HEALTH RESEARCH ABSTRACT SUBMISSIONS #28

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Title of Research *	Inhibiting Glial Tumorigenesis with NF2 Protein Merlin
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Introduction & Purpose *

NF2 (Neurofibromatosis Type II) is a genetic disorder that gives rise to tumors in the brain and spine. These tumors are a result of an inactive tumor suppressor protein called Merlin. While Merlin's suppression of tumor growth has been well correlated in previous publications, its specific functioning in the body is still poorly understood.

The focus of my research is to shed light on the mechanism of the tumor suppressor Merlin by biologically engineering a fluorescent variant of Merlin. This new version of the protein can then be reintroduced into nerve tissue and Merlin's cellular interactions can be directly monitored by fluorescent microscopy

Experimental Design *

The intent of this project is to provide a method to directly view Merlin intracellularly and provide further data for trafficking models. This will involve observing the CFP (cyan fluorescent protein) tagged Merlin DNA construct using FRET microscopy. In brief this requires cutting out CFP DNA and inserting it into a vector with functional Merlin sequence and a Kanamycin antibacterial sequence. This vector can then be inserted and selected for through bacterial culturing. The tagged Merlin will then be inserted into human schwannoma cells lacking functional Merlin and using FRET microscopy, interactions can then be observed.

Results *	This ongoing experiment will be useful for peripheral research projects involving in vitro observation of Merlin in normal and cancerous nerve tissue.

Conclusions *

The prevalence of this variety of sporadic tumors with NF2 suggests Merlin has a broad range of tumor suppressing activity and while this role has been extensively documented and studied, its physiological mechanism is still not well understood. Moreover, while the putative effects of Merlin as a transcriptional regulator are well established, the specific interactions and mechanisms need to be further investigated.
One important aspect that will be observed will be cellular control of the accessibility of transcriptional proteins such as ErbB2, which releases cellular growth factors upon activation. The cell can control the activation of some transmembrane receptors by making them accessible to effectors or by not making them accessible or keeping then within the cell cytosol and not in the cell phospholipid bilayer. Therefore a fluorescently tagged Merlin could shed light on the question of how ErbB2 is activated.

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