

## Early life stressful events impaired enteric antimicrobial activity and triggered commensal E. coli overgrowth responsible for visceral hypersensitivity in adult mice

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# EARLY LIFE STRESSFUL EVENTS IMPAIRED ENTERIC ANTIMICROBIAL ACTIVITY AND TRIGGERED COMMENSAL *E. COLI* OVERGROWTH RESPONSIBLE FOR VISCERAL HYPERSENSITIVITY IN ADULT MICE

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#### 200/200 words

Early life stressful events induce long lasting alterations of intestinal homeostasis associated with susceptibility to develop gastrointestinal disorders at adulthood. Neonatal period is characterized by immature intestinal mucosa. Among others, Paneth cells appear only 2 weeks after birth. Our aim was to analyze the consequences of maternal separation (MS) in mice on enteric antimicrobial activity and its consequences on intestinal microbiota, systemic immune response toward microbiota and visceral sensitivity. In 50-days old mice, MS induced a decrease of enteric antimicrobial activity associated with intestinal E. coli overgrowth and an increase of anti-E. coli IgG and IgA in plasma. Furthermore, MS increased IFN $\gamma$  and TNF $\alpha$  in ileum and induced visceral hypersensitivity in response to colorectal distension. In order to decipher whether or not those alterations were a consequence of E. coli overgrowth, adult mice were force fed daily with  $10^9$  commensal E. coli for 15 days. E. coli gavage reproduced intestinal E. coli overgrowth as well as anti-E. coli IgG and IgA increase and visceral hypersensitivity without modification of enteric antimicrobial defense. Altogether our results highlighted that early life stressful events impair the development of antimicrobial defenses and promote commensal bacterial overgrowth leading to abnormal response toward microbiota and visceral hypersensitivity.