



# Probiotic lactobacilli mediated changes in global epigenetic signatures of human intestinal epithelial cells during *Escherichia coli* challenge

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## Abstract

Host genome environment association is critical for proper development and functioning of an individual. Microbiota and probiotics within the cellular vicinity may serve such critical stimuli that can bring out different epigenetic mediated host responses. The aim of present study was to explore the changes in epigenetic signatures of Caco-2 cells by probiotic strains (*Lactobacillus rhamnosus* MTCC 5897: LR, *Lactobacillus fermentum* MTCC 5898: LF and their mixture: RF), respectively, or during challenge with *Escherichia coli* (ATCC 14948) using exclusion, competition and displacement assays. Adenocarcinoma intestinal epithelial Caco-2 cells were treated with LR, LF, RF and *E. coli* for 6 h, respectively. Caco-2 cells were also challenged with *E. coli* and probiotic lactobacilli during exclusion, competition and displacement assays. Finally, global epigenetic modifications by acetylation of H4 and H3 histone proteins and DNA methylation patterns were determined. Probiotic-treated Caco-2 cells displayed significant ( $p < 0.01$ ) reduction in percent global H4 and H3 acetylation, respectively, in contrast to their elevated ( $p < 0.05$ ) levels after *E. coli* infection. On the other hand, a remarkable ( $p < 0.01$ ) decrease in percent H4 and H3 acetylation were observed when *E. coli* were excluded, competed or displaced by lactobacilli strains. No changes in the global DNA methylation patterns were observed in Caco-2 cells after exposure to probiotic strains or *E. coli*, respectively, but surprisingly, their levels increased significantly ( $p < 0.05$ ) when lactobacilli-treated cells were challenged with *E. coli* during exclusion or competition than displacement assays. Probiotic *L. rhamnosus* and *L. fermentum* modulated the host epigenetic signatures via global histone acetylation individually or during *E. coli* challenge by exclusion, competition and displacement assays. Whilst on the other hand changes in global DNA methylation patterns were obtained significantly during probiotic treatment with *E. coli* in exclusion and competition protocols.

**Keywords** DNA methylation · Epigenome · Histone acetylation · Lactobacilli · Caco-2

## Introduction

Epigenetics is the study of mitotically and meiotically heritable changes in gene function that are independent of DNA sequence (Bhat and Kapila 2017). The epigenome or the overall epigenetic state of an organism is just as important to normal development as is the contribution of the parent genome.

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The relationship between individual genotype and the environment is very essential for the proper host functioning and any perturbation in this association may have lethal consequences (Feinberg 2008; Tollefsbol 2017). Epigenomic reprogramming of the host genome is involved in various life processes such as development, regeneration and postpartum life of higher eukaryotic organisms (Al Akeel 2013). Environmental factors like gut microbiota and their metabolites, nutrients, toxins, infections and hypoxia can have profound effects on the epigenetic signature which may trigger host susceptibility to different disorders (Safronova and Morita 2010; Vel Szic et al. 2015). Epigenetics is therefore considered to be at the epicentre of modern medicine as it helps in understanding the disease aetiology (Feinberg 2008; Tollefsbol 2017). Studies have shown that the bioactive components and gut microbes alter the epigenetic signatures of