lead to new therapeutic strategies to address infertility and oviduct pathologies.

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