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: Functional modulation of p53 via combinatorial modifications
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Training program first author is enrolled in: Senior Postdoc/Visiting Scientist (I am a senior postdoc equivalent position although my official title was re-defined in order to help me maintain visa status in the USA following changes in federal regulation in 2025)
Year of training: 8 (8th year equivalent of a postdoc)
Abstract: The tumor suppressor p53 integrates diverse cellular stresses to elicit distinct transcriptional and cell fate responses. A central but unresolved question is how p53 discriminates among different upstream signals to generate specific downstream outputs. One mechanism to encode the signaling logic is thought to occur via differential post-translational modifications (PTMs) of p53; however, technical limitations have previously prevented comprehensive characterization of *entire* modification patterns on *individual* p53 molecules. Here, we applied a novel intact-protein mass spectrometry approach (I2MS) that circumvents enzymatic fragmentation, enabling direct detection of overall PTM patterns on single p53 to decipher its modification form (modform). Using I2MS, we resolved distinct p53 PTM signatures induced by different activation modes, including DNA damage, MDM2 inhibition (Nutlin) and quantified the distribution of all p53 modforms. We found specific acetylation and phosphorylation sites that were uniquely enriched by different stressors. Guided by these data, we generated combinatorial p53 PTM-mimetic mutants to interrogate how specific modification patterns regulate transcriptional output. We demonstrated that defined PTM combinations selectively activate distinct subsets of p53 target genes, resulting in divergent cell fate decisions such as cell cycle arrest versus apoptosis. Leveraging this mechanistic insight, we developed a therapeutic strategy using self-amplifying RNA (saRNA) encoding selected p53 PTM-mimetic variants. Delivery of these saRNAs enabled single copies of p53 PTM-mimetic RNA to be rapidly amplified within any cells with initial uptake of the saRNA, therefore p53 protein levels to also accumulate which caused selective killing across multiple cancer cell lines in vitro. In vivo mice tumor studies are currently underway with the results imminent. Collectively, this work establishes PTM patterning as a critical determinant of p53 signaling and gene regulation specificity, as well as introducing tunable RNA-based approaches as a promising p53 therapeutic avenue; opening new directions for fundamental understanding and targeted manipulation of the p53 network.

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