O-1(임상) Genetic Factors for Male Infertility

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Background & Objectives: The male factor is at least partly responsible in about 50% of infertile couples. Approximately 2~9% of infertile men attending clinics have a genetic component and in nearly 50% of infertile men are not possible to find a cause. Most of genetic factor of male infertility are Y chromosome microdeletion and polymorphisms or genetic variants in these genes are considered potential risk factors witch may contribute to the severity of spermatogenic failure. In this research, we studied differential gene expression pattern of spermatogenesis stage specific, SNPs and gene specific Y chromosome microdeletion to gain a information of the regulatory mechanism involved in germ cell development and molecular diagnostic tools.

Method: To select a spermatogenesis specific gene, we used a mouse DNA chip to compare the gene expression profiles of mouse pachytene spermatocytes and round spermatids, which were isolated from 9-week ICR mice testes by velocity sedimentation under unit gravity (VSUG). Searched candidate genes or SNPs for infertile males were validated with its association to male infertility by pyrosequencing, PCR, RFLP, semi-quantitative and real-time RT-PCR.

Results: We found that the genes identified include; primarily chromosomal genes related to intracellular enzyme and nucleic acid binding proteins, and kinase and substrate genes that mediated cell cycle transition. The SNPs of folate metabolism related genes (MTHFR, MS, MTRR), cryptorchism related gene (INSL3) and testis specific histone (H2BFWT) were studied whether associated with male infertility. MTHFR 677TT type and MS 2756GG type were associated with azoospermia patients (p=0.0227 and p=0.0063) and MTRR A66G is associated with OAT patients (p=0.0014). H2BFWT -9TT type some meaning (p=0.083), but INSL3 was not associated with male infertility. We also developed molecular diagnostic tools to monitor male infertility. The long arm of the human Y chromosome is required for male fertility. Deletion in three different regions can cause severe spermatogenic defects ranging from non-obstructive azoospermia to oligozoospermia.

Conclusions: These researchs were helpful to understand of spermatogenesis and male infertility. Furthermore, Y chromosome microdeletion detection tools provide economic and high throughput methods for detecting the deletion of genomic DNA sequences of large groups of infertile patients, and a new approach to male infertility screening.