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Journal of Clinical and Cellular Immunology

Commentary

A Commentary on Antibody-Dependent Cellular Cytotoxicity

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DESCRIPTION

ADCC (antibody-dependent cellular cytotoxicity), also known as antibody-dependent cell-mediated cytotoxicity, is a cell-mediated immune defence mechanism in which an immune system effector cell actively lyses a target cell whose membrane-surface antigens have been bound by specific antibodies. It is one of the processes by which antibodies can limit and confine infection as part of the humoral immune response. ADCC is unrelated to the immunological complement system, which lyses targets but does not require the presence of another cell. ADCC necessitates the presence of an effector cell, which are often natural killer (NK) cells that interact with immunoglobulin G (IgG) antibodies. Macrophages, neutrophils, and eosinophils, for example, can induce ADCC by killing parasitic worms known as helminths using IgE antibodies. In general, ADCC is defined as the immune response to antibody-coated cells, which results in the lysis of the infected or non-host cell. Its usefulness in the therapy of malignant cells, as well as a fuller understanding of its deceptively complex pathways, have been areas of increasing interest to medical experts in recent literature.

Antibodies activate NK cells in a multi-tiered process of immunological regulation in a normal ADCC. Fc receptors are expressed on NK cells. These receptors recognise and bind to the antigen-binding component of an antibody, such as IgG, which binds to the target cell's surface. CD16 or FcRIII is the most prevalent Fc receptor on the surface of an NK cell. The NK cell produces cytotoxic substances that kill the target cell once the Fc receptor attaches to the Fc region of the antibody. Some viral proteins are expressed on the infected cell's cell surface membrane during virus replication. These viral proteins can then be recognised by antibodies. Following that, NK cells with reciprocal Fc receptors attach to the antibody, causing the NK cell to release proteins like perforin and granzymes, which cause the infected cell to lyse, preventing the virus from spreading. Large parasites, such as helminths, are too large to be swallowed by phagocytosis and destroyed. They also have an integument on the outside that protects them from the chemicals generated by neutrophils and macrophages. The Fc receptor of an eosinophil will identify IgE once it coats these parasites with IgE. The eosinophil then degranulates as a result of the interaction between FcRI and the Fc component of helminth-bound IgE.

In vitro assays

Antibodies or effector cells' efficiency in generating ADCC can be determined using a variety of laboratory approaches. Typically, an antibody specific for a surface-exposed antigen is incubated with a target cell line expressing that antigen. Effector cells expressing the Fc receptor CD16 are co-incubated with antibody-labelled target cells after washing. PBMCs, of which a tiny percentage is NK cells, are commonly used as effector cells; pure NK cells are used less frequently. A complex formed between the antibody, target cell, and effector cell over the period of a few hours, leading to lysis of the target cell membrane. If a label was pre-loaded on the target cell, the label is released in proportion to the quantity of cell lysis. The amount of label in solution compared to the amount of label that remains within healthy, undamaged cells can be used to quantify cytotoxicity.

The amount of radiolabel released into the cell culture medium is measured using a gamma counter or scintillation counter to detect target cell lysis. A wide range of non-radioactive procedures are now widely used. Direct labelling with a fluorescent dye like calcein or labelling with europium, which becomes fluorescent when released Eu3+ binds to a chelator, are examples of fluorescence-based techniques. Multi-well fluorometers or flow cytometry methods can be used to measure fluorescence. There are also enzymatic-based assays in which the contents of lysed cells contain active cellular enzymes like GAPDH; providing a substrate for that enzyme can catalyse a reaction, the product of which can be measured by luminescence or absorbance.

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Received: 03- Jan-2022, Manuscript No. JCCI-22-15799; **Editor assigned:** 05- Jan-2022, PreQC No. JCCI-22-15799 (PQ); **Reviewed:** 19- Jan-2022, QC No. JCCI-22-15799; **Revised:** 24- Jan-2022, Manuscript No. JCCI-22-15499 (R); **Published:** 7-Feb-2022, DOI:10.35248/2155-9899.22.13.649. **Citation:** Sait H (2022) A Commentary on Antibody-Dependent Cellular Cytotoxicity. J Clin Cell Immunol.13:649.