James Millonig

"Vacuolated Lens (vl) A Mouse Model for Spinal Cord Regeneration" - Completed

"The Development of Spinal Cord Therapies Through a Genetic Analysis of Mouse Spinal Cord Development" – Open

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Two manuscripts have been written and will be submitted by the end of the year. The first manuscript describes the positional cloning of the *vacuolated lens* locus and the characterization of the mutant protein. It is entitled "The orphan G protein coupled receptor, *Gpr161*, encodes the *vacuolated lens* locus and controls neurulation and lens development" and will be submitted to *Genes and Development*. The cloning of an orphan GPCR as the gene responsible for the *vacuolated lens* spina bifida phenotype indicates the presence of an unidentified ligand in the neural environment necessary for neural tube closure. The second manuscript demonstrates that the *vacuolated lens* phenotypes are due to the mutation plus other unlinked modifying loci and describes the mapping of the modifier loci. This manuscript is entitled "Localization of modifier loci for the *vacuolated lens* mutant, a mouse model of spina bifida and congenital cataracts" and will be submitted to *Physiological Genomics*. These findings have established the *vacuolated lens* mutant as a mouse model to study the multi-factorial inheritance of human neural tube defects.

The Commission grants have allowed us to pursue research relevant to human spinal cord injury and disease. The data generated from these grants have led to manuscripts that will be important for my future promotion. Our spinal cord research complements other genetic disease research in the lab and has helped establish the lab as a leader in the genetic research of human neurodevelopmental disorders.

The Commission funding has led to new research in two areas. One, the lab is currently conducting experiments to identify the ligand for the *vacuolated lens* GPCR. The identification of this ligand will be important for understanding spinal cord development and may provide a therapeutic tool for treating spinal cord injury. Two, the lab has demonstrated that one of the modifier loci is sufficient to rescue the *vl* associated lethality that is likely to be due to the spina bifida phenotype. Our plan is to apply for NIH funding to clone the gene responsible for rescuing the *vl* lethality.

The Commission funding has significantly increased our interest in spinal cord disease and injury. Without this funding this interest would have never been stimulated and most of the research would not have been pursued. In addition, the funding of multiple investigators with different expertise at UMDNJ-RWJMS has led to a commitment to spinal cord research and an environment where multiple approaches are being used to address the same scientific problem.