

## XI. IMMUNOLOGY CAN BE ORGANIZED AS PAIRS OF CONCEPTS

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### a. Introduction

Although immunology is one of the least predictable of all the sciences, this situation is mitigated by the fact that many of the concepts in cellular immunology occur as pairs.

For example, many immune cells, such as DCs and T cells, can assume two different cytokine expression patterns, that is, they can express Th1-type cytokines or Th2-type cytokines. Also, T cells occur as two types, CD4<sup>+</sup> T cells and CD8<sup>+</sup> T cells, and once stimulated by a presented antigen, the T cells can undergo two consecutive responses, naive immune response followed at a later time by memory immune response. Such an abundance of pairs is rarely found in any other field of science, except, perhaps for physics. High school students are familiar with the wave/particle duality of light, with positive and negative electric fields, and with matter and antimatter.

### b. Th1-Type Response and Th2-Type Response

By secreting cytokines, DCs can stimulate subsequent Th1-type immune response, or

Th2-type immune response. For example, *Salmonella* bacteria can infect DCs, and once inside, provoke the activation of the DCs, and stimulate the DC to express IL-12 (125). This IL-12, in turn, stimulates downstream Th1-type immune responses that include expression of IFN-gamma (126). IL-12 is a master controller, as it stimulates Th1-type response and inhibits Th2-type response (127). Th1-type response is identified most with expression of IFN-gamma.

To provide another example, certain allergens, and helminths such as *Schistosoma mansoni* (128) and *Nippostrongylus brasiliensis*, stimulate DCs to express Th2-type cytokines (129,130). The separation of immune response into Th1-type and Th2-type is a simplification, in view of the fact that an additional type of response by T cells is Th17-type immune response. Th17 response occurs in the pathology of certain autoimmune disorders, such as multiple sclerosis and ulcerative colitis.

The designation Th, which occurs in the terms Th1 and Th2, refers to T helper cells. T helper cells are CD4<sup>+</sup> T cells. A similar division occurs with CD8<sup>+</sup> T cells, and here the corresponding responses by the CD8<sup>+</sup> T cells, are sometimes called Tc1-response and Tc2-response (131).

<sup>125</sup>Brzoza KL, Rockel AB, Hiltbold EM. Cytoplasmic entry of *Listeria monocytogenes* enhances dendritic cell maturation and T Cell differentiation and function. *J. Immunol.* 2004;173:2641–51.

<sup>126</sup>Lucey DR, Clerici M, Shearer GM. Type 1 and type 2 cytokine dysregulation in human infectious, neoplastic, and inflammatory diseases. *Clin. Microbiol. Rev.* 1996;9:532–62.

<sup>127</sup>Romani L, Puccetti P, Bistoni F. Interleukin-12 in infectious diseases. *Clin. Microbiol. Rev.* 1997;10:611–36.

<sup>128</sup>de Jong EC, Vieira PL, Pawel Kalinski P, et al. Microbial compounds selectively induce Th1 cell-promoting or Th2 cell-promoting dendritic cells in vitro with diverse Th cell-polarizing signals. *J. Immunol.* 2002;168:1704–9.

<sup>129</sup>MacDonald AS, Maizels RM. Alarming dendritic cells for Th2 induction. *J. Exp. Med.* 2008;205:13–7.

<sup>130</sup>Ishiwata K, Watanabe N, Guo M, et al. Costimulator B7-DC attenuates strong Th2 responses induced by *Nippostrongylus brasiliensis*. *J. Immunol.* 2010;184:2086–94.

<sup>131</sup>O'Donnell H, McSorley SJ. *Salmonella* as a model for non-cognate Th1 cell stimulation. *Front. Immunol.* 2014;5: Article 621 (13 pp.).