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Ph.D. DISSERTATION DEFENSE

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Date:	Wednesday, March 11th, 2026
Time/Location:	10:00 a.m. / McLean 510
Title:	Epithelial-Specific Loss of SMAD4 Alleviates the Fibrotic Response in an Acute Colitis Mouse Model
Chairperson:	Dr. Ansu Perekatt, Department of Chemistry and Chemical Biology School of Engineering and Science
Committee Members:	Dr. Woo Lee, Department of Chemistry and Chemical Biology, School of Engineering and Science Dr. Paola DiMarzio, Department of Chemistry and Chemical Biology, School of Engineering and Science Dr. Shang Wang, Department of Biomedical Engineering, School of Engineering and Science

ABSTRACT

Mucosal healing is strongly linked to improved clinical outcomes in patients with inflammatory bowel disease; however, the specific role of the epithelium in driving this process in vivo remains poorly defined. To address this, we examined mucosal repair in an acute dextran sulfate sodium–induced colitis model in which epithelial-specific deletion of Smad4 results in an attenuated colitis response. We find that enhanced epithelial wound healing alleviates the fibrotic response. Dextran sulfate sodium caused increased mesenchymal collagen deposition—indicative of fibrosis—within a week in the WT but not in the Smad4 KO colon. The fibrotic response correlated with decreased epithelial proliferation in the WT, whereas uninterrupted proliferation and an expanded zone of proliferation were observed in the Smad4 KO colon epithelium. Furthermore, the Smad4 KO colon showed epithelial extracellular matrix alterations that promote epithelial regeneration. Our data suggests that epithelium is a key determinant of the mucosal healing response in vivo, implicating mucosal healing as a strategy against fibrosis in inflammatory bowel disease patients.