

A REPOSITORY OF ENU MUTANT MOUSE LINES AND THEIR POTENTIAL FOR MALE FERTILITY RESEARCH

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One in 25 western men are infertile and the causal factor is frequently unknown, although it is expected that many are genetic in origin. My project aims to identify genes critical to mouse spermatogenesis using ENU mutagenesis. A further aim was to develop a repository of mutant mice and data on their fertility parameters for use by the reproductive biology community. This research will aid the diagnosis and development of specific treatments for human infertility and the development of contraceptive agents. The potent mutagen *N-ethyl-N-nitrosourea* (ENU) was utilized to generate libraries of C57BL/6 mice with random point mutations throughout their genomes. A 3 generational breeding program produced mice that were homozygous for a number of mutations. I subsequently performed a number of large scale screens on 3rd generation males, identifying lines carrying recessive mutations specifically affecting male fertility. Thus far we have observed a wide range of abnormal testis phenotypes including Sertoli Cell only, hypospermatogenesis, meiosis arrest, abnormal sperm morphology and abnormal hormone levels. From these analyses a repository including all data and tissues collected from 1200 3rd generation male mice from 122 different lines has been developed and will become publicly available. This includes testis and epididymal histology and serum levels of FSH, LH, activin A and inhibin. Further, I have stored gDNA long term and cryopreserved sperm to enable regeneration of lines in the future. In addition, I have developed a high throughput mutation screening protocol for the detection of mutations within genes of interest using denaturing high performance liquid chromatography (DHPLC). Collectively, our repository and gene screening techniques can be used in conjunction with artificial reproductive technologies to generate mouse models reflective of human conditions and altered specific gene function.