

**P003** Generation and analysis of a mouse mutant deficient for the adhesion molecule MAdCAM-1

**A. Schippers<sup>1</sup>, C. Leuker<sup>2</sup>, O. Pabst<sup>3</sup>, A. Kochut<sup>1</sup>, A.D. Gruber<sup>4</sup>, N. Wagner<sup>5</sup>, W. Müller<sup>1,6</sup>**

*Department of Experimental Immunology, Helmholtz-Centre for Infection Research, Braunschweig<sup>1</sup>; Institute for Genetics, University of Cologne, Cologne<sup>2</sup>; Institute for Immunology, Medical University Hanover, Hanover<sup>3</sup>; Institute of Pathology, Dept. of Veterinary Medicine, Freie Universität Berlin, Berlin<sup>4</sup>; Department of Paediatrics, University Hospital Aachen, Aachen<sup>5</sup>; Faculty of Life Sciences, University of Manchester, Manchester<sup>6</sup>*

$\beta$ 7-integrin directs the migration of immune cells into the gut associated lymphoid tissues (GALT). In order to elucidate the *in vivo* function of mucosal addressin cell adhesion molecule-1 (MAdCAM-1), the principal ligand of  $\beta$ 7-integrin, we generated a MAdCAM-1 deficient mouse strain. In adult human or mouse MAdCAM-1 is constitutively expressed in GALT and intestinal venules. Consistently, lack of MAdCAM-1 results in a reduced size of Peyer's patches (PP) and decreased numbers of IgA secreting plasma cells in the small intestinal lamina propria. The earliest differences in the size of the PP anlagen become visible at day 3 after birth, indicating that  $\beta$ 7-integrin-MAdCAM-1 interaction is dispensable for embryonic PP development, but affects the recruitment of mature lymphocytes into the organ. Competitive adoptive transfer experiments with transgenic T cells demonstrated that homing of antigen-experienced effector CD4 and CD8 T cells into mesenteric lymph nodes and the lamina propria required MAdCAM-1. Reduced numbers of intestinal plasma cells correlate with impaired humoral responses after oral immunization, suggesting that also plasma cell homing into the intestine requires MAdCAM-1. In conclusion these data reveal that MAdCAM-1 directs the migration of effector T cells and plasma cells into GALT and the intestinal lamina propria. This emphasizes the significant contribution of the  $\beta$ 7-integrin and MAdCAM-1 receptor/ligand interactions for proper functioning of the GALT.