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Spermatid specific thioredoxin (SPTRX3) as a novel human male infertility marker

Clayton Buckman & Peter Sutovsky

Spermatid Specific Thioredoxin (SPTRX3) is a protein that accumulates in the superfluous cytoplasm of defective human spermatozoa. We researched the relationship between SPTRX3 and male infertility in men from 239 couples undergoing IVF or ICSI fertility treatment. The SPTRX3 content of human sperm was evaluated by flow cytometry, epifluorescence microscopy, western blotting, and a novel Image Stream technology. Extremely high sperm SPTRX3 levels (>15% SPTRX3-positive sperm) were discovered in 51% of male infertility patients (n=72, but also in 20% of men from couples with idiopathic infertility (n=61) and in 14% of men from couples with female infertility (n=85). Men with greater than 15% SPTRX3-positive sperm produced fewer pronuclear zygotes and had a significantly reduced chance of conceiving (16.7% pregnant couples vs. 43.8% pregnant with less than 5% SPTRX-positive sperm). SPTRX3-levels were significantly lower in couple treated with IVF compared to couples undergoing ICSI treatment. High sperm SPTRX3 compounded female infertility in couples diagnosed with combined male and female infertility and had a profound effect on pregnancy rates in the subgroup of women over the age of 35. Image Stream confirmed that the SPTRX3 containing cells were spermatozoa with a variety of morphological effects. Flow cytometric data SPTRX3 values positively correlated with light microscopy SPTRX3 evaluation, offering a simple clinical version of SPTRX3-assay. Men with greater than 15% of SPTRX3-positive spermatozoa have their chance of fathering children by IVF or ICSI reduced by nearly two thirds. SPTRX3 protein is a suitable biomarker for unbiased, objective diagnosis of male infertility relevant to decision making in ART.