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Effects of different dietary treatments on epigenetic mechanisms in children with IgE-mediated cow’s milk allergy

Lorella Paparo, Rita Nocerino, Maurizio Mennini, Linda Cosenza, Carmen Di Scala, Antonio Amoroso, Rosita Aitoro, Roberto Berni Canani
University of Naples, Italy

Aims: We showed that the acquisition of oral tolerance in children with cow’s milk allergy (CMA) is driven by a different DNA methylation pattern of Th1 and Th2 cytokines. In this study we evaluated comparatively the effect of different dietary treatments on DNA methylation pattern of cytokine genes involved in Th2 (IL-4) and Th1 (IL-10) response in children with IgE-mediated CMA.

Methods: Prospective randomized study in subjects with IgE-mediated CMA randomized into two groups of dietary treatment: 1. extensively hydrolyzed casein formula containing the probiotic L. rhamnosus GG (LGG); 2. soy formula. At enrollment, and after 6 and 12 months of treatment a venous blood sample was collected to perform DNA methylation analysis of the CpGs in the promoter region, and the determination of serum concentrations of IL-4 and IL-10 by ELISA. At 12 months, the possible acquisition of oral tolerance to cow’s milk proteins was evaluated by oral food challenge.

Results: 16 children (11 males, ages 6-12 months) were prospectively randomized: 8 in Group 1 and 8 in Group 2. At enrollment DNA methylation rate of CpGs in the promoter region of IL-4 and IL-10 cytokines and respective serum levels were similar between the two groups. After 6 and 12 months of dietary treatment subjects treated with extensively hydrolyzed casein formula containing LGG showed significant higher rate of IL-4 and lower rate of IL-10 gene methylation associated with significant differences in serum levels. In addition, after 12 months of exclusion diet, the number of patients acquiring oral tolerance resulted double in Group 1 (50 vs 25%).

Discussion/Conclusions: Dietary treatment with extensively hydrolyzed casein formula containing LGG induces a more rapid and pronounced epigenetic effect on IL-4 and IL-10 DNA methylation pattern. These epigenetic mechanisms might be involved in the positive effects of this dietary strategy on the acquisition of oral tolerance.