Profiling signaling proteins in human spermatozoa: biomarker identification for sperm quality evaluation

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The molecular biology of the spermatozoa has been neglected in the last decade due to the use of assisted reproduction technologies (ART) that bypassed the need for a "normal" ejaculated sperm sample. However, it is preferable to rise sperm quality and avoid ART. Identification of the male infertility factors and biomarkers will improve fertility management and even allow for conception through intercourse.

In this study, we unraveled the signaling pathways involved in regulating human sperm function and correlated them with clinical data. A total of 37 semen samples, obtained from a randomized group of donors, were included in this study. We examined 18 signaling proteins for their phosphorylation or cleavage status. Data was then correlated with basic semen parameters and spermatozoa DNA integrity. The results indicated that the activity of several proteins was significantly correlated with spermatozoa clinical parameters (Figure 1, green and pink nodes). Moreover, we established a profile for the expression of a large number of protein kinases in human spermatozoa. Thirty-four protein kinases were identified as expressed in their total levels in normozoospermic samples (Figure 1, orange and pink nodes). From those, 8 kinases (CDK2, PAK3, KSR1, BMX, DAPK1, CSNK1D, MAP4K2 and ZIPK) were identified for the first time in human spermatozoa.

We have identified several proteins that showed a high degree of differential activity and have the potential to integrate a quantitative array, which may have several applications: explain idiopathic infertility, failure in ART or repeated abortion; choice of the appropriate ART; and assess the efficacy of medical interventions.

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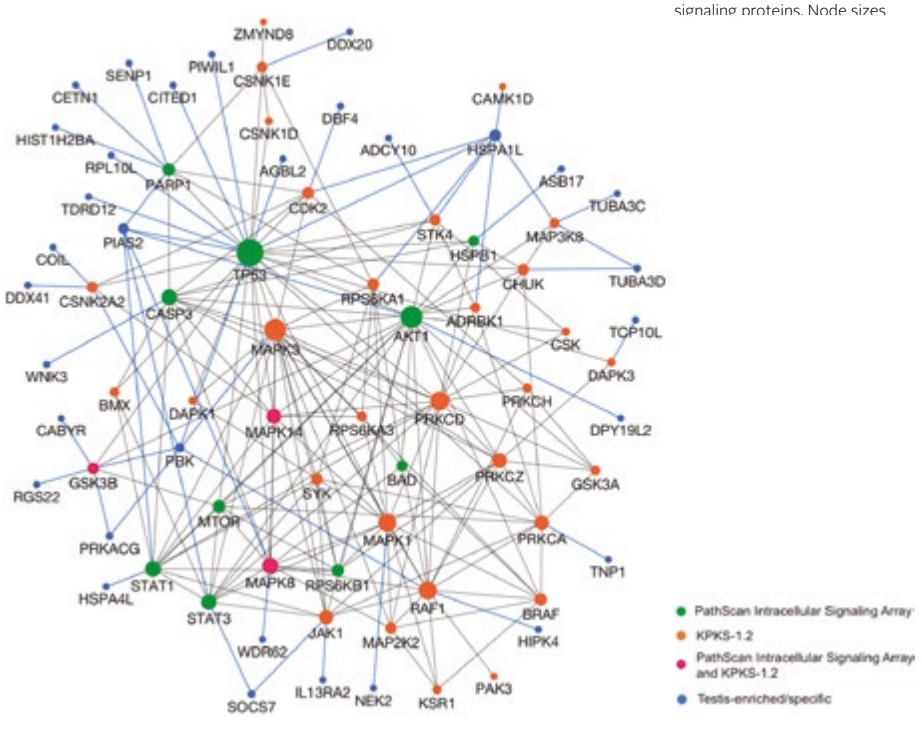

FIGURE 1
Network of the signaling proteins identified as correlated with clinical sperm parameters (green and pink nodes) and in the kinases screen (orange and pink nodes). Blue nodes and edges represent direct testis-enriched/specific interactors/interactions of those signaling proteins. Node sizes