Characterization of colonic apoptosis following DSS induced colitis in the absence of Lrig3

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Introduction

Abstract

Research in the Powell lab focuses on the epithelium of the small intestine and colon during hematopoietic and immune diseases. Heterozygous Lrig1 individuals display increased intestinal inflammation and colitis compared to wildtype mice. This effect can be reversed by classic inflammatory cytokine inhibitors. Previous research in the Powell lab has shown that the transcriptional repressor and chaperone Lrig1 is required for this phenotype. This study also showed that Lrig1 directly controls cell death and differentiates between epithelial and immune cells. This cell death requires the presence of Lrig1 but not Lrig3, which is a similar transcriptional repressor in other tissues. This study has shown that Lrig1-mediated cell death is tissue specific and is required in the intestine to control the inflammatory response.

Methods

1. Does Lrig3 play a role in colonic tissue repair after DSS induced colitis?

• The Powell lab is investigating this question by examining apoptosis, leukocyte infiltration, proliferation, and the morphology of a DSS induced colitis in models with and without Lrig3.

2. Hypothesis: Loss of Lrig3 causes a decrease in apoptosis after DSS induced colitis

Background

The Colonic Epithelium

Lrig and Ulcerative Colitis

Lrig1 is known to control immune and epithelial cell functions. Lrig1 is a known tumor suppressor and induces apoptosis in the colon. It has been shown that Lrig1 regulates the inflammatory response in the gut. Lrig1 was found to be critical for the resolution of inflammation in the colon. Lrig1 is also a transcriptional repressor that can control cell proliferation and differentiation. It has been shown that Lrig1 expression is necessary for the resolution of inflammation in the colon.

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Apoptosis

Programmed cell death (apoptosis) is an essential process within all types of tissues. The colon-specific epithelial repressor inhibits control of proliferation at the base of the crypt and apoptosis as the cells shed at the top of the crypt. Studying the factors that influence these homeostatic mechanisms may be an important step towards understanding the etiology of ulcerative colitis.

Apoptosis

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Future Directions

Acknowledgements

• Further investigation of the role of Lrig3 in apoptosis pathways
• B-catenin activity
• Leukocyte infiltration, proliferation, and differentiation in the colon with and without Lrig3

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Conclusion

No significant difference in the amount of apoptotic cells that occur during DSS induced colitis was observed between models that had Lrig3 versus models that did not have Lrig3. That being said, there was a slight decrease in the amount of apoptosis that occurred in the cohort with Lrig3 excised compared to the cohort with two functional Lrig3 alleles. Additional research should be conducted to further explore the potential role of Lrig3 in DSS induced ulcerative colitis recovery.