Synopsis of Original Research Paper

How do cosmetics sensitize humans? Analysis of a possible role of platelets.

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To investigate the role of platelets in the process of sensitization of allergic contact dermatitis, we first examined that hapten stimulates CD40 ligand release from platelets in vitro. When platelets obtained from healthy volunteers were stimulated with a representative hapten, DNCB and one of danger signals, ATP, they significantly released CD40L in a dose-dependent fashion. Next, we examined using DNA microarray how ATP, which is released from platelets by various stimuli, e.g., thrombin, collagen, von Willebrandfactor, ADP, vasopressin, platelet-activating factor, and Ca^{2+} ionophores affects immune response by keratinocytes. We identified several immune-related genes whose expression is augmented in ATP-stimulated human keratinocytes by DNA microarray. The statistical analysis of the microarray data revealed that, besides IL-6, the expression of several novel genes such as IL-20, CXCL1-3, and ATF3 was significantly augmented in ATP-stimulated keratinocytes. These data were validated by quantitative real-time RT-PCR. We also confirmed the augmented production of IL-6, IL-20, CXCL1 by ELISA and that of ATF3 by Western blotting. These studies characterized (1) production of IL-6 and IL-20, (2) chemotaxis for neutrophils via CXCL1-3, and (3) ATF3 activation as possible roles of ATP-stimulated keratinocytes. Finally, we demonstrated the presence of extracellular ATP in the sensitization phase of allergic contact dermatitis in vivo by using agarose beads coupled with lucifearase. These studies suggest that platelets may play a crucial role in sensitization of allergic contact dermatitis and that platelets may surrogate the role of irritant dermatitis in sensitization.