A novel genomic diagnostic tool for sperm quality?

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Abstract  Male factor infertility is a growing problem worldwide. Considering that a male factor is involved in at least 20% of infertility cases, there is a need for better predictive markers of sperm function. The traditional sperm analysis based on sperm count and motility has been used for the diagnosis of male fertility for several decades, however, a significant number of men with normal sperm features remain unable to reach pregnancy. This fact clearly indicates the need to develop new male infertility tests to accurately diagnose the sperm samples from these individuals. Furthermore, the classic spermogram has limited predictive power to predict pregnancy in assisted reproductive techniques. Microarray technology is a powerful tool for detecting gene expression of thousands of genes at the same time. There is a great interest in the sperm transcriptome as a source from which to develop markers of male infertility. This commentary discusses the current advances in the microarray technology and sperm quality. It is believed that microarray-based fertility testing of sperm potential in infertility treatment could be close at hand.

Male factor infertility is a growing problem worldwide and in infertile couples male factor is involved in at least 20% of infertility cases (Moldenhauer et al., 2003). The basic sperm analysis in assessing natural male fertility potential and predicting pregnancies in assisted reproduction has been the subject of ongoing debate with a continued call for the development of new markers of sperm function. The traditional sperm analysis based on sperm count and motility has been used for the diagnosis of male fertility for several decades. It is an easy, inexpensive and useful tool to determine the fertile status of a male, but a considerable number of men with normal sperm features remain unable to attain natural pregnancy (Garrido et al., 2004). This fact clearly indicates the need to develop new male infertility tests to accurately diagnose the sperm samples from these individuals. Furthermore, the classic spermogram has limited power to predict pregnancy in IVF or intracytoplasmic sperm injection (ICSI).

In a previous issue of Reproductive BioMedicine Online, García-Herrero et al. (2011) presented a novel molecular approach to semen analysis for predicting pregnancy outcome in ICSI patients. In an ICSI procedure involving an ovum donation programme, the authors characterized the mRNA of spermatozoa that achieved implantation and compared it to the mRNA of spermatozoa that did not. The oocytes from a single donor were divided between the two recipients exhibiting opposite pregnancy outcomes, making the study design unique by allowing elimination of oocyte quality and concentrating on interindividual differences in sperm quality. A further strength of their study design was the analysis of the same sperm sample that was used for further ICSI treatment. They found significant differences in the gene expression pattern in spermatozoa that resulted in pregnancy compared with those that did not, supporting the hypothesis that microarray-based diagnostic tools can be used to predict the potential of spermatozoa to initiate...
a pregnancy in ICSI and also contribute to a better knowledge of male infertility. The presence and importance of mRNA transcripts in sperm cells has been confirmed by several studies (Meseguer et al., 2006; Miller and Ostermeier, 2006a,b; Miller et al., 2005; Ostermeier et al., 2004), but the functional significance of mRNA in mature spermatozoa remains essentially unexplored (Lalancette et al., 2008). The results from Garcia-Herrero et al. (2011) complement, from a clinical point of view, the seminal works of integrating transcriptional and functional data on spermatozoa and function in sperm cells, as well as its relationship with male fertility (Garcia-Herrero et al., 2010; Miller and Ostermeier, 2006a;b; Miller et al., 2005; Ostermeier et al., 2004). Several authors have postulated that sperm microarray analysis will be the future in the diagnosis of male infertility (Krawetz, 2005; Miller and Ostermeier, 2006a; Miller et al., 2005; Ostermeier et al., 2005), but no consensus gene list has been proposed so far.

Microarrays are now a widely recognized tool for effective assessment of gene expression of thousands of genes at the same time. There is a great interest in the sperm transcriptome as a source from which to develop markers of male infertility. In previous studies, the utility of sperm cell RNA to provide clinical markers of infertility has been explored (Miller, 2000; Steger et al., 2008) and differences in specific transcript levels in spermatozoa of different motility (Lambard et al., 2004), as well as between morphologically normal and abnormal sperm samples, have been reported (Garcia-Herrero et al., 2010; Garrido et al., 2009; Platt et al., 2007; Steger et al., 2003, 2008; Yatsenko et al., 2006). The Garcia-Herrero et al. (2011) study, together with the previous studies, could serve to inspire new molecular approaches for the evaluation of male fertility and additionally to make the move from anatomical to molecular medicine. The information obtained by Garcia-Herrero et al. (2011), together with that from earlier studies, could lead to a microarray-based fertility test for assessing the sperm potential in infertility treatment.

In today’s genomic era, new perspectives of the analysis and classification of subclasses of different disease emerging, especially tumour classification (Bloom et al., 2004; Eschrich et al., 2005; Golub et al., 1999) and complex functions (Medina et al., 2007; Quackenbush, 2006), and the seminal works of integrating transcriptional and functional data on spermatozoa and function in sperm cells, as well as its relationship with male fertility (Garcia-Herrero et al., 2010; Miller and Ostermeier, 2006a;b; Miller et al., 2005; Ostermeier et al., 2004). Several authors have postulated that sperm microarray analysis will be the future in the diagnosis of male infertility (Krawetz, 2005; Miller and Ostermeier, 2006a;b; Miller et al., 2005; Ostermeier et al., 2005), but no consensus gene list has been proposed so far.

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Still, much remains to be clarified. RNA microarrays are a powerful tool for gene discovery but the large number of transcripts that get pooled and the limited number of samples used in the microarray-based studies narrow the statistical power to discriminate the differentially expressed genes. Integration and cross-validation of data sets of sperm gene expression profiles produced by different groups could increase confidence in the expression results and should provide the list of genes that together orchestrate male fertility. Additionally, the bioinformatic capacity to efficiently process all the information generated by these types of studies must be increased and, to a certain degree, researchers must begin to think more along the lines of ‘systems biology’, while focusing on gene pools rather than outcomes based upon single gene analysis.

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