

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

NAME OF PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR: **Monica Roth**

Project Title: **Targeting Hematopoietic Stem Cells for Cancer Therapy**

Description: **The research aims at introducing drug resistance genes to hematopoietic progenitor cells using modified retroviral vectors that specifically recognize these stem cell populations.**

Chemotherapy involves the use of toxic drugs to eliminate the cancerous cells. However, the use of high dose chemotherapy often results in deleterious effects on the normal cells required for recovery. Methods are being developed to protect the hematopoietic stem cells, needed to replenish the body, from high dose chemotherapy. These methods introduce protective genes that provide drug resistance to the chemotherapeutic agents. Methods currently available to introduce these protective genes into cells do not work with high specificity or efficiency with human hematopoietic stem cells. The studies in this application aim at improving the specificity and ultimately, the efficiency of delivering genes to human hematopoietic stem cells. The approach randomizes a small domain on the surface protein of the retroviral gene delivery particles that bind to the target cell receptor proteins. It has been shown that changing this small stretch of eleven amino acids can direct the viral vectors to enter the cell through new receptor proteins. The experiments in this proposal aim at screening the library of vector particles for isolates that bind to receptor proteins that are specifically expressed on human hematopoietic stem cells. Stem cells and progenitor cells have unique properties and protein expression patterns. It is strongly believed that these proteins can be targeted to be receptors for gene delivery particles. For example, stem cells are known to express proteins that eliminate toxins, known as multidrug resistance genes. These pumps allow the stem cells to exist in the body for long periods of time without accumulating mutations. One goal of our research is to see if these multidrug resistance genes could serve as viral receptors. Multidrug resistance genes are also expressed on numerous cancer cells, including breast cancer. The ability to direct gene delivery to cells overexpressing multidrug resistance genes would have a broad impact on other cancers, beyond those of the hematopoietic lineages.