IN BRIEF

MACROPHAGES

Responding to a chill by alternative activation

Non-shivering thermogenesis, which is required to maintain core body temperature, involves the induction of lipolysis and the expression of thermogenic genes in adipose tissues. Ajay Chawla and colleagues now show a role for interleukin-4 (IL-4) and alternatively activated macrophages in this process. The expression of alternative activation markers was increased in the brown and white adipose tissue (but not in other tissues) of mice acutely exposed to 4°C compared with expression levels in control mice, and this increase depended on IL-4 and IL-13. Cold-exposed mice that lacked alternatively activated macrophages or lacked IL-4 and IL-13 had impaired metabolic adaptations to cold — that is, defects in the induction of lipolysis in white adipose tissue and the upregulation of thermogenic genes in brown adipose tissue. Administration of IL-4 increased non-shivering thermogenesis in a macrophage-dependent manner in wild-type mice housed at normal temperatures. Finally, in response to cold exposure, alternatively activated macrophages from brown and white adipose tissue were shown to produce catecholamines, such as noradrenaline, in an IL-4-dependent manner to mediate the metabolic adaptations to cold.

ORIGINAL RESEARCH PAPER Nguyen, K. D. *et al.* Alternatively activated macrophages produce catecholamines to sustain adaptive thermogenesis. *Nature* **480**, 104–108 (2011)

T CELLS

Heating up T cell activation

Infections are often accompanied by fever. But what effect does this increase in temperature have on immune cell activation? This study found that incubation of naive $CD8^+$ T cells at 39.5°C prior to antigen-specific activation resulted in enhanced differentiation of these cells into effector $CD8^+$ T cells compared with cells incubated at 33°C or 37°C. Furthermore, enhanced naive $CD8^+$ T cell differentiation was observed in mice following whole-body hyperthermia. But, the rate of T cell proliferation was not affected. However, clustering of $GM1^+$ cholesterol-dependent microdomains on $CD8^+$ T cells was increased at 39.5°C both *in vitro* and *in vivo*, as was the rate of T cell–antigen-presenting cell (APC) conjugate formation. So, physiologically relevant increases in temperature enhance the antigen-specific differentiation of effector $CD8^+$ T cells by increasing T cell–APC conjugation.

ORIGINAL RESEARCH PAPER Mace, T. A. *et al.* Differentiation of $CD8^+$ T cells into effector cells is enhanced by physiological range hyperthermia. *J. Leukoc. Biol.* **90**, 951–962 (2011)

B CELLS

Maturity matters for IgE class switch

Class-switch recombination (CSR) in mature B cells activated under T helper 2 (T_H2)-type conditions generates IgG1 and IgE isotypes. Now, Wesemann *et al.* report that CSR during early B cell developmental stages favours the IgE over the IgG1 isotype. Activated immature B cells derived from fetal liver progenitors, as well as activated $CD93^+$ transitional B cells, showed an increased preference for switching to the IgE isotype compared with activated mature B cells. Whereas activated mature B cells have been previously shown to switch to IgE in a two-step process, through an intermediate IgG1 stage, activated immature B cells were observed to undergo direct IgM to IgE transition. The underlying mechanism may involve decreased levels of phosphorylated signal transducer and activator of transcription 6 (STAT6) and altered histone methylation at the germline promoter region upstream of the constant IgG1 heavy chain gene. These findings can explain the elevated serum IgE levels in children and in immunodeficient patients with defective B cell development.

ORIGINAL RESEARCH PAPER Wesemann, D. R. *et al.* Immature B cells preferentially switch to IgE with increased direct Sμ to Sε recombination. *J. Exp. Med.* 5 Dec 2011 (doi:10.1084/jem.20111155)