

IJAE

Italian Journal of Anatomy and Embryology

Official Organ of the Italian Society
of Anatomy and Histology

71° CONGRESSO
della Società Italiana di Anatomia e Istologia

71TH MEETING
of the Italian Society of Anatomy and Histology

Taormina 20-22 september 2017



Vol. 122
N. 1 (Supplement)

2017

ISSN 1122-6714

Role of CX₃CR1⁺ cell in the protection of the intestinal mucosa

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During infection intestinal CX₃CR1⁺ cells can either extend transepithelial cellular processes to sample luminal bacteria or, very early after infection migrate into the intestinal lumen to capture bacteria. However, up to date, the biological relevance of the intraluminal migration of CX₃CR1⁺ cells remained to be determined. We addressed this by using a combination of mouse strains differing in their ability to carry out CX₃CR1-mediated sampling and intraluminal migration. We observed that, the number of *S. Typhimurium* traversing the epithelium did not differ between sampling-competent/migration-competent C57BL/6 and sampling-deficient/migration-competent Balb/c mice. By contrast, in sampling-deficient/migration-deficient CX₃CR1^{-/-} mice the numbers of *S. Typhimurium* penetrating the epithelium were significantly higher. However, in these mice the number of invading *S. Typhimurium* was significantly reduced after the adoptive transfer of CX₃CR1⁺ cells directly into the intestinal lumen, consistent with intraluminal CX₃CR1⁺ cells preventing *S. Typhimurium* from infecting the host. This interpretation was also supported by a higher bacterial faecal load in CX₃CR1^{+/-gfp} compared to CX₃CR1^{gfp/gfp} mice following oral infection. Furthermore, by using real time in vivo imaging we observed that CX₃CR1⁺ cells migrated into the lumen moving through paracellular channels within the epithelium. Also, we reported that the absence of CX₃CR1-mediated sampling did not affect antibody responses to a non-invasive *S. Typhimurium* strain that specifically targeted the CX₃CR1-mediated entry route. These data showed that the rapidly deployed CX₃CR1⁺ cell-based mechanism of immune-exclusion is a defence mechanism against pathogens that complements the mucous and secretory (s)IgA antibody-mediated system in the protection of intestinal mucosal surface.