RC17 Characterization and study of Goblet cells involved in mucus layer secretion in a rat model of metabolic syndrome associated to catch-up growth

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Introduction: Accumulating evidence indicates that perinatal growth-restriction followed by catch-up growth increases the susceptibility to metabolic diseases in adulthood. We previously demonstrated that one possible mechanism of this association was the early endotoxemia development together with a marked dysbiosis. In the present study we focused on the colonic barrier integrity analysis, mainly on the mucin-producing Goblet cells physiology and replenishment.

Material and Methods: Offspring of Wistar rat dams fed ad libitum (control [C]) or 65% food-restricted during pregnancy and lactation (undernourished [U]) were weaned onto a high-fat (HF) diet (CHF and UHF) to drive catch-up growth. Akkermansia muciniphila and colonic Tff3, Muc2, IL6, IL1β, TNFα expression levels were analyzed by RT-qPCR. Colonic integrity was analyzed using Alcian blue-PAS staining and transmission electron microscopy (TEM). Insulin, glycemia, lipid profile and cytokines levels were determinated in serum. For CD68+ cell infiltrate identification we immunostained colonic tissue.

Results: U rats showed significant mucolytic-bacteria A.muiniphila expansion before and after the catch-up growth. This event was accompanied by colonic mucus thickness reduction, increased CD68+ macrophage abundance and expression of proinflammatory cytokines in UHF as compared to CHF animals. To determine whether altered mucin production might also be contributing to defective intestinal barrier, ultrastructural analysis was performed in Goblet cells. Reduced number of mucin-granules per cell was detected in the U and UHF colon rats because granules were merged. Moreover, food-restriction and HFD promoted ER-distension in Goblet cells from the colon. This fact might be attributable to an aberrant Goblet cell autophagy or immaturity, as we observed in the specific analysis with TEM and gene expression.