Introduction of Sensitive and Specific Biomarkers Can Improve Infertility Treatment Success Rates

Approximately 20% of couples of reproductive age need assisted reproductive technologies to conceive, in spite of sophisticated improvement in the diagnosis and treatment of infertility. The cause of 30% of infertilities is unknown and less than 50% of couples are conceived by each treatment cycle using advanced assisted reproductive technologies. In the present clinical practice, many steps in the whole spectrum of diagnosis to treatment of infertility are based on the use of ambiguous biomarkers or less related ones. Moreover, there are even no specific bio-markers available to determine the causes and outcomes of infertility. Consequently, this condition leads to the blind performance of many diagnostic and treatment procedure with less desirable outcomes (1).

Fortunately, introduction of more specific and sensitive biomarkers with less invasive methods has lead to early detection and efficient treatment of most diseases. Biomarkers have found wide application in research and clinic and they are useful for screening, risk assessment, diagnosis, stage determination and grading of diseases. They are also useful for the selection of treatment procedures and monitoring cure or recurrence of diseases. Application of new technologies such as genomics, proteomics, transcriptomics, metabolomics, microarray, CGH and other high throughput techniques has provided several potential biomarkers at four basic levels of cell biology including DNA, RNA, protein and metabolites for early diagnosis and treatment of diseases (2).

Reproduction and infertility has not been left out from this progress. Most research on human reproduction and infertility aiming to increase the rate of take home baby and fetal-maternal health will not materialize without the availability of more sensitive, specific and non-invasive biomarkers. Moreover, efficient treatment of male or female infertility is dependent on the identification of a vast range of biomarkers to represent the exact information on ovarian reserve, ovarian response to stimulation protocols, number and quality of oocytes during stimulation, sperm quality, presence and quality of sperm in non-obstructive azoospermia, embryo quality, and endometrial receptivity.

Nowadays, most biomarkers are based on the morphological criteria of gonads, gametes and embryos. Several studies have shown a poor correlation between clinical and functional outcomes with the results of conventional fertility evaluations (3). For example, sperm criteria including concentration, motility and morphology are well accepted as biomarkers for semen analysis and are first line biomarkers in evaluating male fertility, but in large numbers of men results of these biomarkers have been in contrast with the function and fertilizing ability of sperm. This means that many fertile men with severe abnormality in semen or vice versa many infertile men would seemingly have normal results (4). Therefore, it is the time to shift form morphological and invasive biomarkers to non-invasive molecular biomarkers with high sensitivity and specificity. In the case of sperm biomarkers, molecular and functional biomarkers such as chromatin maturity and integrity are available now. Different staining and flow cytometric methods could detect and separate non-functional sperm with defective chromatin, but the evaluation procedure could lead to the destruction of the sperm before it can be used for ART.

New generation of biomarkers should provide the exact information about ovaries, testis, sperm, oocytes, embryos and endometrium without any deleterious effects on their function during an IVF cycle. Although scientists actively are in search of new efficient biomarkers and verification process of biomarker function takes a long time, but it should be pointed out that infertile couples are eagerly awaiting increased ART success rates.

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