

ABSTRACT

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The Danger Model

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For over 50 years immunologists have based their thoughts, experiments and clinical treatments on the idea that the immune system functions by making a distinction between self and non-self. Although this paradigm has often served us well, years of detailed examination have revealed a number of inherent problems. This presentation describes a model of immunity based on the idea that the immune system is more concerned with entities that do damage than with those that are foreign. Working with the model over a space of about 10 years, the author has come to the realization that the cells that control immunity are not the cells of the adaptive

immune system, nor those of the innate immune system. The cells that control immunity are the cells of the tissues that the immune system is meant to protect: namely, the tissues of the body. It is a tissue cell that emits alarm signals that initiate an immune response. It is a tissue cell that expresses MHC molecules and its own antigens, without costimulatory signals, and thus induces tolerance. And it is a tissue cell that dies a normal programmed cell death, allowing its antigens to be processed and presented by resting antigen presenting cells to induce another form of tolerance. From these considerations, a new extension will be presented of the Danger model, in which the model begins to explain how the effector class of an immune response is controlled. Although it is currently broadly accepted that the class of a response is tailored to the pathogen being fought, the extended Danger model suggests that this might be incorrect. The class of immunity is tailored to the tissue in which the immune response occurs.

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