STRONG CHILDREN'S RESEARCH CENTER

Summer 2014 Research Scholar

Name: Leti Nunez

School: University of Rochester

Mentor: Craig Mullen M.D., Ph.D.

ABSTRACT

Title : Identifying the Median Lethal Dosage of Common Chemotherapy Drugs in Primary B-cell Acute Lymphoblastic Leukemia

Background: B-cell acute lymphoblastic leukemia (B-ALL) is the most prevalent childhood malignancy.[1] While many of patients respond well to current chemotherapies (80-90%), there still remains a subset of patients that are more resistant to common therapies after relapse; these relapse patients generally have a significantly reduced survival outcome.[2-4] Furthermore, this has generated a necessity for current research efforts to develop different types of therapies to treat these resistant patients.

Objective: Our group's focus is on therapies that target the bone marrow microenvironment. Since B-ALL is known to only grow in vitro in the presence of mesenchymal stromal cells, this further suggests the importance of the microenvironment to the malignancy. Our group aims to combine siRNA targeting stromal cell genes with common chemotherapy drugs to determine if the combination leads to synergistic effects. This study focused on determining the median lethal dosage for five commonly used chemotherapy drugs: dexamethasone, vincristine, L-asparaginase, 6-mercaptopurine, and methotrexate.

Methods: Immortalized recombinant human mesenchymal stromal cells, with human TERT and GFP, were plated 20,000 per well in a 96-well plate in RPMI with 10% fetal calf serum and 100 moles of hydrocortisone.[5] After 24 hours of incubation, media was removed and the stromal monolayer was washed with RPMI 1640. Subsequently, primary B-ALLPAL3 Tw 0..2(d)3.8-1(9)-48(ed)-7,000 p

combine the chemotherapy drugs at the median lethal dosage with siRNA targeting stromal cell genes and determine the outcome.

References:

1.