FACULTY OF BIOSCIENCE ENGINEERING

DEPARTMENT OF FOOD TECHNOLOGY, SAFETY AND HEALTH
RESEARCH UNIT FOOD MICROBIOLOGY AND FOOD PRESERVATION

TRANSCRIPTIONAL PROFILING OF HUMAN INTESTINAL EPITHELIAL CACO-2 CELLS INFECTED WITH *BACILLUS CYTOTOXICUS*

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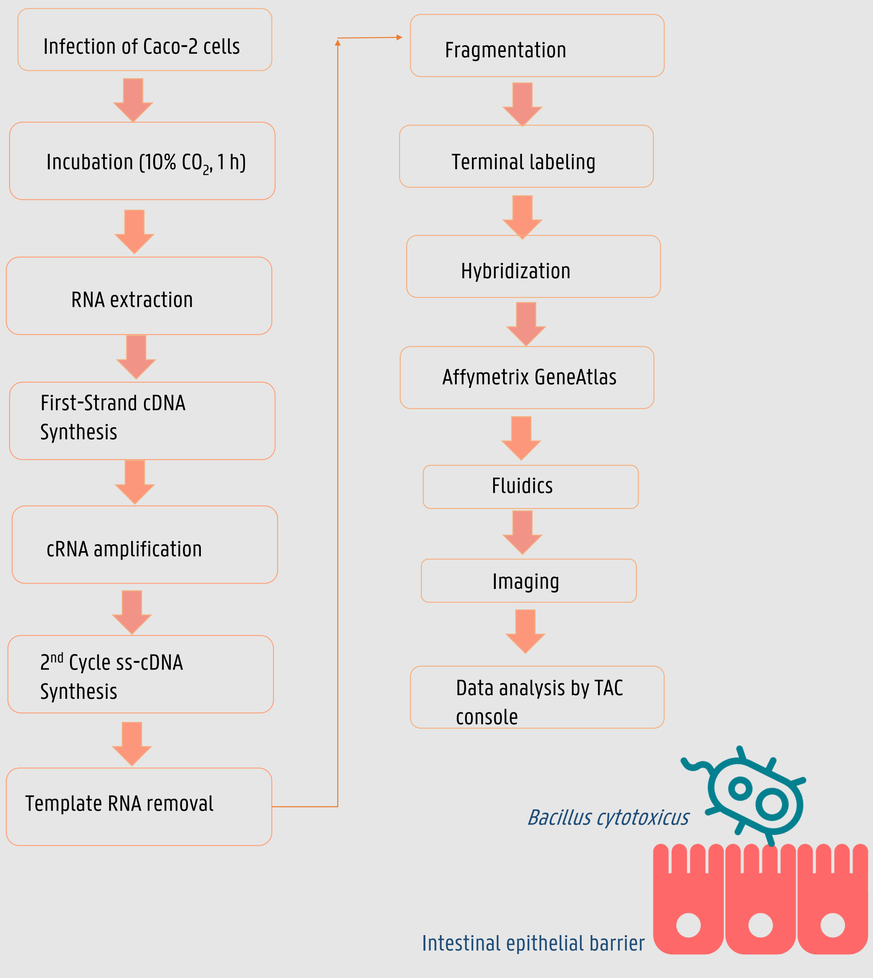
Objectives

Bacillus cytotoxicus is a highly cytotoxic species identified as a causal agent of severe necrotic enteritis. Specifically, this species produces the CytK-1 variant of the Cytotoxin K, which is highly toxic to human intestinal Caco-2 and Vero cells. To better characterize the pathogenesis of intestinal epithelial Caco-2 cells after infection with *B. cytotoxicus*, gene expression of whole transcriptome was analyzed by the microarray system.

Methods



Results

Total number of genes: 48226
- Genes passed filter criteria: 6528 (13,54%)
- Up-Regulated: 3281 (50,26%)
- Down-Regulated: 3247 (49,74%)

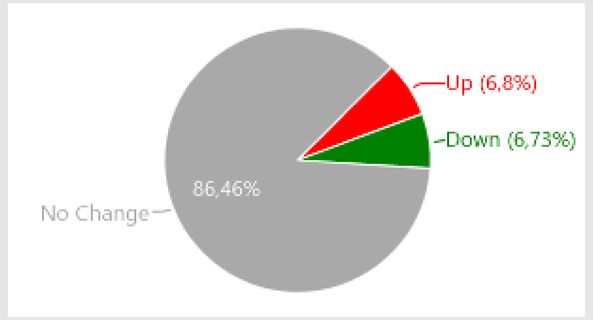


Figure 1. % of induced genes (red-upregulated; green-down-regulated)

Most of the induced genes appeared to be involved in nucleic acid metabolism, transcription, protein synthesis, cell modifications, as well as regulation of surface protein production. In this study, alterations were noted for mucin family genes, from which mucin 16 (MUC16), associated with cell surface integration, was the highest upregulated gene. Gene encoding fibrillin-1 (FBN1), a structural component of microfibrils of the extracellular matrix, significantly induces upon exposure to *B. cytotoxicus*. Further, the macrophage receptor MARCO-like, which has an important role in the removal of pathogens from the body was highly affected, as well as serine peptidase inhibitors Kazal types 13 and 6 (SPINK13, SPINK6) and carbamoyl-phosphate synthetase 1 (CPS1). Myosin ID (MYO1D), required for normal planar cell polarity of some cells, also upregulated. On the other hand, downregulation was noted for epidermal growth factors, such as epiregulin (EREG) and amphiregulin (AREG), epithelial cell adhesion molecule (EpCAM), and fibrinogen beta chain (FGB). Significant alterations in the expression levels of APO family members APOA4, APOC3, APOD, and APOH were observed.

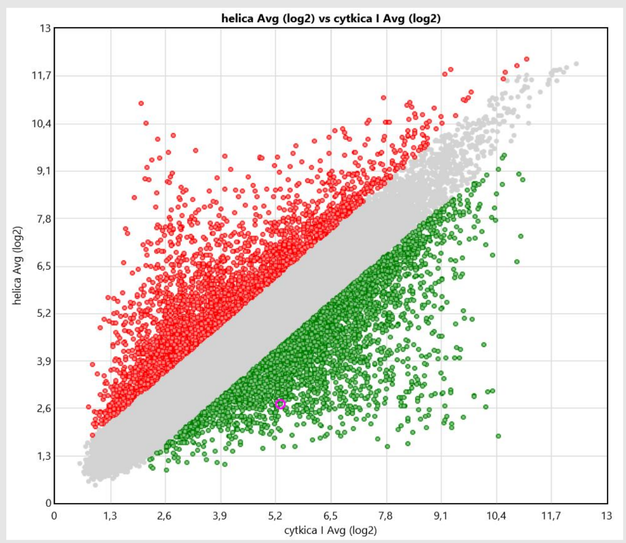


Figure 2. Differential expression of Caco-2 cells infected *with B. cytotoxicus.*

Conclusion

The Caco-2 cell line has served a historically important role as in vitro model for molecular and cellular biology of polarized intestinal epithelia. The present study demonstrates transcriptomic profiles of infected intestinal epithelial Caco-2 cells providing novel insights into molecular events underlying *B. cytotoxicus* pathogenesis. Induced genes indicate that *B. cytotoxicus* damage epithelial barrier and affects mucus production. Additionally, it affects genes related to macrophages and immunity, important for elimination of pathogens from organism. The identification of transcripts unique to this work will be useful as functional and regulatory networks can be interrogated to clarify the molecular and cellular function of individual factors and to unravel the complex mechanisms involved in the host response and bacterial adaptation to host environments during infection.

Acknowledgments

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