20th International p53 Workshop- Abstract Submission Template

Submission Deadline: December 31, 2025 (5pm EDT)
Notification of acceptance: January 30, 2026

Title of study/project: **The role of p53 in early primary invasion**

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Training program first author is enrolled in: PhD in biomedical science

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Abstract:

Purpose: Loss of the tumor suppressor p53 is strongly associated with metastatic progression and poor prognosis in colorectal cancer, yet its role in restraining the earliest stage of invasion remains unclear. This study investigates how p53 loss enables epithelial cells to acquire invasive and tumor-initiating properties during primary invasion.

Materials and Methods: We used an inducible, intestinal-specific CKIα and p53 double-knockout (DKO) mouse model to capture early invasive events in vivo. Cellular states and lineage transitions were examined by high-definition spatial transcriptomics, with spatial proximity analyses to assess tumor–microenvironment interactions.

Results: Combined loss of p53 and CKIα caused rapid epithelial destabilization and enrichment of $Prox1^{+}$ epithelial cells invading the villous lamina propria. These cells exhibited strong tumor-initiating capacity ex vivo, indicating a stem-like invasive state normally suppressed by p53. Spatial analyses identified a non-canonical stem-like population distinct from $Lgr5^{+}$ intestinal stem cells. Cell trajectory inference demonstrated that $Prox1^{+}$ cells originate from differentiated villus epithelium, revealing a p53-dependent barrier to

epithelial plasticity. Spatial profiling further uncovered coordinated remodeling of the tumor microenvironment, with enrichment of myeloid cells adjacent to invading Prox1^{+} cells, suggesting that p53 loss promotes invasion through both epithelial reprogramming and microenvironmental signaling.

Conclusions: These findings reveal a previously unappreciated role for p53 in suppressing primary invasion by constraining epithelial plasticity and tumor–microenvironment communication. Loss of p53 activates a Prox1-associated early primary invasion that highlight new opportunities for early prognosis and clinical interventions.

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