



Medical Education and Research Grant Outcome Report

Name: Role of Ikaros in Cellular Proliferation

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Department: Pediatrics

Program: New Investigator Program

Grant Duration: 03-01-06 to 02-28-08 (24 months)

Expenditures: \$100,000 (100% expended)

Use of Funds (Taxonomy): Basic research

Research Keywords: Leukemia, tumor suppression, signal transduction, phosphorylation, Ikaros

► **Description:** The aim of the research was to discover the mechanism that controls the multiplication of leukemia cells by gaining insight into normal vs malignant blood cell formation. The aims of the research were to: (1) study how the Ikaros gene affects cellular differentiation and multiplication and (2) determine the role of Ikaros in responding to DNA damage. Altering a cell's DNA-damage response has been proposed as a means of improving chemotherapies. By examining how Ikaros influences normal and aberrant cell proliferation, the researchers expected to gain insight into potential new treatment strategies.

► **Results:** The research results produced novel information on the mechanisms that control the growth of leukemia cells. In addition, insights into the mechanisms of response to DNA damage from irradiation may help design therapies that enhance current chemotherapy drugs.

Discoveries included:

- Ikaros plays an important role in tumor suppression and cellular proliferation in acute leukemia.
- The activity of the Ikaros gene is controlled by specific enzymes.
- A new signaling pathway was identified, which regulates differentiation and multiplication of acute leukemia cells.
- Activity of the Ikaros gene changes during induction of DNA damage, suggesting that Ikaros plays an important role in this process.

The discovery of the enzymes controlling genetic activity can potentially lead to a new target for specific, less toxic chemotherapy for this type of leukemia. Similarly, the discovery of the signaling pathway can potentially contribute to more effective combination therapies for leukemia.

This research provides new and important information and will yield insights into the pathophysiology and treatment of leukemia and other malignancies.

► **Met Objectives:** Project completed

► **Timeline for Application of Results:** 5-7 years

► **New Partnerships or Collaborations:** Collaborations with researchers at UW School of Medicine and Public Health and at two other universities.

► **Matched Dollars (cash or in-kind):** \$0

► **Dissemination:**

- Published article: *Journal of Biological Chemistry*
- Two articles submitted for publication

► **Additional Funding:** \$330,000 (3-year funding) from St. Baldrick's Foundation.