

# Epithelial GPR35 protects from *Citrobacter rodentium* infection by preserving goblet cells and mucosal barrier integrity

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The Manuscript Microscope Sentence Audit is a research paper introspection system that parses the text of your manuscript into minimal sentence components for faster, more accurate, enhanced proofreading.

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The combined approaches ensure easier, faster, more effective proofreading.

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- Depending on the source of the input text, the Sentence Audit may contain occasional html artefacts that are parsed as sentences (E.g. "Download figure. Open in new tab").
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### Research Paper Sections:

The sections of the research paper input text parsed in this audit.

[illegible]

Title      **Epithelial GPR35 protects from Citrobacter rodentium infection by preserving goblet cells and mucosal barrier integrity**

**S1 [001]      Summary**

**S1 [002]**      Goblet cells secrete mucin to create a protective mucus layer against invasive bacterial infection and are therefore essential for maintaining intestinal health.

Goblet cells secrete mucin ...  
... to create a protective mucus layer ...  
... against invasive bacterial infection ...  
... and are therefore essential ...  
... for maintaining intestinal health.

**S1 [003]**      However, the molecular pathways that regulate goblet cell function remain largely unknown.

However, ...  
... the molecular pathways ...  
... that regulate goblet cell function remain largely unknown.

**S1 [004]**      Although GPR35 is highly expressed in colonic epithelial cells, its importance in promoting the epithelial barrier is unclear.

Although GPR35 is highly expressed ...  
... in colonic epithelial cells, ...  
... its importance ...  
... in promoting the epithelial barrier is unclear.

**S1 [005]**      In this study, we show that epithelial Gpr35 plays a critical role in goblet cell function.

In this study, ...  
... we show ...  
... that epithelial Gpr35 plays a critical role ...  
... in goblet cell function.

**S1 [006]**      In mice, cell type-specific deletion of Gpr35 in epithelial cells but not in macrophages results in goblet cell depletion and dysbiosis, rendering these animals more susceptible to Citrobacter rodentium infection.

In mice, ...  
... cell type-specific deletion ...  
... of Gpr35 ...  
... in epithelial cells ...  
... but not ...  
... in macrophages results ...  
... in goblet cell depletion ...  
... and dysbiosis, ...  
... rendering these animals more susceptible ...

... to *Citrobacter rodentium* infection.

**S1 [007]** Mechanistically, scRNA-seq analysis indicates that signaling of epithelial Gpr35 is essential to maintain normal pyroptosis levels in goblet cells.

Mechanistically, ...  
... scRNA-seq analysis indicates ...  
... that signaling ...  
... of epithelial Gpr35 is essential ...  
... to maintain normal pyroptosis levels ...  
... in goblet cells.

**S1 [008]** Our work shows that the epithelial presence of Gpr35 is a critical element for the function of goblet cell-mediated symbiosis between host and microbiota.

Our work shows ...  
... that the epithelial presence ...  
... of Gpr35 is a critical element ...  
... for the function ...  
... of goblet cell-mediated symbiosis ...  
... between host ...  
... and microbiota.

**S1 [009]** Figure1

Figure1

## **S2 [010] Introduction**

**S2 [011]** Goblet cells are the most abundant secretory epithelial cells in the colon.

Goblet cells are the most abundant secretory epithelial cells ...  
... in the colon.

**S2 [012]** Their principal functions involve the production and secretion of mucins, thereby providing a thick mucus layer covering the apical surface of the intestinal epithelium.

Their principal functions involve the production ...  
... and secretion ...  
... of mucins, ...  
... thereby providing a thick mucus layer covering the apical surface ...  
... of the intestinal epithelium.

**S2 [013]** This mucus layer acts as the first line of defense by fending off luminal bacteria, thus reducing bacterial exposure of epithelial and immune cells.

This mucus layer acts ...  
... as the first line ...  
... of defense ...  
... by fending off luminal bacteria, ...

... thus reducing bacterial exposure ...  
... of epithelial ...  
... and immune cells.

**S2 [014]** Gel-forming O-linked glycosylated Muc2 polymers are the main component of the intestinal mucus and play a crucial role in maintaining a regular microbial community in the gut (Wu et al., 2018).

Gel-forming O-linked glycosylated Muc2 polymers are the main component ...  
... of the intestinal mucus ...  
... and play a crucial role ...  
... in maintaining a regular microbial community ...  
... in the gut ...  
... (Wu et al., 2018).

**S2 [015]** Mucus layer impairment leads to infection and inflammation, as described for inflammatory bowel disease (IBD) (Cornick et al., 2015; Wells et al., 2017).

Mucus layer impairment leads ...  
... to infection ...  
... and inflammation, ...  
... as described ...  
... for inflammatory bowel disease ...  
... (IBD) ...  
... (Cornick et al., 2015; ...  
... Wells et al., 2017).

**S2 [016]** Indeed, ulcerative colitis (UC) has been associated with a reduced number of goblet cells, defective production and secretion of mucins, and increased bacterial penetration (van der Post et al., 2019).

Indeed, ...  
... ulcerative colitis ...  
... (UC) ...  
... has been associated ...  
... with a reduced number ...  
... of goblet cells, ...  
... defective production ...  
... and secretion ...  
... of mucins, ...  
... and increased bacterial penetration ...  
... (van der Post et al., 2019).

**S2 [017]** Muc2-deficient mice display excessive bacterial contact with their colonic epithelium and spontaneously develop chronic colitis (Johansson et al., 2011a; Johansson et al., 2011b; Johansson et al., 2008; Zarepour et al., 2013).

Muc2-deficient mice display excessive bacterial contact ...  
... with their colonic epithelium ...  
... and spontaneously develop chronic colitis ...  
... (Johansson et al., 2011a; ...  
... Johansson et al., 2011b; ...  
... Johansson et al., 2008; ...  
... Zarepour et al., 2013).

**S2 [018]** The lack of Muc2 also impairs clearance of the attaching and effacing (A/E) pathogen *Citrobacter rodentium* (*C. rodentium*) (Bergstrom et al., 2010).

The lack ...  
... of Muc2 also impairs clearance ...  
... of the attaching ...  
... and effacing ...  
... (A/E) ...  
... pathogen *Citrobacter rodentium* ...  
... (*C. rodentium*) ...  
... (Bergstrom et al., 2010).

**S2 [019]** Intriguingly, the precise mechanisms that alter the mucus layer leading to defective barrier integrity remain largely unknown.

Intriguingly, ...  
... the precise mechanisms ...  
... that alter the mucus layer leading ...  
... to defective barrier integrity remain largely unknown.

**S2 [020]** Supporting the hypothesis that the microbiota and their metabolites strongly contribute to the modulation of the intestinal mucus layer which appears thinner in germ-free mice than in conventionally housed mice (Johansson et al., 2015).

Supporting the hypothesis ...  
... that the microbiota ...  
... and their metabolites strongly contribute ...  
... to the modulation ...  
... of the intestinal mucus layer ...  
... which appears thinner ...  
... in germ-free mice ...  
... than in conventionally housed mice ...  
... (Johansson et al., 2015).

**S2 [021]** The microbiota-mediated establishment of intestinal barrier integrity is dependent on signaling through G protein-coupled receptors (GPCRs) (Melhem et al., 2019; Tan et al., 2017).

The microbiota-mediated establishment ...  
... of intestinal barrier integrity is dependent ...  
... on signaling ...  
... through G protein-coupled receptors ...  
... (GPCRs) ...  
... (Melhem et al., 2019; ...  
... Tan et al., 2017).

**S2 [022]** Genome-wide association studies on GPR35 single nucleotide polymorphisms indicated that the rs3749171 variant of GPR35, responsible for T108M substitution, might be related to the pathogenesis of UC (Ellinghaus et al., 2013; Imielinski et al., 2009).

Genome-wide association studies ...  
... on GPR35 single nucleotide polymorphisms indicated ...  
... that the rs3749171 variant ...

## **End of Sample Audit**

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