In This Issue

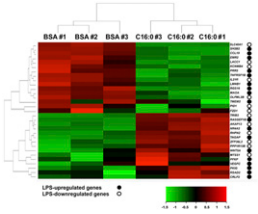
J Immunol 2017; 199:3713; ;
doi: 10.4049/jimmunol.1790021
http://www.jimmunol.org/content/199/11/3713

The Journal of Immunology is published twice each month by
The American Association of Immunologists, Inc.,
1451 Rockville Pike, Suite 650, Rockville, MD 20852

Print ISSN: 0022-1767 Online ISSN: 1550-6606.

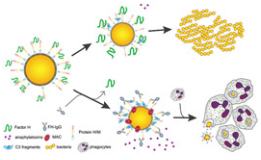
The Journal of Immunology

Proinflammatory Palmitate



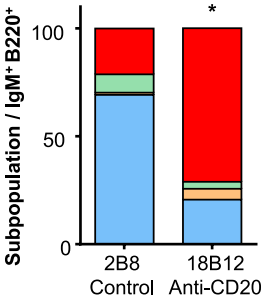
Obesity has been shown to influence immune responses, and the accumulation of saturated fatty acids (SFA) in particular has been associated with proinflammatory responses. Macrophages have been suggested to play a critical role in mouse models of obesity-induced inflammation, but less is known about how human macrophages respond to SFAs. In this issue, Riera-Borrull et al. (p. 3858) examine how treatment of monocyte-derived macrophages with pathological concentrations of the SFA palmitate affects transcriptional and functional responses. Macrophages were polarized with M-CSF to induce anti-inflammatory gene expression, and palmitate treatment of these macrophages induced a shift toward greater proinflammatory gene expression. Palmitate treatment was also associated with JNK activation, which resulted in decreased expression of *MAFB*, a gene that encodes a positive regulator of IL-10 expression, and a downstream decrease in anti-inflammatory gene expression, including not only *IL10*, but also *CCL2*, *HTR2B*, and *HTR7*. Palmitate pretreatment also altered macrophage responses to LPS by significantly enhancing production of proinflammatory cytokines (including TNF-α, IL-6, and IL-1β), and this response was also driven by JNK activation. Taken together, these results show that the SFA palmitate can promote a proinflammatory state in human macrophages that is dependent on JNK activation, providing insight into the triggers of obesity-associated inflammation

Factoring in a New Antibacterial Approach



Gram-positive bacterial infections have become increasingly difficult to manage due to antibacterial resistance and a lack of effective vaccines. Blom et al. (p. 3828) now examine a different therapeutic approach to treating *Streptococcus pyogenes* infection using a chimeric protein comprised of domains 6 and 7 of the complement inhibitor human factor H linked to an IgG1 Fc domain (FH6-7/hFc). Previous studies have shown that domains 6 and 7 of human factor H can bind to the surface of bacterial pathogens, and inclusion of this Fc domain promotes activation of the classical complement pathway as well as opsonophagocytosis mediated by phagocytes expressing FcγR. FH6-7/hFc has also been shown previously to be an effective treatment of Gram-negative bacterial infections. In this study, investigators observed that domains 6 and 7 of factor H can bind to *S. pyogenes* proteins H and M, and FH6-7/hFc-bound *S. pyogenes* can compete out serum factor H and promote complement activation in vitro. Human polymorphonuclear cells showed increased phagocytosis of FH6-7/hFc-treated *S. pyogenes* compared with untreated bacteria. Critically, FH6-7/hFc treatment of *S. pyogenes*–infected transgenic mice engineered to express human factor H showed reduced mortality and sepsis. These results suggest that FH6-7/hFc can be used to treat Gram-positive infection and may offer a unique strategy for targeting multidrug-resistant bacterial pathogens.

Transfusion Tactics



Transfusion of RBCs can be a critical intervention for sickle cell disease patients and individuals with severe blood loss due to injury or surgery. However, transfusions can also trigger alloimmune responses against RBC Ags, and in rare situations, can cause targeted destruction of a patient's RBCs through a delayed hemolytic transfusion reaction (DHTR). Previous studies have examined whether B cell depletion by anti-CD20 treatment can prevent subsequent RBC alloimmunization in patients with severe DHTR. Here, Elayeb et al. (p. 3771) use a mouse model of polytransfusion to determine if anti-CD20 treatment can prevent primary RBC alloimmunization. Transgenic HOD mice that display a fusion protein between hen egg lysozyme, OVA, and Duffy b Ag on the RBC membrane were used as a source of RBCs for transfusion into B10BR mice as a way to measure RBC Ag–specific responses. Prophylactic anti-CD20 treatment depleted B cells from the spleen and periphery and prevented alloantibody production during primary transfusion. But therapeutic anti-CD20 treatment initiated after RBC transfusion only attenuated the levels of peripheral B cells and alloantibodies. Anti-CD20 treatment was also associated with the expansion of alloreactive RBC Ag–specific $CD4^+$ T cells, although compared with cells induced in the absence of anti-CD20, this subset had higher CD40 expression and lower CD134 expression, which was consistent with a less activated phenotype. Taken together, these results indicate that anti-CD20 treatment may offer therapeutic benefits for managing transfusion-associated alloimmunization.