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Commentary

Note on expression of lymohocyte receptor gene

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OVERVIEW

The production of specific lymphocyte receptors employs a number of genetic mechanisms that are unique to the immune system. In 1987, Susumu Tonegawa won the Nobel Prize for Physiology or Medicine "for his discovery of the genetic principle for generation of antibody diversity," a discovery that challenged the fundamental concept that one gene encoded one polypeptide chain. Tonegawa and his colleagues showed that the antibody light chain was encoded in the germ line by not one but three families of gene segments separated by kilobases of DNA. The germ-line DNA is the genetic information encoded in the sperm and egg, which can be passed on to future generations. Their work demonstrated that two DNA segments, one from each family, are conjoined, only in B-lymphocytes, to create the mature form of the light-chain variable region of the immunoglobulin gene. A third segment encodes the constant region of the gene.

To protect its host, the immune system must recognize a vast array of rapidly evolving microorganisms. To accomplish this, it must generate a diverse and flexible repertoire of receptor molecules, while minimizing the expression of receptors that recognize self antigens. As described in, each B-lymphocytes or T-lymphocyte expresses a unique antigen-specifi c receptor. When these receptors bind to their corresponding antigens under the appropriate conditions T-lymphocytes and B-lymphocytes proliferate and differentiate into effector cells that eliminate the microbial threat. In, we described the biochemistry of the T-lymphocytes and B-lymphocyte receptors and the secreted antibodies formed by B-lymphocytes following antigen stimulation. We also outlined the experiments which demonstrated that secreted antibodies are identical in antigen-binding specificity to the B-cell receptors of the secreting cell. In this chapter, we address the question of how an organism can encode and express receptors capable of recognizing a constantly evolving universe of microbial threats using a finite amount of genetic information.

Different combinations of The Organization and Expression of Lymphocyte Receptor Genes segments are used in each B-cell, to create the diverse repertoire of light-chain receptor genes. Subsequent experiments have shown that all of the B-cell and T-cell receptor genes are assembled from multiple gene segments by similar rearrangements. We describe below the unique genetic arrangements of T-cell and B-cell receptor gene segments, and the mechanisms by which they are rearranged and expressed. We will address here only those mechanisms that shape the receptor repertoires of mouse and human naïve B- cell and T-cells, which have not yet been exposed to antigen.

The immune system relies on a vast array of B-cell receptors that possess the ability to bind specifically to a correspondingly large number of potential pathogens. The first indication of the immense size of the antibody repertoire was provided by immunologists using synthetic molecules to stimulate antibody production. They discovered that antibodies can discriminate between small synthetic molecules differing in as little as the position of an amino or hydroxyl group on a phenyl ring. T-cells and B-cells are the major cellular components of the adaptive immune response. T-cells are involved in cell-mediated immunity, whereas B-cells are primarily responsible for humoral immunity (relating to antibodies). The function of T-cells and B-cells is to recognize specific "non-self" antigens, during a process known as antigen presentation. Once they have identified an invader, the cells generate specific responses that are tailored maximally to eliminate specific pathogens or pathogen-infected cells. B-cells respond to pathogens by producing large quantities of antibodies which then neutralize foreign objects like bacteria and viruses. In response to pathogens some T-cells, called T helper cells, produce cytokines that direct the immune response, while other T-cells, called cytotoxic T-cells, produce toxic granules that contain powerful enzymes which induce the death of pathogen-infected cells. Following activation, B-cells and T-cells leave a lasting legacy of the antigens they have encountered, in the form of memory cells. Throughout the lifetime of an animal, these memory cells will "remember" each specific pathogen encountered, and are able to mount a strong and rapid response of the same pathogen is detected again this is known as acquired immunity.

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