

SUMMARY OF PROPOSED RESEARCH

(250 words or less)

Do not exceed the space provided

Describe clearly and concisely, in language readily understandable to a biomedical scientist who may not be a specialist in the research project's field, the broad objectives, specific aims, general procedures, and the potential significance of the research.

SUMMARY

High oxidative stress (OS) appears to be a common pathway for multiple infertility-related disorders (varicocele, morphological aberration, spinal cord injury, oligospermia, etc). Disorders of spermatogenesis and epididymal dysfunction are responsible for the majority of alterations in morphology and motility parameters. In the ejaculate, sperm cells are at different stages of maturation and different subsets contribute dramatically to the maturity of the cells when isolated. Immature or dysgenic spermatozoa can produce large quantities of highly unstable free radicals called reactive oxygen species (ROS). These are responsible for the deleterious effects on sperm motility and viability. Several studies have implicated high ROS levels with reduced rates of acrosomal reaction, decreased fertilization capacity of spermatozoa and DNA damage. Several techniques have been developed to improve semen quality for assisted reproductive techniques. The basic principle of all these techniques is to isolate a highly mature and motile spermatozoa population from immature, immotile or dead spermatozoa, and provide high quality sperm for assisted reproduction programs

Our preliminary results show a marked correlation between the presence of residual cytoplasm and high ROS levels. The goal of this study is to identify the efficiency of the spermatogenesis. We will examine the effect of oxidative stress in spermatozoa and cells isolated following density gradient separation from both normal healthy donors and infertile patients before and after complete leukocyte removal. In addition, we will study how defective spermatogenesis as well as alterations in the spermiogenesis influence these recovery rates in presence of high oxidative stress. We will attempt to establish the biochemical link between the type of ROS produced, morphological abnormalities, high cytoplasmic metabolic activity markers such as creatine kinase (CK), and the extent of DNA damage in patients with different clinical diagnosis.

The results of our study will help explain the impact of OS on the different cell population present in a given sample. It will also explain how spermatozoa with low fertility potential and high ROS production can induce deleterious effects on mature and motile spermatozoa present in the same sample. The study will allow us to understand the impact of ROS in the spermiogenesis process, establishing its efficiency in patients with different clinical diagnoses.

Please provide five key words that best describe your project:

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|------------------------|---|----------------------------|
| (1) <u>Infertility</u> | (3) <u>Oxidative stress</u> | (5) <u>Creatine kinase</u> |
| (2) <u>DNA damage</u> | (4) <u>Spermatogenesis/spermiogenesis</u> | |