

**New Jersey State Commission on Cancer Research
LAY ABSTRACT OF RESEARCH PROJECT**

NAME OF PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR: **Patrizia Casaccia-Ben nefil**

Project Title: **Defective epigenetic changes in the genesis of gliomas**

Description: **This grant asks two main questions: what is the cell of origin of brain tumor ? what renders a neural stem cell undergo transformation ?**

Malignant gliomas are the most frequent adult brain tumor, with an incidence of almost 12 per 100,000 people in the US and slightly higher incidence in New Jersey. Unfortunately, gliomas are also the most common childhood brain tumors after leukemias. Due to their characteristic infiltrative behavior in the brain parenchyma, these tumors cannot be completely removed by surgery and are typically non-responsive to chemotherapeutic schemes that are used for the treatment of other types of cancer. The result is an extremely elevated mortality rate. Due to the high incidence of brain tumors in both adult and children and to the extremely high mortality of these forms of cancer, it becomes critical for the general public and for the population of New Jersey in particular, to promote a better understanding of the mechanisms of generation of glial tumors.

The discovery of novel therapeutic approaches for gliomas begins with the answer to two fundamental questions:

- 1.) WHICH CELLS GENERATE GLIAL TUMORS ?
- 2.) WHAT ARE THE MECHANISMS RESPONSIBLE FOR TRANSFORMATION OF THESE CELLS INTO CANCER ?

This grant is aimed at providing answers to these two basic and essential questions.

Based on our previous studies and several other reports on the characterization of glial brain tumors (including the early loss of a protein called p53), we have hypothesized that these tumors originate from NEURAL STEM CELLS residing in a special region of the brain called the subventricular zone. According to our model, these cells first lose the ability to stop proliferating (by losing p53) and then gradually become unable to follow the normal program of differentiation into glial cells, due to loss or decreased activity of enzymes called HDACs. A combination of studies in cultured rodent cells and transplantation experiment in mice will be adopted to test this model.

The results of the proposed studies will provide a critical insight on the generation of glial tumors from adult neural stem cells. The relevance of this research proposal is two-fold: on one hand it will provide essential information for the study of cancer biology, on the other hand it will address issues related to the potential risks associated with stem cell replacement therapies.

