

**SUMMARY OF PROPOSED RESEARCH**  
(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.

**Project Summary**

Since the initial reported pregnancies using assisted reproductive techniques (ARTs), especially intracytoplasmic sperm injection (ICSI), tremendous progress has occurred in the treatment of male factor infertility.<sup>1</sup> However, there is a great deal of debate in the scientific and medical community on the possible short and long-term adverse effects of bypassing the physiological selection process to achieve fertilization with abnormal spermatozoa using ICSI.<sup>2</sup> In addition, sperm preparation techniques used prior to ARTs are considered as an iatrogenic cause of fertilization failure, as repeated centrifugation of sperm preparations induces damage to spermatozoa via mechanisms mediated by the generation of reactive oxygen species (ROS).<sup>3</sup>

Human spermatozoa are known to be especially sensitive to oxidative stress because of the high content of polyunsaturated fatty acids in their cell membranes.<sup>4</sup> Lipid peroxidation of these membranes appears to be the most important pathologic process responsible for spermatozoal dysfunction, including loss of motility<sup>5</sup>, impaired capacitation<sup>6</sup> and midpiece morphological defects.<sup>7</sup> DNA bases are also susceptible to oxidative stress, and peroxidation of these structures can cause strand breaks and cross-linking of the DNA leading to disrupted transcription, translation and DNA replication.<sup>8</sup> It has been suggested that damaged genomic DNA of the spermatozoa can be transmitted to the progeny and lead to increased incidence of abortions, fetal anomalies and birth defects.<sup>9</sup> High levels of oxidative DNA damage may be involved in the mechanism of male infertility.<sup>10</sup> However, there is still very little information available on the levels of endogenous DNA damage in human spermatozoa.

The aim of our proposed study is to correlate the sperm characteristics with the levels of ROS and DNA damage in the semen samples of patients with male infertility who may undergo assisted reproduction. Also, we will determine the effect of sperm preparation techniques on the levels of oxidative stress-induced DNA damage. We will then determine if the exogenous addition of antioxidants prior to these sperm preparation techniques could reduce the amount of DNA damage. If our hypothesis is correct, then we may be able to reduce the risks like childhood cancer which could be transmitted to the offspring of the couples undergoing ARTs. These results may allow us to decide whether exogenous antioxidant supplementation can minimize collateral DNA damage.

Please provide five Key Words that best describe your project:

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|----------------|----------------------------|--------------------------|
| 1. Infertility | 2. Reactive oxygen species | 3. Assisted reproduction |
| 4. DNA damage  | 5. Antioxidants            |                          |