Novel *Escherichia coli* Derived Therapeutic Immunotherapies Reduce Innate Immune Responses to Protect Muc2 deficient mice from Spontaneous Colitis

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*QBECO* treatment reduced RegIIIβ expression and modulates the gut microbiome

**Abstract**

Ulcerative Colitis (UC) is a form of inflammatory bowel disease (IBD) in which the intestinal mucosal barrier, including the mucus layer, is compromised -leading to ulceration. Mice that lack the major mucin found in the intestinal mucus, mucin 2 (Muc2), develop spontaneous colitis that mimics UC. QBECO, an immunomodulator derived from an inactivated strain of *Escherichia coli* that holds potential as a novel immunotherapeutic agent for UC by restoring normal innate immune function, was tested in Muc2 deficient (Muc2−/−) mice. Specifically, QBECO treatment markedly improved the overall histological score, reduced T cell infiltration and decreased neutrophil numbers in the colonic tissues. These observations were accompanied with a reduction in pro-inflammatory mediators IL-17A in the colon and keratinocyte-derived chemokine (KC) in serum. QBECO treatment did not impact regulatory T cell marker (Foxp3) and anti-inflammatory growth factor (TGF-β) expressions in affected tissues. Additionally, QBECO treated mice attenuated levels of the antimicrobial lectins, RegIII-β and RegIII-y, which favorably affected the gut microbiome by limiting the growth of gamma-proteobacteria and increasing the probiotic lactobacilli. These data demonstrate QBECO treatment ameliorates spontaneous colitis in aged Muc2−/− mice. Together, these findings may have broader implications for our understanding of IBD pathology and aid in the development of novel immunotherapeutic focused on reconstituting normal immune function in the context of IBD.

**Background**

- Ulcerative colitis is a form of inflammatory bowel disease thought to occur when mucosal barrier is damaged or defective
- Therapeutic approach has been limited and not fully effective
- Mice lacking the mucus protein mucin 2 (Muc2) develop spontaneous colitis that mimics ulcerative colitis
- QBECO is a microbe-based investigational therapeutic (Qu Biologics Inc.) that is an immunomodulator derived from inactivated *E. coli*

**Hypothesis**

QBECO ameliorates spontaneous colitis in Muc2−/− mice by selectively dampening the innate immune response

**Methods**

- Three months old Muc2−/− mice (when colitis is established) were subcutaneously injected with placebo or QBECO every other day for 30 days
- Tissues were collected for histology, immunostaining and gene expression analysis
- Blood was collected for cytokine analysis

**Conclusion**

QBECO, derived from inactivated *E. coli*, beneficially modulates the spontaneous colitis developed in Muc2−/− mice by:
- Ameliorating intestinal pathology
- Decreasing neutrophils numbers and CD3 positive T cells
- Modulating RegIII-β, with a reduction in γ-proteobacteria and an increase in lactobacilli

This study highlights the potential of using bacterial-derived products for innate immune stimulation as a therapeutic for ulcerative colitis

**References**


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