From Proteins to Potency: An Integrative Proteomic Approach Towards Male Infertility Management

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Comprehensive evaluation of the underlying causes and a personalized approach is necessary to the individual patient for the accurate diagnosis and effective treatment of the male infertility. Low number, poor motility or morphological abnormality of spermatozoa constitutes the reason for infertility in 20-25 % of the total cases. The current study compares the global proteome profiles of spermatozoa from fertile men and infertile men of various infertility phenotypes with the aim to identify differentially displayed proteins in relation to human male factor infertility employing label-free liquid chromatography coupled with tandem mass spectrometry. A total of 22 semen samples were collected and analysed, comprising 5 samples from fertile men, 7 samples from men with oligospermia, 5 samples from men with teratospermia, and 5 samples from men with asthenozoospermia. In total, of 551 proteins detected, 513 proteins were identified by UniProt and 309 proteins were observed to be expressed differentially or uniquely among various groups of infertile and fertile spermatozoa. The foldchange of <0.50 or >2 was used as cut-off threshold to identify the differentially expressed proteins associated with specific infertility phenotypes. 34 proteins were found to be unique to fertile individuals. Conversely, 71, 6, and 22 proteins exhibited their unique presence in the spermatozoa from asthenozoospermic, oligozoospermic and teratozoospermic individuals respectively. PANTHER classification of differentially expressed proteins identified majority of proteins involved in hydrolase activity, oxidoreductases and enzyme modulators; Rho GTPase signalling and Parkinsons disease pathway be severely altered in infertile groups. Further, STRING network analysis of differentially expressed proteins predicted the clusters of cytoskeletal proteins, proteasomal degradation, regulators of oxidative stress, stress response and protein synthesis pathways to be significantly altered in infertile groups. The present study systematically explored the global proteome changes associated with defective spermatozoa. These findings may also pave the way for the development of new diagnostics strategies for screening male infertility and, for the discovery of new drug targets and the development of personalized therapies to improve fertility outcomes.