20th International p53 Workshop- Abstract Submission Template

Submission Deadline: January 31st 2026 (5pm EDT)
Notification of acceptance: By or before February 27, 2026

Title of study/project: **Elucidating Mechanisms of TP53-mediated Leukemia Immune Escape**

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Training program first author is enrolled in: **MIT Biology PhD Program**

Year of training: **GY 3**

Abstract: *Suggested format: Purpose, Materials and Methods, Results, Conclusions*

Purpose: The immune system is a potent barrier to malignant cellular transformation, yet many humans develop and unfortunately succumb to cancer. In the context of acute leukemias, such as acute myeloid leukemia (AML) and B-cell acute lymphoblastic leukemia (B-ALL), immunotherapies have been widely used and achieved cures in some cases. Despite this, specific genetic subsets of leukemia have been documented to lead to worse treatment outcomes, and the roles of many of these mutations in immunotherapy resistance remain elusive. Leukemias with mutations in *TP53* are a notable example of a disease subset known to lead to worse treatment outcomes, even when treated with immunotherapy. Thus, we hypothesize that *TP53* mutations promote immune evasion and immune suppression in the leukemia microenvironment, contributing to therapy resistance. **Methods:** We developed a novel *in vivo* screening approach using an immunogenic murine B-ALL model combined with high-throughput base editing to screen thousands of patient-derived mutations to identify immune-evasive genetic variants. This immunogenic B-ALL model was also leveraged to test the role of specific *Trp53* mutations in disease progression under strong immune pressure. **Results:** *Trp53* mutations, among many others, were associated with immune escape in our screen. Certain *Trp53* variants were particularly enriched in leukemia populations retaining antigen expression. Studies of individual *Trp53* mutations showed significantly fewer leukemia-specific T-cells in the bone marrow compared to isogenic controls. Interestingly, mutant *Trp53* escaping populations retained antigen expression, whereas *Trp53* wild type leukemias predominantly escaped through stochastic antigen silencing. **Conclusions:** Together, these findings suggest *Trp53* mutations can alter the response to T-cell based anti-leukemia immunity in our models, contributing to immune escape and therapy failure. Ongoing studies aim to further define the molecular pathways underlying this phenotype and to determine its relevance across additional leukemia contexts and treatment modalities.

Please email your submission to us at p53workshop2026@uhn.ca . Please use the following subject heading: Abstract- p53 International workshop