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EARLY MATERNAL SEPARATION IN MICE IMPAIRS SPECIFIC IMMUNE RESPONSE TOWARD LUMINAL CONTENT AT ADULTHOOD.

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Early life stressful events contribute to development of functional gastrointestinal disorders such as irritable bowel syndrome (IBS). Using maternal separation (MS) as an experimental model mimicking IBS, we investigated whether early life stressful events in mice may trigger inappropriate immune responses toward luminal content and as a consequence induce IBS symptoms.

MS leads to IBS-like symptoms (intestinal hyper-permeability and visceral sensitivity) and impairs immune system in adult male C₃H/HeN mice. Indeed, MS decreased by 20% fecal IgA concentration MS significantly increased anti-*E. coli* IgG (Optical-Density 0.089±0.012 vs. 0.033±0.005; p<0.05) but not IgA in plasma without affecting Ig response in Gut Fluid lavages (GFL). Furthermore, MS decreased levels of anti-food IgG in plasma (OD 1.277±0.160 vs. 0.785±0.125; p<0.05) and anti-food IgA in GFL (OD 00000 vs. 00000; p<0.05). *Ex vivo* stimulation of splenocytes with *E. coli* lysate induced higher IFN γ secretion (594±72 vs. 357±72pg/ml; p<0.05) and lower IL10 (278±100 vs. 535±115pg/ml ; p<0.05) and IL17 (289±159 vs. 539±189pg/ml ; p<0.05) secretion in MS mice compared to controls.

These data show that early life stressful events trigger inappropriate immune response toward luminal content (food antigens and microbiota) that may contribute to IBS symptoms and highlight perinatal period as a critical window for immune system development.