Characterization of a New Gene Causing Male Infertility in the M366 Mouse Model

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Abstract

Spermatogenesis is a complex process involving hundreds of genes, and a malfunction of any protein involved in gamete maturation could potentially result in nonfunctional sperm. Spermatogenesis is very similar between mice and humans, making mice good models for infertility studies. The M366 mouse model involves a mutation in a novel gene called Nup210l. This mutation causes infertility in homozygous male mice. Preliminary studies suggest the mutation may affect the function of Sertoli cells, which are vital to spermatogenesis. The purpose of this study is to further explore the nature of this novel gene and the infertility-causing mutation in the M366 mouse model. Characterization of the normal Nup210L gene will include identification of splice variants using mouse testicular RNA and confirmation of the existence of a NUP210L transcript in human testes. The nucleotide sequence of the mutated Nup210l gene carried by affected M366 mice will be compared to the nucleotide sequence of the wild-type Nup210l gene so that the exact nature of the mutation may be determined. These preliminary studies to characterize both wild-type and mutant variants of the Nup210l gene and their expression will form the basis of future work to define the precise role of the Nup210l protein in spermatogenesis.

Introduction

○ The mouse strain M366 carries a mutational insertion in a novel gene called Nup210. The exact nature of the mutation is unknown.
○ Homozygous affected male M366 mice are infertile and have defects in Sertoli cells and spermatogenesis.
○ The NUP210L gene in humans has been predicted but not yet shown to produce transcripts.

Nup210l Transcript Sequence Alignment

Evidence for Mouse Nup210l Splice Variants

Confirmation of Human NUP210L Transcript

Conclusions

○ Nucleotide sequence analysis done to date does not show any major differences between the M366 allele of Nup210l and the wild-type allele.
○ There is evidence that mouse Nup210l is alternatively spliced in tests.
○ We have demonstrated experimentally the presence of a human NUP210L transcript.

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