IL-1β maintains the DNA hypermethylation of anti-inflammatory IL-10 gene in a human intestinal epithelial cell line

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Intestinal inflammation is a natural process crucial to maintain gut integrity, but its deregulation is involved in the pathogenesis of severe intestinal disorders[1]. Intestinal epithelial cells play a crucial role in the inflammatory response, modulating the immune cell exposure to antigens and by their ability to secrete many inflammatory mediators. IL-1β represents a pivotal player: secreted by infiltrated leucocytes, it induces the expression of several pro-inflammatory genes. Also the anti-inflammatory IL-10, whose function is to terminate the inflammatory process, modulates the intestinal physiology[2]. Recent clinical reports showed that patients with ulcerative colitis in remission phase have significantly higher *IL10* gene expression in mucosa compared with active patients and controls[3]. Moreover, in the latest years aberrant epigenetic mechanisms were put in binomial relationship with chronic inflammatory diseases[4].
Previously, we described a demethylation of pro-inflammatory *IL6* and *IL8* genes in human colonic Caco-2 cells differentiated into an enterocyte-like phenotype and exposed to the inflammatory action of IL-1β[5].
In the present study we evaluate whether the IL-1β treatment affected the methylation status of the anti-inflammatory *IL10* gene, in the same *in vitro* model. Our results showed that IL-1β treatment did not change the hypermethylation status of the *IL10* promoter. Moreover, in cell lysates from IL-1β-treated Caco-2 cells, we observed a dose-dependent increase of DNMTs activity and, surprisingly, a decrease of DNMT3b expression. These findings put in evidence the complexity of relationship between IL-1β and DNMTs, and may suggest a potential role of IL-1β as pleiotropic modulator of DNA methylation in Caco-2 cell line.

References

[1] Martin GR, Wallace JL. *Gastrointestinal inflammation: a central component of mucosal defense and repair*. Exp Biol Med (Maywood); 231(2):130–7 (2006).

[2] Latorre E, Mendoza C, Matheus N, Castro M, Grasa L, Mesonero JE, Alcalde A. *IL-10 modulates serotonin transporter activity and molecular expression in intestinal epithelial cells.* Cytokine; 61(3):778-84 (2013).

[3] Fonseca-Camarillo G, Furuzawa-Carballeda J, Llorente L, Yamamoto-Furusho JK. *IL-10 and IL-20 expressing epithelial and inflammatory cells are increased in patients with ulcerative colitis.* J Clin Immunol; 33(3):640-8 (2013).

[4] Shanmugam MK, Sethi G. *Role of epigenetics in inflammation-associated diseases.* Subcell Biochem; 61:627-57 (2013).

[5] Schifano I, Gentile C, Naselli F, Sposito L, Allegra M, Tesoriere L, Livrea MA, Caradonna F. *IL-1β induces DNA demethylation at genome level and in specific CpG sites of IL-6 and IL-8 genes in human intestinal epithelial cells.* 86° Congresso Nazionale della Società Italiana di Biologia Sperimentale (SIBS), Palermo (Italy) (2013).