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There are a host of methods used to assess the functional integrity of spermatozoa in an attempt to predict their subsequent fertility. Traditional parameters such as motility, viability and morphology are now combined with more complicated assessments, such as acrosome integrity, capacitation status, and the sperm chromatin structure assay, to provide a better understanding of sperm physiology and an improved prediction of fertility to be obtained post-insemination (Gillan et al. 2008). However, these analyses fail to explain the poor fertility of spermatozoa in circumstances where no obvious problems with sperm function or female reproductive physiology exist. A possible explanation lies in the discovery that sperm maturation, function and fertility are governed by a complex interaction between the sperm cells and the female reproductive tract (Fazeli and Pewsey 2008; Rath et al. 2008). This so called ‘maternal communication’ with spermatozoa must be taken into consideration if the issue of fertility is to be fully understood.

Spermatozoa interact with the female tract in a variety of ways during transit from the site of semen deposition in the anterior vagina, cervix or uterus, to the site of fertilisation in the ampulla of the oviduct. Taking a vaginal depositor such as the sheep as an example, spermatozoa must first traverse the physical barrier of the cervix before entrance into the uterus, which is only achieved by a select portion of the initial ejaculate or inseminate. Within the uterus, spermatozoa interact with uterine epithelial cells as well as polymorphonuclear neutrophilic granulocytes and leucocytes (particularly in uterine depositors such as the pig and horse; Rath et al. 2008), before establishing a reservoir at the utero-tubal junction (UTJ; Rodriguez-Martinez et al. 1990; Taylor et al. 2008; Druart et al. 2009). This site appears to serve as a second selective barrier for spermatozoa, as the concentration of sperm cells is significantly lower in the isthmus of the oviduct when compared to the UTJ (Hunter et al. 1980; Druart et al. 2009). Once through the UTJ, uncapacitated sperm cells bind with oviducal epithelial cells (OECs) of the isthmus to form the final sperm reservoir (Hunter 1981; Suarez 1998). Following capacitation, spermatozoa disengage from the OEC (Lefebvre and Suarez 1996; Fazeli et al. 1999; Revah et al. 2000) and make their way to the ampulla. Here, a spermatozoon may fertilise the oocyte after binding with the zona pellucida and undergoing the acrosome reaction (Evans 2003). Whereas there is some species variation in this chain of events, this is a reasonably accurate description of the physical interaction between sperm and the female reproductive tract in all species studied. These physical events have been relatively well elucidated, but the molecular basis for their regulation – the precise nature of the pathways of maternal communication with spermatozoa – remains poorly understood. There are no reported pathways in the vagina, cervix and uterus, but their presence in the oviduct has been established and the molecular basis of the interaction relatively well studied. It is known that specific sperm surface proteins are required for sperm to be able to pass the UTJ (Cho et al. 1998), that binding to OECs is mediated by sperm lectin and OEC carbohydrate residues, and that their subsequent release is controlled by glycosidases in the oviduct epithelium (Rath et al. 2008). Controversially, it is now apparent that this maternal communication is not unidirectional, that is to say, that signalling occurs from maternal sources to sperm cells as well as from spermatozoa to the cells of the reproductive tract (Fazeli and Pewsey 2008). The presence of spermatozoa within the oviduct has been shown to elicit sperm-specific changes to the production of mRNA transcripts.
(Fazeli et al. 2004), secretion of proteins (Georgiou et al. 2005; Georgiou et al. 2007) and prostaglandins (Kodithuwakku et al. 2007) by the oviduct. These findings have considerable implications for fertility, as it is evident that spermatozoa are able to influence the oviducal microenvironment in which sperm transport, sperm binding and release, capacitation, transport of oocytes, fertilization, and early cleavage stage embryonic development occur (Fazeli and Pewsey 2008). The oocyte and embryo are also capable of similar control over the microenvironment in which they reside (Fazeli and Pewsey 2008). Clearly, successful fertilisation and subsequent establishment of a pregnancy is the result of a complex ‘interactome’ of signalling pathways with any disturbances causing potential adverse effects on fertility.

Knowledge of these interactions has helped shed light on fertility problems with otherwise normal spermatozoa, which have been described as highly functional by traditional means of assessment. One such example is ram spermatozoa liquid stored for 24 h prior to cervical artificial insemination. Despite excellent motility, the fertility of ram spermatozoa stored using this technique appears to be compromised unless delivered by intrauterine insemination (Maxwell and Salamon 1993). Direct observation of the patterns of sperm migration within the reproductive tract of the ewe by fibred confocal fluorescence microscopy has since demonstrated that liquid storage causes a diminished capacity for migration of the cervix and a subsequent decrease in the number of spermatozoa at the UTJ and within the oviduct (Druart et al. 2009). The molecular basis for this altered interaction of liquid-stored spermatozoa with the cervix of the ewe has not been established. A further example is the diminished fertility of sex-sorted bull spermatozoa in samples with seemingly acceptable levels of motility, viability and acrosome integrity (Underwood et al. 2010). Using the sheep as a model, recent results suggest that sex-sorted spermatozoa alter the expression of genes within the oviduct and by inference the microenvironment of fertilisation and early embryonic development (Beilby, de Graaf, Grupen et al. unpublished observations). Although this does not appear to affect the in vivo fertility of sex-sorted ram sperm (de Graaf et al. 2007), it may have implications for the poor fertility obtained in cattle (Schenk et al. 2009), pigs (Bathgate et al. 2008), and horses (Clulow et al. 2008).

Clearly, further work is required to ascertain the full extent of the interaction between sperm and the female reproductive tract. As further details of molecular pathways and sperm-tract signalling come to light, it will be essential to investigate the precise effects of assisted reproductive technologies such as sex-sorting and sperm cryopreservation on the maternal communication interactome and any subsequent relationship to fertility.

References


