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## ANTIBODY TECHNOLOGY: Glossary of Terms

**ANTIBODIES:** Proteins of the immune system that seek out and help destroy antigens. Antibodies are highly specific, i.e. each antibody binds to one particular antigen. It is this trait that makes antibodies effective therapeutics.

**ANTIGENS:** Any substance that can induce the production of antibodies (**antibody generating substances**). These substances are usually foreign to an organism and include disease-causing bacteria, viruses, and other infectious agents. A human protein introduced into a mouse will induce mouse antibodies, i.e. the human protein functions as an antigen in the mouse. The resulting mouse antibodies (or engineered forms thereof) can then be used to target the human protein in the human system (the human system does not normally make antibodies against its own proteins).

**EX VIVO LIBRARY:** Method of obtaining antibodies by creating a repertoire of antibodies *ex vivo* which can be screened for binding to a specific target.

**FAB (fragment for antigen binding):** A Fab is the arm of the Y of an antibody. It functions in recognizing the antibody's target, the molecule against which the antibody is directed.

**GAMMA GLOBULINS:** One of the classes of proteins found in human blood plasma. Sometimes referred to as immune globulins, most of the antibodies in body fluids are gamma globulins. Injections of gamma globulins are used to create rapid but temporary immunity in patients who have been exposed to certain diseases (e.g. measles), to people who cannot produce enough antibodies, or to patients who have low blood platelet counts due to autoimmune diseases.

**HAMA: Human Anti-Mouse Antibodies.** A mouse antibody administered to a human is seen by the human immune system as a foreign protein (antigen). The human immune system generates its own human antibodies against the introduced mouse antibody (the HAMA response). The HAMA response can create problems such as allergic-like reaction to the mouse antibody, rapid removal of the mouse antibody, and weak ability to recruit human immune system processes necessary to clear the targeted antigen (e.g. tumor cell). The first may generate additional health problems in a patient while the latter two reduce the efficacy of the mouse antibody as a therapeutic.

**HYBRIDOMA**: A cell line made by fusing an antibody-producing spleen or B cell with a myeloma cell. Generally, the antibody-producing cell is taken from a mouse that has been immunized with (i.e. exposed to) a human antigen. The hybridoma combines the antibody-producing capability of the spleen cell with the long life of the myeloma cell, resulting in a cell line that can be cultured indefinitely and produces large quantities of an antibody.

**LIGANDS**: A molecule that binds to another molecule, particularly used to refer to a small molecule that binds specifically to a larger one. The antigen that binds to a specific antibody is an example of a ligand.

**MYELOMA**: A tumor of the bone marrow that can be adapted to grow permanently in cell culture. Myeloma (immortal) cells are fused with antibody-producing mammalian (mortal) cells to produce hybridomas.

**POLYCLONAL ANTIBODIES**: Because the human immune system cannot know in advance what pathogens it will confront, it prepares for future infections by creating millions of different antibodies. Each of these highly selective proteins recognizes and binds to a specific target, or antigen, then signals other components of the immune system to destroy the target. These naturally-occurring polyclonal antibodies play a crucial role in triggering an immune response.

**RECOMBINANT DNA**: Made by combining DNA from more than one source – often from very different species – recombinant DNA is also referred to as genetic engineering, gene splicing or genetic modification. This technique is now the basis for many biotechnology advances. Usually, a human or other animal gene is inserted into the bacterium *E. coli*, the most common bacterium in the human intestine. Because this bacterium divides quickly, the new gene can be cloned in a short time.

**THERAPEUTIC ANTIBODY**: A single clone of a specific antibody that is produced from a cell line, including hybridomas. There are four classifications of therapeutic antibodies: murine antibodies; chimeric antibodies; humanized antibodies; and fully human antibodies. These different types of antibodies are distinguishable by the percentage of mouse to human parts making up the antibodies. A murine antibody contains 100% mouse sequence, a chimeric antibody contains approximately 30% mouse sequence, and humanized and fully human antibodies contains only 5-10% mouse residues. These groups are defined below.

**MURINE ANTIBODY**: A mouse antibody. While approved for transplant rejection and colorectal cancer, murine antibodies administered to humans are seen by the human immune system as foreign and can have serious side effects, including an allergic-like response (see HAMA). Murine antibodies may also be ineffective as human therapeutics due to their rapid removal from human blood and their weak ability to recruit human immune system processes necessary to clear the targeted antigen (e.g. tumor cell).

**CHIMERIC ANTIBODY**: A genetically engineered fusion of parts of a mouse antibody with parts of a human antibody. Generally, chimeric antibodies contain

approximately 33% mouse protein and 67% human protein. Developed to reduce the HAMA response elicited by murine antibodies, they combine the specificity of the murine antibody with the efficient human immune system interaction of a human antibody. However, chimeric antibodies can exhibit a HACA response (**H**uman **A**nti-**C**himeric **A**ntibodies; similar to HAMA response) and thereby may show reduced efficacy as a therapeutic.

*HUMANIZED ANTIBODY*: A genetically engineered antibody in which the minimum mouse part from a murine antibody is transplanted onto a human antibody; generally humanized antibodies are 5-10% mouse and 90-95% human. Humanized antibodies were developed to counter the HAMA and HACA responses seen with murine and chimeric antibodies. Data from marketed humanized antibodies and those in clinical trials show that humanized antibodies exhibit minimal or no response of the human immune system against them.

*"FULLY HUMAN" ANTIBODY*: Recently the term "fully human" and "human" antibody has been used to label those antibodies derived from transgenic mice carrying human antibody genes or from human cells. To the human immune system, however, the difference between "fully human", "human", and "humanized" antibodies may be negligible or nonexistent and as such all three may be of equal efficacy and safety.

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