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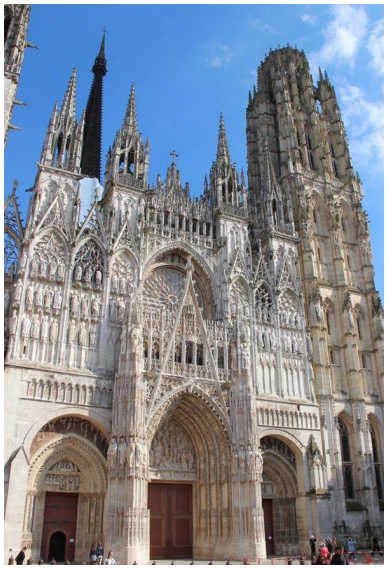

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Cryptosporidium parvum can subvert the host immune response through manipulation of CRAMP expression during neonatal infection

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Due to the immaturity of their immune system, neonates are highly sensitive to intestinal infections. During the neonatal period, antimicrobial peptide (AMP) composition differs substantially from that of adults. This is the case in the small intestine for the cathelicidin-related antimicrobial peptide (CRAMP) expressed preferentially in the neonatal period while conversely other AMPs such as Reg3γ are expressed later in life. Among enteric neonatal diseases, Cryptosporidiosis is a zoonotic disease and is highly prevalent in children less than 5 years old in developing countries and in neonatal ruminants worldwide. *Cryptosporidium parvum* is the etiological agent of this diarrheal disease and infects exclusively epithelial cells. Innate immunity is important to control the acute phase of infection in neonates with dendritic cells and IFNγ playing a major role. Antimicrobial peptides are important contributors of innate immunity, but the role of CRAMP, which is elevated in the intestine of neonates has never been investigated during Cryptosporidiosis so far.
In this work, we observed in the neonatal murine model of cryptosporidiosis that unlike other antimicrobial molecules such as Reg3© and Lysozyme, CRAMP expression was significantly reduced in the intestine during infection. By using different genetically modified mouse models, we demonstrated that the reduced CRAMP expression was independent of IFN©, a pro-inflammatory cytokine strongly produced during infection, but also of Myd88, an adaptor molecule involved in innate immune signalling. We also excluded the role of gut flora in this response. When C. *parvum* infected neonatal mice orally received exogenous CRAMP to compensate the reduced expression of this AMP, the parasitic load of neonates was significantly decreased. In addition, when free parasites were in direct contact with CRAMP, this AMP affected the viability of sporozoites. All together, these data suggest that C. *parvum* induces the reduction of CRAMP expression to escape the anti-parasiticidal effect of CRAMP.