

SUMMARY OF PROPOSED RESEARCH

Please provide five Key Words that best describe your project:

- (1). Apoptosis (2). DNA damage (3). Magnetic cell separation
(4). PARP (5). Sperm

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

Sperm DNA damage plays an important role in the pathogenesis of male infertility. Failure of fertilization in assisted reproduction (ART) despite the use of morphologically normal and motile spermatozoa may be due to such damage. Poly(ADP-ribose) polymerase (PARP) is nuclear enzyme that plays an important role in repairing damaged DNA. The main objective of our study is to investigate the role of PARP in ejaculated sperm and to attempt to modulate its function with in order to decrease the incidence of DNA damage. In addition, we shall test the ability of the magnetic cell separation technique to extract DNA damaged sperm based on the activity of PARP.

In order to achieve our aims, mature human sperm will be collected from healthy donors and infertile male patients. DNA damage will be induced in sperm using standardized protocols that promote apoptosis and oxidative stress. In addition, PARP and caspase (PARP deactivator) inhibitors will be used to test their ability to modulate PARP. Finally, magnetic cell separation will be performed using PARP as a marker for DNA damaged sperm.

The potential significance of our study lies in elucidating and attempting to modulate the role PARP in sperm DNA damage. The success of magnetic cell separation to extract DNA damaged sperm shall provide a novel in vitro model to study the mechanisms of sperm DNA damage and its role in male infertility. Alternatively, it may also be used as a sperm preparation technique that positively impacts ART success rates.