MHC-II expression on resident colonic macrophages is partially regulated by the microbiota

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Intestinal macrophages (Mϕs) play a vital role in controlling the balance of immunity and tolerance. The majority of the gut Mϕ pool relies on monocyte replenishment, but recently it has been shown that a long-lived, prenatally-derived Mϕ population can be distinguished by the expression of Tim4. Unlike most tissue resident Mϕs from other organs, most intestinal Mϕs express high levels of the antigen-presenting molecule MHC-II. However, it is not currently clear what mechanisms regulate MHC-II expression specifically on Mϕs in the intestine.
We observed that MHC-II expression in mouse small intestinal and colonic Mϕs exhibited different kinetics during neonatal development and in particular around weaning. Since colonic Mϕs are in close contact with the gut microbiota, we hypothesised that this interaction may play a major role in regulating their MHC-II expression. In accordance with this, we observed 10-20% higher frequencies of MHC-II low/negative Mϕs in the colon but not in the small intestine of antibiotics-treated, germ-free and MyD88-/- mice compared to WT mice. Notably, in all cases, the MHC-II negative Mϕs were Tim4 positive, suggesting that MHCII expression on resident colonic macrophages is at least partially dependent on the microbiota. In accordance with this, we observed that CCR2-/- mice, which have a severely impaired monocyte trafficking to the intestine, had increased frequencies of Tim4 positive and MHC-II negative Mϕs.
In conclusion, our data suggests that MHC-II expression on resident colonic but not monocyte-derived or small intestinal Mϕs is partially regulated by the microbiota. We are currently performing experiments to further characterise the molecular mechanisms responsible.

Keywords : Macrophage, MHC-II, antigen presentation, intestine, microbiota
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