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EPIGENETIC MECHANISMS ELICITED BY BUTYRATE IN PERIPHERAL BLOOD MONONUCLEAR CELLS FROM CHILDREN WITH IGE-MEDIATED COW MILK ALLERGY

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Butyrate is a short chain fatty acid derived from fermentation of dietary fibers by gut microbiota. Butyrate modulates several immune function and epigenetic mechanisms. These effects could lead to more effective strategies for food allergy (FA) prevention and treatment. We aimed to evaluate the direct effects of butyrate on (PBMCs) from children affected by IgE-mediated cow milk allergy (CMA).

PBMCs from 4 children with challenge-proven IgE-mediated CMA (2 male; all Caucasian and no farm-living; mean age 3.5, range 1–5 yrs) were stimulated with beta-lactoglobulin (β -LG; 100 μ g/ml) in the presence or absence of butyrate at different doses (0.1–2.0 mM) for 48 h. Production and DNA methylation rate of IL4, IL5, IL-10 and IFN- γ were assessed by ELISA and HRM Real Time PCR, respectively. DNA methylation rate and expression of Forkhead box Protein 3 (FoxP3), histone deacetylase 6 and 9 (HDAC6 and HDAC9) mRNA were assessed by RT PCR.

PBMCs stimulation with BLG resulted in a significant increase in IL-4 and IL-5 production. No modulation of these two cytokines production and DNA methylation was observed after stimulation with 0.5 mM butyrate. Instead, butyrate stimulated, in a dose-dependent manner (maximal effective dose 0.5 mM), IL-10 and IFN- γ production and decreased DNA methylation rate of these two cytokines. Same effective butyrate dose induced FoxP3 promoter region demethylation and HDAC6/HDAC9 expression down-regulation.

These data pave the way to a preventive/therapeutic use of butyrate against FA.

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BREAST MILK BUTYRATE AS PROTECTIVE FACTOR AGAINST FOOD ALLERGY

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Conflicting evidences suggest a role for breast milk as protective factor against food allergy. The major short chain fatty acids, butyrate produced by gut microbiota exerts positive effect on immune system. We aimed to see whether butyrate concentration in human milk is able to prevent food allergy in an animal model of cow milk allergy.

Mature breast milk butyrate concentration from 40 healthy women (aged 21–42 yrs) was assessed by gas chromatography. 4-Week-old female C3H/HeOJ mice were sensitized by oral route with β -lactoglobulin (BLG, 20 mg) plus cholera toxin (CT, 10 μ g) as an adjuvant in the presence or absence of butyrate. Acute allergic skin response, anaphylactic symptom score, body temperature, intestinal permeability, anti-BLG IgE, IL-4 and IL-10 production were assessed soon after oral challenge. Mean butyrate concentration in breast milk was 0.75 mM (SD \pm 0.15). Based on this concentration a daily dose of 30 mg/kg body weight was calculated. The same butyrate concentration was able to significantly prevent acute allergic skin response, anaphylactic symptom score, body temperature decrease, intestinal permeability increase, anti-BLG IgE, IL-4 and IL-10 production in CMA animal model ($p < .05$).

Our data suggest a pivotal role for butyrate as an effective human milk component in food allergy prevention.

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