Characterization and biological roles of oviduct-specific, oestrogen-dependent glycoprotein

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During late follicular growth, oestrus, fertilization and early embryonic development, the oviduct, under specific hormonal control, produces fluid and contributes secretory macromolecules that optimize the microenvironment for gamete maturation and transport, fertilization and early cleavage-stage embryonic development. This review describes the state of knowledge concerning the physiological and biochemical characterization of the major oviduct secreted protein, the oviduct-specific, oestrogen-dependent glycoprotein. The identification, localization within the oviduct, binding and association with oocytes, embryos and spermatozoa, hormonal control of gene expression, cloning, gene organization, protein sequences and post-translational modifications of oviduct-specific, oestrogen-dependent glycoprotein are discussed. Identification of biological functions for this glycoprotein, its interactions with spermatozoa, oocytes and embryos and its potential as a paracrine regulator of fertilization and development are also discussed.

The mammalian oviduct undergoes significant endocrine-induced morphological, biochemical and physiological changes during the oestrous or menstrual cycle. These changes establish an essential microenvironment within the oviduct for final maturation of gametes, capacitation of spermatozoa, transport of gametes and embryos, fertilization and early cleavage-stage embryonic development. These complex functions are dependent on activities of the ciliated and secretory, non-ciliated epithelia that line the deep longitudinal mucosal folds. These functions and cells are controlled by the ovarian steroids, oestrogen and progesterone. During the follicular phase of development, oestrogen is essential for differentiation of the epithelium and development and maturation of secretory cells concomitant with production of macromolecules. The resultant luminal environment (for reviews, see Hunter, 1988; Leese, 1988; Buhi *et al.*, 2000) consists of proteins and macromolecules derived from either serum transudate or secretory epithelium. In the last decade, it has been recognized that the oviduct and its secretions play roles in various reproductive events. Detection and analyses of *de novo* synthesized and secreted proteins from the oviduct epithelia have demonstrated a temporal and spatial distribution of macromolecules and differences in protein distribution among species. Furthermore, these analyses have permitted identification of the major secretory product, a high molecular weight, oestrogen-dependent, oviduct-specific glycoprotein.

In this review, the family of glycoproteins identified as

the oviduct secretory glycoprotein (pOSP; Buhi *et al.*, 1996), oestrus-associated glycoprotein (EAP; Buhi *et al.*, 1990; King and Killian, 1994), oviduct-specific, oestrus-associated glycoprotein (EGP; Hill *et al.*, 1996a), oviduct glycoprotein (sOP92; Gandolfi *et al.*, 1991), oviductin (Robitaille *et al.*, 1988), MUC-9 (Lagow *et al.*, 1999), glycoprotein GP 215 (Kapur and Johnson, 1988) and oviduct-specific glycoprotein (OGP; Sendai *et al.*, 1995; O'Day-Bowman *et al.*, 1996) will be identified collectively as oviduct-specific, oestrogen-dependent glycoproteins (OGPs). OGPs with different molecular masses and carbohydrate contents are synthesized and released exclusively by oviduct secretory epithelium in all mammals examined with two possible exceptions, rats (Arias *et al.*, 1994) and mares (Buhi *et al.*, 1996). Differences in the expression of OGPs in the infundibulum, ampulla and isthmus have also been demonstrated. Expression of OGPs appears to be regulated and is oestrogen-dependent or oestrogen-associated. However, differences in species (Komiya *et al.*, 1996) and effectors (Sun *et al.*, 1997) are apparent. At least eight OGPs have been cloned and a high degree of conservation in both nucleotide and amino acid sequence demonstrated across species. A universal characteristic of OGPs is their association with the zona pellucida and perivitelline space of oocytes and embryos, with the possible exception of the mouse zona pellucida. A variety of functional roles for OGPs have been proposed, but relatively few studies have been performed. Although these studies *in vitro* indicate a biological effect of OGP on spermatozoa, eggs and embryos, some studies have contradictory findings. Thus, although specific mechanisms and functions underlying

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Fig. 1. The oviduct secretory epithelium at oestrus or during the mid-late follicular phase and the influence of oestrogen on synthesis, secretion and function of oviduct-specific, oestrogen-dependent glycoprotein (OGP) with spermatozoa, oocyte and embryo. Oestrogen transported via the circulation to the epithelium, induces OGP synthesis and secretion. Within the lumen, OGP may interact with spermatozoa to affect motility and viability and has potential to participate in capacitation and the acrosome reaction. Effects of OGP on the oocyte include increased sperm penetration, increased fertilization rates and decreased polyspermy. Potential developmental alterations include changes in cleavage rates and increased number of embryos to the blastocyst stage. Autocrine effects on oviduct epithelium are unknown.

OGP activities remain elusive, the objective of this review is to consider current knowledge of the biochemical and physiological characteristics, localization, hormonal control of expression, cloning, sequence analyses, molecular weight, isoforms, post-translational modifications, and to examine potential functional roles of OGPs with regard to spermatozoa, oocytes and embryos (Fig. 1).

Oviduct-secreted OGPs

Numerous investigators have proposed that the oviduct expresses specific macromolecular components that interact with gametes or embryos. Pioneering experiments revealed that under oestrogen control, non-ciliated epithelial cells of the rabbit oviduct synthesize a protein *de novo* that is localized in apical secretory granules. This protein is released into luminal fluid and ultimately becomes part of the egg coat (Oliphant *et al.*, 1984). OGPs have since been identified and characterized using one- and two-dimensional SDS-PAGE, fluorography and immunological detection techniques in other species, including baboons (Verhage *et al.*, 1989), cattle (Boice *et al.*, 1990a), goats (Abe *et al.*, 1995a), hamsters (Robitaille *et al.*, 1988), humans (Verhage *et al.*, 1988), mice (Kapur and Johnson, 1988), pigs (Buhi

et al., 1990), rhesus monkeys (Verhage *et al.*, 1997a) and sheep (Sutton *et al.*, 1984). In most species, maximum OGP synthesis and secretion occur during oestrus, the mid- to late follicular phase, fertilization and early cleavage-stage embryonic development (Fig. 2). Furthermore, in pigs, production of OGP is greatest in the ampulla, and second and third greatest in the infundibulum and isthmus, respectively (Fig. 2) (Buhi *et al.*, 1990), and is not detected in any other tissue or fluid compartment, as it is exclusively of oviduct origin. Comparison of proteins revealed OGP to be a high molecular weight glycoprotein with a native undissociated molecular weight of $> 1 \times 10^6$, whereas the reduced and denatured glycoprotein had molecular masses ranging from 66 to 350 kDa. Cow, pig, sheep, human, baboon and hamster OGPs consist of several molecular weight forms and at least two isoforms, acidic and basic molecules. Pig OGP has three major isoforms and two molecular weight variants (Kouba *et al.*, 2000), whereas bovine OGP consists of seven isoforms (Vieira *et al.*, 1999). Immunological crossreactivities, N-terminal amino acid, lectin and carbohydrate analyses demonstrate that, within a species, variants appear to be structurally related. It is unclear why there should be multiple OGP molecular weight variants and isoforms.

Localization of OGPs

Oviduct

Immunolocalization and *in situ* hybridization studies demonstrate that OGPs are products only of non-ciliated oviductal epithelium. Immunoreactive protein is localized in the rough endoplasmic reticula, Golgi and putative secretory granules at apical regions or protrusions primarily in the ampullary epithelium at oestrus, after oestradiol treatment or during the follicular phase of the menstrual cycle. Tissues obtained at the luteal phase, after ovariectomy or after ovariectomy and progesterone treatment demonstrate undetectable or barely detectable OGP (Verhage *et al.*, 1990). Regional differences are apparent as OGPs are not detected immunologically or by *in situ* hybridization in sheep or mouse isthmus (Kapur and Johnson, 1988; Gandolfi *et al.*, 1991; Murray and DeSouza, 1995). In cattle, sheep, pigs and mice, OGPs have also been immunolocalized to the infundibulum. Why some species do not produce OGP in a specific region is not clear, although lack of production may relate to function within that region.

Oocytes and embryos

The onset of OGP expression and secretion during late follicular development through early cleavage-stage embryonic development implies an interaction with gametes and embryos. Association or binding of OGP with oocytes from numerous species has been amply demonstrated using immunofluorescent or immunogold localization (for a review, see Buhi *et al.*, 2000). In most species examined, OGPs

have been localized throughout the zona pellucida, perivitelline space and vitelline or blastomere membrane of oviductal and uterine oocytes and embryos. However, in mice, OGP is found only in the perivitelline space (Kaput and Johnson, 1988).

Distribution of OGPs in the zona pellucida appears uniform and non-dissociable, remaining associated with embryos until day 7 of pregnancy in cattle (Wegner and Killian, 1991) and until pig embryos hatch (Buhi *et al.*, 1993). Although uptake of OGP into baboon (Boice *et al.*, 1990b) and hamster (Kan *et al.*, 1993) blastomeres has been reported, these findings are contradictory to evidence in other species (Gandolfi *et al.*, 1991; Buhi *et al.*, 1993). Taken together, these findings demonstrate that OGP binding and association with ovulated oocytes and embryos is common to all mammalian species examined and indicate that OGPs may play a substantial role as a regulator of fertilization and embryonic development. Because OGPs within species have different molecular weight forms, different isoforms and potentially different post-translational modifications, further studies are necessary to determine whether OGPs associated with zona pellucida, perivitelline space, or vitelline or blastomere membrane consist of different OGP forms, each with a different target and activity. For example, OGP isoforms may differ in their oligosaccharide content, number and distribution of side-chains, and affinity for zona pellucida or vitelline membrane receptors and therefore differ in their ability to regulate biological functions.

Spermatozoa

The hypothesis that OGPs interact with gametes and embryos is supported in part by the immunolocalization of OGPs with both oocytes and embryos. Immunofluorescent studies with lectin-purified hamster OGP revealed binding to the acrosomal region of spermatozoa before and after capacitation (Boatman and Magnoni, 1995). Furthermore, OGP binding to bovine sperm head and midtail regions differs from that in hamster spermatozoa (King and Killian, 1994). In contrast, studies with human spermatozoa by O'Day-Bowman *et al.* (1996) did not demonstrate homologous OGP binding. Thus, it remains unclear whether OGP binding to mammalian spermatozoa affects their function.

Hormonal control of expression of OGPs

In most species examined, expression of OGP mRNA and protein is dependent on the stage of the oestrous cycle, menstrual cycle or early pregnancy and is correlated with circulating concentrations of oestrogen. Regulation of OGP expression appears to show a differential response in species with long oestrous cycles compared with those with short cycles (that is, rodents). In hamsters, differences in expression of OGP mRNA and protein during a normal oestrous cycle were not detected (Komiya *et al.*, 1996). *In*

situ hybridization experiments indicated that OGP mRNA was constitutively expressed, although its signal intensity was attenuated only in ampulla. GnRH analogue treatment decreased oestrogen and OGP mRNA, whereas subsequent administration of oestrogen stimulated the expression of OGP mRNA. Furthermore, oestrogen administered to pre-pubertal hamsters induced OGP expression (Abe *et al.*, 1998). In contrast to the findings in rodents, as serum oestrogen increases, OGP mRNA in oviduct tissue increases to a maximum value during the late follicular phase in women (Arias *et al.*, 1994) and on days 0–2 of oestrus in pigs (Buhi *et al.*, 1996). Furthermore, during these periods of maximum OGP mRNA expression in oviduct tissue, there are increases in the number of oviduct epithelial apical secretory granules containing OGP and in the amount of OGP protein in oviductal fluid or conditioned culture media. Moreover, during dioestrus or the luteal phase, OGP mRNA and protein are weakly expressed or are undetectable (Fig. 2) (Verhage *et al.*, 1988; Buhi *et al.*, 1991, 1996; Arias *et al.*, 1994).

Ovariectomy and hormone replacement with oestrogen maintains or restores expression of OGP mRNA and protein, whereas addition of progesterone antagonizes the effect of oestrogen, strongly suppressing mRNA and protein. OGP mRNA expression in pig oviduct is significantly greater in the ampulla than in the infundibulum or isthmus throughout the oestrous cycle (Fig. 2b) or after ovariectomy and oestrogen treatment (Buhi *et al.*, 1996). Although the hypothesis that induction and upregulation of OGP expression is oestrogen-dependent is supported by these studies, several laboratories have demonstrated that LH receptors are present and functional in human, pig and cow oviduct. The presence of LH receptors and changes in quantity depend on hormonal status and may affect oviduct function (Shemesh, 2001). Sun *et al.* (1997) suggested that LH has a direct effect on OGP expression as treatment with hCG of bovine epithelium *in vitro* increases the half-life of OGP mRNA. The functional significance of LH in other species and *in vivo* remains to be examined.

Cloning, sequences and modifications of OGPs

OGP cDNA sequences have been determined in baboons (Jaffe *et al.*, 1996), cows (Sendai *et al.*, 1994), hamsters (Suzuki *et al.*, 1995), humans (Arias *et al.*, 1994), mice (Sendai *et al.*, 1995), pigs (Buhi *et al.*, 1996), rhesus monkeys (Verhage *et al.*, 1997a) and sheep (DeSouza and Murray, 1995a). These OGPs appear to be highly conserved, and share 70–78% identity and 76–87% similarity in the overall deduced amino acid sequence. However, the N-terminal region of the mature polypeptide has a high degree of identity (77–84%) and similarity (86–90%) compared with a low identity (37–63%) and similarity (50–75%) in the C-terminal end. The open reading frames of cDNAs code for a preprotein with a 21 amino acid signal sequence and a total protein of 527–721 amino acids. The predicted molecular masses range from 58.5 to 76.5 kDa,

Fig. 2. For legend see facing page.

which is considerably less than the calculated mass of reduced, denatured glycoprotein. Bovine, ovine and pig OGP are more similar in sequence and length to one another, whereas human, baboon and rhesus monkey OGP appear more similar to each other.

Major sequence differences are localized in the carboxy terminal region (Buhi *et al.*, 1996), which corresponds to exon 11 of the gene (Verhage *et al.*, 1997b). Significant differences in protein length, amino acids at 141–335, insertions, deletions and truncations are described for this region which contains numerous Ser-Thr residues. The hamster OGP C-terminal region contains a mucin-type, tandem-repeat sequence (six repeats) of 15 amino acids each (Paquette *et al.*, 1995). In contrast, human, baboon and rhesus monkey C-terminal regions contain only four tandem-repeat sequences, whereas those of cattle, sheep and pigs contain incomplete or no tandem-repeat sequences. However, the mouse C-terminal region contains 21 repeat sequences composed of seven amino acids each. Putative *N*-glycosylation sites, ranging from one to seven, and putative *O*-glycosylation sites, ranging from 10 to 20 (except in mice, in which there are 67 predicted sites), are localized within the carboxy terminal region. In general, tandem repeats are a feature of mucins, although they are exhibited by other proteins. In agreement with the reported characteristics of some OGP, tandem repeats contain all the *O*-linked glycosylations and are usually found within one exon. Thus, hamster and mouse OGP may be more closely related to mucins than are other OGP. Although methods are available for removal of carbohydrate, only one study *in vitro* (Satoh *et al.*, 1995) investigating the biological role of OGP devoid of carbohydrate has been performed to date. Removal of sialic acid and *N*-linked glycosylation significantly reduces the ability of bovine OGP to maintain sperm viability. Completely deglycosylated OGP is insoluble. Therefore, these glycosylation sites appear to be important for biological activity and for maintaining extracellular solubility. The carbohydrate may also have roles in protection from protease degradation, protein folding and protein–protein interaction. Differences in tandem repeats, the presence and distribution of *N*- and *O*-linked carbohydrate, the diversity of side chains, and the length of the C-terminal region may confer species specificity, mediate specific recognition events and directly regulate the biological activity of OGP.

The organization and structure of genomic sequences

have been described for human (Jaffe, 1996), mouse (Takahashi *et al.*, 2000) and hamster (Merlen and Bleau, 2000) OGP. The coding sequence was contained in 11 exons with the signal sequence localized in exons 2 and 3 and the mature peptide found in exons 3–11. A TATAA box was identified in human 5'-flanking sequence, whereas mouse and hamster lacked typical TATA, CAAT and CG boxes. However, atypical nucleotide sequences were identified in both species. An imperfect oestrogen-response element (ERE) was detected in hamsters and mice and ten half-palindromic ERE were located in the putative promoter in mice. Transfection experiments in MCF-7 cells using various sections of the mouse 5'-flanking region demonstrate that promoter activity for oestrogen responsiveness resides in this region. Additional experiments are required to examine functional analyses, oestrogen receptor binding and other regulatory domains that may control tissue specificity and gene expression.

All OGP demonstrate a similarity to a growing group of mammalian gene products, which include human cartilage glycoprotein 39 (Hakala *et al.*, 1993) and human macrophage chitotriosidase (Boot *et al.*, 1995), and a group of enzymes (chitinases) not found in mammals. All these proteins belong to family 18 glycosyl hydrolases, proteins of the chitinase gene family. Comparison of the structural organization of genes (Takahashi *et al.*, 2000), protein sequence comparisons and the number and position of conserved cysteine residues (Buhi *et al.*, 1996) in OGP and mammalian gene products indicates that these proteins have arisen from a common ancestral gene. Hydrophobic cluster analyses and sequence comparisons among all groups indicate that identity and similarity are greater in the N-terminal domain, defined as the catalytic domain, of chitinases. Four residues in chitinases appear to be necessary for activity, but two have been shown by site-directed mutagenesis to be absolute requirements for chitinase activity (Watanabe *et al.*, 1993). Consistent with this finding, all OGP examined lack an essential glutamic acid residue and chitinase activity. Hydrophobic cluster analysis indicates that amino acids 386–525 in pig OGP correspond to a C-terminal binding domain found in some cellulases and chitinases (Buhi *et al.*, 1996). Owing to divergence in the C-terminal domain, it has been hypothesized that this region constitutes both a binding and species-specific recognition domain.

Post-translational modifications of OGP may provide

Fig. 2. Temporal and spatial distribution of pig oviduct-specific, oestrogen-dependent glycoprotein (OGP) mRNA and protein in the oviduct. (a) Representative fluorographs of the two-dimensional SDS-PAGE separation of proteins present in culture media conditioned by the infundibulum (i,ii), ampulla (iii,iv) and isthmus (v,vi) from tissues collected on day 0 (i,ii,iii,v) and day 12 (ii,iv,vi). Arrows 1–3 indicate the location of the three major molecular mass and isoelectric forms of pig OGP (previously described as pOSP-E1 (75–85 kDa, pI 4), pOSP-E2 (100 kDa, pI 5–6) and pOSP-E3 (100 kDa, pI 8.5)). Arrowheads identify several minor 100 kDa and isoelectric forms of OGP. Significantly reduced synthesis and secretion of all OGP forms into culture media is shown in the isthmus at day 0 and in all three segments from day 12 tissues. (b) Dot blot hybridization analyses of pig OGP mRNA from the (i) infundibulum, (ii) ampulla and (iii) isthmus on days 0 and 2 of oestrus and day 12 of dioestrus. Blots were probed with a 0.8 kb fragment of OGP mRNA and quantified by densitometry and relative pOGP:GAPDH expression (mean $\pm$ SD) calculated. Bars with different letters are significantly different ((i) $P < 0.01$; (ii,iii) $P < 0.05$). Location $\times$ day differences in OGP mRNA expression were detected and OGP mRNA abundance in the ampulla was significantly greater than it was in the infundibulum and isthmus, regardless of day (for a review, see Buhi *et al.*, 1996).

specific biological properties (Satoh *et al.*, 1995) and these modifications may influence protein–protein or protein–cell interactions with sperm membranes, zona pellucida, the vitelline membrane of oocytes, or the blastomere membrane of early embryos. Carbohydrate precursor, lectin binding, chemical deglycosylation, enzyme and inhibitor studies indicate that both *N*- and *O*-linked glycosylation occur. Carbohydrates include terminal *N*-acetylneuraminic acid (sialic acid) in $\alpha(2,3)$ and $\alpha(2,6)$ linkages, galactose, *N*-acetylgalactosamine, α -fucose, galactosyl- $\beta(1,3)$ -*N*-acetylgalactosamine, *N*-acetylglucosamine and mannose (Buhi and Alvarez, 1991; DeSouza and Murray, 1995b; Satoh *et al.*, 1995). Furthermore, metabolic labelling studies have demonstrated that rabbit (Oliphant *et al.*, 1984), pig (Buhi *et al.*, 1990), and hamster (Malette and Bleau, 1993) OGP are modified by the addition of inorganic sulphate. Although phosphorylation sites are predicted, only pig OGP has been shown to be phosphorylated (Buhi and Alvarez, 1991). Thus, variable isoforms of OGP within a species may be the result of heterogeneous addition of sialic acid residues, other carbohydrates, sulphation or phosphorylation.

Function of OGPs

Co-incubation of spermatozoa, oocytes or embryos with oviductal fluid, epithelium or conditioned media indicate that OGPs are involved in a variety of roles during fertilization and early embryonic development (Fig. 1). The physiological significance of OGPs binding to oocytes, spermatozoa and embryos is not known, but apparent targets are the zona pellucida, and the perivitelline space and membranes of oocytes or blastomeres. The fact of OGP binding to spermatozoa indicates, but does not establish, an effect on sperm activity. Moreover, in species in which OGP has not been shown to bind spermatozoa, effects on sperm activity have been demonstrated. Treatment of bovine spermatozoa with enriched or semi-purified OGP significantly increased capacitation and ability to fertilize bovine oocytes (King *et al.*, 1994) or increased motility and viability when added in a dose-dependent manner (Abe *et al.*, 1995b). Similarly, pig spermatozoa showed increased viability with semi-purified OGP at lower concentrations (McCauley *et al.*, 2001). OGP added in increasing concentrations to pig spermatozoa during a homologous IVF maintained high penetration rates at low concentrations ($<20 \mu\text{g ml}^{-1}$) with a significant decrease in polyspermy (Kouba *et al.*, 2000). However, with increased OGP concentrations ($\geq 50 \mu\text{g ml}^{-1}$), sperm penetration and binding were significantly reduced.

Co-incubation of the homologous OGP and human spermatozoa and hemizona or hamster spermatozoa and ovarian oocytes demonstrated increased sperm binding and penetration (Boatman and Magnoni, 1995; O'Day-Bowman *et al.*, 1996). Despite high homology between human and baboon OGP, human sperm binding to hemizona was decreased with addition of the heterologous baboon OGP, indicating the importance of a homologous system

(O'Day-Bowman *et al.*, 1996). Incubation of ovine spermatozoa, oocytes and enriched OGP during fertilization showed significant increases in cleavage rate and in numbers of blastocysts (Hill *et al.*, 1996b). However, addition of OGP during culture after IVF showed no effect on cleavage rates (Hill *et al.*, 1996a). Similarly, during pig IVF, no effects on cleavage rates were noted, but increased numbers of embryos at the blastocyst stage were found with OGP treatment at fertilization (Kouba *et al.*, 2000). Embryotrophic effects of OGP in the development of bovine zygotes to blastocysts have not been detected. In contrast, pig OGP added to zygotes fertilized *in vivo* showed a significant increase in incorporation of radiolabelled amino acid into protein at the four-cell stage (Wallenhaupt *et al.*, 1996). Taken together, these results support a possible role for OGP during embryonic development *in vitro* and indicate a window of importance during fertilization and first cleavage events.

OGP pretreatment of spermatozoa alone, before fertilization, has produced contradictory results. Bovine spermatozoa preincubated with OGP showed increased capacitation and fertilization rates compared with controls (King *et al.*, 1994). However, a second study in cattle (Martus *et al.*, 1998) found that OGP pretreatment of spermatozoa did not alter fertilization rates. In pig spermatozoa treated with OGP concentrations lower than those in bovine studies, there was a significant increase in the penetration rate compared with that in controls (McCauley *et al.*, 2001) and an increase in polyspermy. Differences in study design, protein purity and concentration, and sperm concentration may explain these disparities.

OGP pretreatment of bovine and porcine ovarian oocytes alone, before fertilization, showed positive effects. In pigs, high penetration and fertilization rates were maintained and polyspermy was significantly reduced when oocytes were treated with low OGP concentrations (McCauley *et al.*, 2001), identical to results after both oocytes and spermatozoa were treated with OGP (Kouba *et al.*, 2000). Similarly, bovine oocytes preincubated with OGP demonstrated significant increases in fertilization rates (Martus *et al.*, 1998). These results indicate an effect of OGP on the oocyte. Furthermore, studies by Martus *et al.* (1998) and Kouba *et al.* (2000) extend this concept by demonstrating that biological effects of OGP are blocked with inclusion of specific anti-OGP antibody. Taken together, these studies demonstrate that OGPs have biological effects on both spermatozoa and eggs. However, overall results indicate that the effects of OGPs on reproductive events are mediated primarily through interactions with the oocyte, which may extend into embryonic development.

Conclusion

OGP has been demonstrated to be the major secretory glycoprotein and to be expressed exclusively by the oviduct. This protein, under oestrogen control during oestrus and the follicular phase of the menstrual cycle, is conserved across

all species examined. OGP binding to the extracellular matrix, the zona pellucida, and membranes of gametes and embryos indicates a potential biological role during fertilization and development. Functional studies indicate that OGPs affect sperm capacitation, motility and viability. Moreover, evidence indicates that OGPs have direct effects on egg penetration, fertilization and development that may be mediated through interactions with the oocyte.

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