The induction of genes related to differentiation of intestinal absorptive cells and adipocytes via epigenetic memory

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Intestinal absorptive cells and adipocytes rapidly mature during the transient period from sucking to weaning when plasma glucocorticoid hormone concentration increases and p44/42 mitogen-activated protein kinase (MAPK) activity is inhibited in these cells. Thus, glucocorticoid hormones and p44/42 MAPK inactivation are thought to be important in gene expression of intestinal absorptive cells and adipocytes. In addition, recent studies have shown that abrupt changes in gene expression, which occur frequently in differentiating cells, are accompanied with a major chromatin structural change that is triggered by modifications of epigenetic memory. In this study, the author examined whether the inductions of genes related to differentiation of the intestinal absorptive cells and adipocytes are regulated by Brd4-P-TEFb complex, which is known to bind to acetylated histones and regulate transcriptional elongation.

The author found that the bindings of acetylated histones on an intestinal gene GLUT5 and on an adipocyte gene adiponectin were enhanced throughout the upstream/transcribed regions of these genes when human intestinal cell line Caco-2 cells or mouse adipocyte cell line 3T3-L1 cells were treated with a medium suitable for differentiation [Caco-2 cells: p44/42 MAPK inhibitor, PD98059 (PD) and glucocorticoid hormone agonist dexamethasone (Dex); 3T3-L1 cells: insulin, 3-isobutyl-1-methylxanthine (IBMX) and Dex]. In addition, the bindings of Brd4-P-TEFb complex and acetylated histones on the GLUT5 gene were enhanced by the stimulation of differentiation in Caco-2 cells. Furthermore, the bindings of P-TEFb, which stimulates transcriptional elongation by phosphorylating serine 2 of RNA polymerase II (Pol II) carboxy-terminal repeat domain (CTD), were enhanced by the treatment with the medium for the differentiation in Caco-2 cells.

In conclusion, the author has demonstrated in this study that the induction of genes related to differentiation in intestinal absorptive cells and adipocytes are associated with the enhancement of the bindings of acetylated histones and Brd4-P-TEFb complex to the promoter/enhancer and transcribed regions of the genes.