ORAL ABSTRACTS

124. Altered CCL2 Signaling Delays Clearance of Pneumococcal Colonization in Infant Mice

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Background. *Streptococcus pneumoniae* is a significant cause of morbidity and mortality, especially in children. Colonization is the prerequisite to invasive pneumococcal disease, and is particularly common and prolonged in children.

Methods. We studied prolonged carriage using a mouse model of pneumococcal colonization by intranasally inoculating infant (7-day old) and adult (6-8 week old) mice.

Results. Adult mice had completely cleared colonization by 21 days postinoculation (dpi), while mice colonized as infants still carried pneumococci by 45 dpi. We used this model to examine the mechanisms underlying delayed pneumococcal clearance in infants. Macrophages, the effector cells in clearing pneumococci from adults, exhibited delayed recruitment into the nasopharyngeal lumen of infant mice. Inflammation was not completely impaired in infant mice, however, as they appropriately recruited neutrophils into the nasopharynx during the acute phase of colonization. This lack of macrophage recruitment was paralleled by a failure to upregulate *Ccl2 (Mcp-1)*, a macrophage chemoattractant that is required in adult mice to promote clearance. Surprisingly, baseline levels of *Ccl2* expression were significantly higher in the infant upper respiratory tract compared to the adult URT. Furthermore, infant mice expressed more CCL2 protein in serum than adult mice, suggesting a systemic effect on expression of CCL2 in infants. Peritoneal macrophages isolated from infant mice also expressed more *Ccl2* than those cultured from adults, additional evidence of a systemic effect on infant CCL2 signaling.

Conclusion. Taken together, these results demonstrate that CCL2 signaling is altered at baseline in infant mice, which prevents the development of appropriate innate cell infiltration in response to pneumococcal colonization, leading to delayed clearance of pneumococcal carriage.

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