Commentary

Immunomodulation at the receptor-mediated cell-signalling, molecular level for fertility treatment

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An increase in incidence of infertility has been seen in recent times. Infertility is often associated with significant psychological stress to the couple. Unfortunately, success rate of fertility treatment has not improved dramatically. Targeting biochemical-signalling pathways at the molecular and cellular level is emerging as a treatment strategy, wherein focussed research is required. Individualized immunotherapeutic treatment strategies by targeted manipulation of Toll-like receptor (TLR) signalling regulatory network could be quite promising to improve the success rate of fertility treatment.

TLRs[1] are a class of proteins that play a key role in the innate immune system. They are single, membrane-spanning, non-catalytic receptors usually expressed as macrophages and dendritic cells, which recognize structurally conserved molecules derived from microbes. TLRs are now counted among the key molec ules that alert the immune system to the presence of microbial infections. They were named so in 1985 because of their similarity to the protein coded by the toll gene identified in *Drosophila*. Female reproductive tract is in close contact with allogenic sperms and transmitted microorganisms during intercourse and with semi-allogenic foetus during pregnancy.[2] Zandieh *et al.*[3] described TLRs as one of the main components of the innate immune system.

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Poor ovarian response (POR) to gonadotropin stimulation has led to a significant decline in the success rate of fertility treatment. The immune system may play an important role in pathophysiology of POR by dysfunctions of cytokines and the growth factor network, and the presence of ovarian auto-antibodies.[4] Taghavi *et al.*[4] investigated the expression of Toll-like receptors and cyclooxygenase (COX) 2 genes in follicular cells and concentration of interleukin and macrophage migration inhibitory factor, as major parts of innate immunity, in follicular fluid obtained from POR women in comparison with normal women. TLR and COX2 gene expression were found to be significantly higher in POR. Toll-like receptor 2 (TLR2) and interferon-gamma (IFN-γ) coordinate with a diverse array of cellular programs through the transcriptional regulation of immunologically relevant genes and play an important role in immune system, reproductive physiology and basic pathology. Alterations in the functions of TLR2, IFN-γ and signalling molecules that result from polymorphisms are often associated with susceptibility or resistance, which may, in turn, establish the innate host response to the various infectious diseases.[5]

There are different areas in infertility wherein receptor-based cell signalling could be primarily responsible for reproductive disorders like oocyte maturation, sperm

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function, pre-embryo morphology, genital infections, impaired endometrial implantation, etc. Molecular biology research-oriented experimental studies are required in the future. The article ″Dissecting Toll-like Receptor Molecular Regulatory Network(s) in Reproductive Medicine, Primarily Infertility: A Snapshot″ is an interesting article and will encourage researchers to do further studies on this topic. Hopefully, it will be a step towards the next level of advancement by providing personalized immunotherapeutic treatment.

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Conflicts of interest

There are no conflicts of interest.

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