


 INNATE IMMUNITY

# 'Natural helper' cells identified

A recent paper published in *Nature* describes a new population of innate lymphocytes that are found in a previously unrecognized lymphoid structure associated with adipose tissue. The authors propose that these T helper 2 ( $T_H2$ )-type innate lymphocytes be termed 'natural helper' cells.

In this study, the authors identified a lymphoid structure in the peritoneal cavity of mice composed of clusters of lymphocytes that was distinct from other lymphoid tissues and surrounded by adipose tissues. These structures were also found in the adipose tissues around the kidney and genitalia, as well as in the human mesentery, and were termed fat-associated lymphoid clusters (FALCs). Within these structures,  $KIT^+SCA1^+$  cells were identified that do not express lineage (LIN) markers but express interleukin-7 receptor- $\alpha$  (IL-7R $\alpha$ ) and ST2 (a subunit of IL-33R), along with several other cell surface molecules. Further analysis showed that these cells are of lymphoid lineage but are

distinct from B and T cells, natural killer cells, lymphoid-tissue inducer cells and IL-22-producing NKp46 $^+$  cells.

Stem cell factor and IL-7 were shown to support the survival of FALC  $KIT^+SCA1^+$  cells, and IL-2 induced cell proliferation and the production of the  $T_H2$ -type cytokines IL-5, IL-6 and IL-13 *in vitro*. These cells also produced  $T_H2$ -type cytokines, as well as low levels of interferon- $\gamma$ , in response to PMA (phorbol 12-myristate 13-acetate) plus ionomycin, and incubation with IL-33 or IL-2 plus IL-25 induced high levels of IL-5 and IL-13 production.

Furthermore, FALC  $KIT^+SCA1^+$  cells support the proliferation of B-1 but not B-2 B cells and have a helper function for IgA production *in vitro*. To confirm this observation *in vivo*, the authors transferred B-1 B cells with or without FALC  $KIT^+SCA1^+$  cells into immunodeficient mice and found that FALC  $KIT^+SCA1^+$  cells enhanced the proliferation of B-1 B cells.

In addition, FALC  $KIT^+SCA1^+$  cells were shown to be the main producers of IL-5 and IL-13 *in vivo* in response to IL-33, and mice lacking these cells did not produce IL-5 and IL-13 or induce goblet cell hyperplasia in response to infection with the helminth *Nippostrongylus brasiliensis*.

So, FALC  $KIT^+SCA1^+$  cells are a newly described innate lymphocyte population present in FALCs that produce high levels of  $T_H2$ -type cytokines, support B-1 B cell proliferation and promote goblet cell hyperplasia in response to helminth infection.

Olive Leavy

**ORIGINAL RESEARCH PAPER** Moro, K. *et al.*  
Innate production of  $T_H2$  cytokines by adipose tissue-associated c-Kit $^+$ Sca-1 $^+$  lymphoid cells.  
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