IN BRIEF

REGULATORY T CELLS

Expanding T_{Reg} cell numbers *in vivo*

There is great interest in harnessing the suppressive powers of regulatory T (T_{Reg}) cells in the clinic. Although it is possible to numerically expand T_{Reg} cells *ex vivo*, concerns over their purity and stability remain. An alternative approach is to expand pre-existing populations of T_{Reg} cells *in vivo*. This study showed that a monoclonal antibody specific for CD45RB (which has a role in T cell receptor signalling) increased the frequency and absolute number of T_{Reg} cells in mice. This increase required the presence of cognate antigen and was due to homeostatic proliferation of thymus-derived T_{Reg} cells rather than increased thymic output or conversion from effector T cells. CD45RB-specific antibody was shown to inhibit T_{Reg} cell motility, thereby increasing the contact time of the cells with dendritic cells. This increased contact time resulted in increased activation of nuclear factor of activated T cells (NFAT), which is required for T_{Reg} cell proliferation. These data describe a novel method by which T_{Reg} cell numbers may be increased *in vivo*.

ORIGINAL RESEARCH PAPER Camirand, G. *et al.* CD45 ligation expands Tregs by promoting interactions with DCs. *J. Clin. Invest.* http://dx.doi.org/10.1172/JCI74087 (2014)

IMMUNOGENETICS

Human *CTLA4* mutations described

Cytotoxic T lymphocyte antigen 4 (CTLA4) is a crucial negative regulator of T cells. A new study describes for the first time the consequences of *CTLA4* mutations in humans. Six subjects from four unrelated families suffering from severe immune dysregulation were identified as having heterozygous germline mutations in *CTLA4*. Although the subjects had different mutations, they all had reduced CTLA4 mRNA and protein expression. The *CTLA4* haploinsufficiency resulted in defective regulatory T cell function and hyperproliferative T cells, and lymphocytic infiltration of non-lymphoid organs was observed in these patients. B cells were also affected, with patients exhibiting circulating B cell lymphopenia and increased numbers of autoreactive $CD21^{low}$ B cells. The identification of these patients confirms the essential role of CTLA4 in maintaining B cell and T cell homeostasis.

ORIGINAL RESEARCH PAPER Kuehn, H. S. *et al.* Immune dysregulation in human subjects with heterozygous germline mutations in *CTLA4*. *Science* http://dx.doi.org/10.1126/science.1255904 (2014)

MACROPHAGES

Gut needs a steady supply of reinforcements

Recent studies have suggested that macrophages in steady-state tissues originate from embryonic yolk sac-derived progenitors and are maintained by self-renewal *in situ*. Bain *et al.* now report that this paradigm does not hold true for intestinal macrophages. They have found that embryonic precursor cells seed the intestinal mucosa and show extensive proliferation during the neonatal period. However, these cells are replaced around the time of weaning by $LY6C^{hi}$ monocytes, which are recruited to the intestine in a CC-chemokine receptor 2 (CCR2)-dependent manner and mature into anti-inflammatory macrophages. Recruitment of monocytes to the intestine required signals from the microbiota and was responsible for maintaining intestinal macrophage populations throughout adulthood. The authors suggest that this unique mode of replenishing macrophages may reflect the continuous threat of infection and tissue damage in the intestine.

ORIGINAL RESEARCH PAPER Bain, C. C. *et al.* Constant replenishment from circulating monocytes maintains the macrophage pool in the intestine of adult mice. *Nature Immunol.* http://dx.doi.org/10.1038/ni.2967 (2014)