Morphologically Distinct Phenotypes of Spermatozoa in Infertile Men
Reveal Down Regulation of Multiple Signaling Pathways
Ashok Agarwal, PhD, 1, Zhihong Cui, MD,1,2, Rakesh Sharma, PhD, 1, Luna Samanta, PhD, 1,3, Rola Turki, PhD, 4,5, Muhammad Abu-Elmagd, MD, 2
1 Center For Reproductive Medicine, Cleveland Clinic, Cleveland, OH, 1Institute of Toxicology, Third Military Medical University, Chongqing, China, 2Redox Biology Laboratory, School of Life Science, Ravenshaw University, Orissa, India, 3Ob/Gyn, Mobil, AL, 4CEGMR, Center of Excellence in Genomic Medicine Research, King AbdulAziz University, Jeddah, Saudi Arabia.

Abstract

Objective: Seven morphologically distinct spermatozoal phenotypes can be detected in human semen and electron microscopy, sperm with an argyrophilic fibrous sheath, sperm with flagellum defect, sperm with dysplasia of the fibrous sheath, sperm with hypoacrosomal head, dysplasia of acrosomal process, sperm with hypoplastic flagellum, and even sperms without heads. It is hypothesized that these spermatozoal defects, immotile cilia syndrome, acrosomal hypoplasia, defective chromatin, and sperm defects may be the causes of some patients' infertility. We hypothesize that these spermatozoal defects may be related to the underlying pathology of infertility.

Design: A total of 1202 proteins were studied in the first mature (mid-morphological stage) 1186. Conserved proteins were identified in the F1-F4 fractions. The number of conserved proteins in each fraction was determined to determine the number of proteins present in the mature spermatozoa. The number of conserved proteins was 487, followed by 455, 415, and 357, respectively.

Methods: Sperm were obtained from 12 infertile patients; all patients provided written consent to participate in the study. Following liquefaction, manual semen analysis was performed according to WHO 2010 guidelines to determine sperm concentration and motility. Spermatozoa in the ejaculated semen were analyzed to determine the number of spermatozoa with morphological defects. The number of spermatozoa with morphological defects was determined by dividing the number of spermatozoa with morphological defects by the total number of spermatozoa. The percentage of spermatozoa with morphological defects was determined by dividing the number of spermatozoa with morphological defects by the total number of spermatozoa.

Results: A total of 1202 proteins were identified in the F1-F4 fractions. The number of conserved proteins was 487, followed by 455, 415, and 357, respectively.

Conclusions: A defective signaling cascade is responsible for the defective sperm function in infertile patients. Decline in mitochondrial function and oxidative phosphorylation in the F4 fraction implies an energy deprived hypoxic state. The small colored hexagons represent the proteins, red shapes represent factors involved in the regulation of transcription, blue shapes, transfactors (red shapes), and other proteins (blue shapes). Blue circles show the proteins in the network within the immediate vicinity of those identified proteins. The small colored hexagons are vectors between nodes describe positive interaction (green), unphosphorylated (blue), or negative phosphorylated (red). Each connection (vector) represents a direct interaction between proteins.