

# Regulation of HDACs and Histone Acetylation in Intestinal Epithelial Cells by Lipopolysaccharide

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## Introduction

The gut microbiota interacts directly with intestinal epithelial cells (IECs) that line the intestinal tract. These cells play a critical role in responding to commensal bacterial-derived signals to dynamically maintain intestinal homeostasis. In addition, epigenomic modifications regulate gene expression in response to environmental cues without altering the genetic sequence. Our lab identified that a specific epigenomic-modifying enzyme, histone deacetylase 3 (HDAC3), is a critical factor that regulates histone acetylation in IECs and integrates commensal bacterial-derived signals to regulate intestinal homeostasis. Furthermore, deletion of IEC-intrinsic HDAC3 results in increased susceptibility to intestinal damage and inflammation in the presence of the microbiota. However, how the microbiota affects HDAC3 activity and expression in host IECs is not well understood.

## Hypothesis

We hypothesize that lipopolysaccharide (LPS), a product derived from gram negative bacteria, impacts the expression and activity of HDAC3 in IECs, and thus may mediate how microbes regulate gene expression through histone acetylation.

## Methods

The goal of the project is to understand whether HDAC activity and expression in CMT93 (mouse intestinal epithelial) cells is affected after treatment with LPS. To evaluate this, CMT93 cells were treated with LPS at increasing concentrations for 4 hours. Following treatment, cells were lysed and HDAC activity was assayed and HDAC expression was measured by Western blot. Immunohistochemistry was used to examine whether LPS induces altered HDAC3 localization and expression along with differences in acetylated histone 3 (AcH3).

## Results

Treatment of the CMT93 cells with LPS led to a significant dose-dependent increase in HDAC activity. However, results from the Western blots revealed that HDAC expression was unaffected in the epithelial cell line post-LPS treatment. However, immunohistochemistry revealed decreased AcH3 within the nucleus, and an increase in nuclear localization of HDAC3 following LPS treatment.

## Conclusions

The data supports that LPS induces HDAC activity and HDAC3 nuclear localization in IECs. LPS-triggered regulation by HDAC3 may affect the expression of microbiota-dependent genes responsible for maintaining intestinal homeostasis. The findings from this project may shed light on the pathogenesis of Inflammatory Bowel Disease (IBD), highlighting how certain bacterial-derived products may alter the epigenomic pathways and therefore modulate gene expression in the intestine.

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