

ANTIBODIES



IN THERAPY AND RESEARCH





MorphoSys is currently active in two areas, therapeutic antibodies and research antibodies. In the therapeutic sector, MorphoSys is developing new antibody-based drugs, both for its own account and in collaboration with partners. In the research sector, MorphoSys is a major provider of antibodies and related technologies which are used as tools to support scientific research. Since HuCAL GOLD, MorphoSys's core technology, is the source of highly specific antibodies for both markets, the Company is able to participate in the growth of both sectors. HuCAL antibodies function in various ways to meet the demands of biological research, diagnosis, and therapy.

Antibodies can accurately find and detect almost any molecule. These binding partners, also known as target molecules or antigens, are often parts of proteins, which are the most important components of living cells. Antibodies are therefore ideal "search engines" for detecting minuscule amounts of a particular target molecule, and are used daily as tools, or reagents, in research laboratories worldwide. In 2004, researchers spent approximately US\$ 800 million on antibodies.

Antibodies also play a crucial role in diagnosing various conditions, such as testing blood serum for the presence of various pathogens. Arguably their most important application is as drug treatments. Companies must invest in many years of intensive research and trials as well as meeting part of the high development costs before an antibody is approved for use as a therapeutic agent. At the moment, 17 antibodies are available as drugs.



Antibodies as Tools in Basic Research and Diagnostics

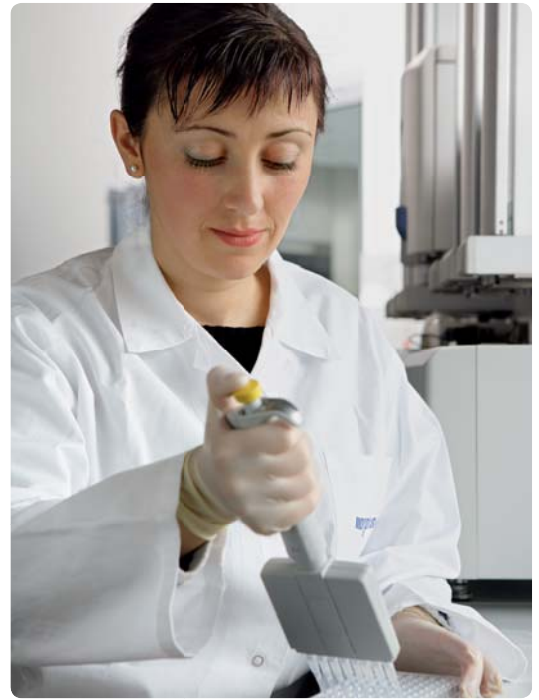
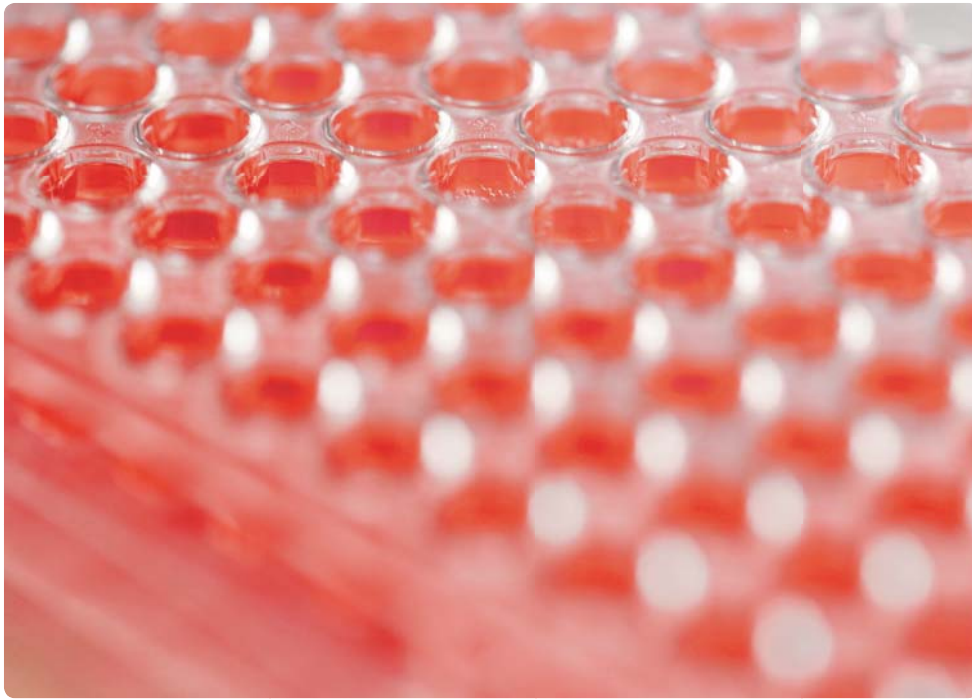
All methods of discovery in biotechnology and medicine are based on an understanding of fundamental biological processes and living systems. Which structures in the cells of living organisms carry out which functions? How do these structures communicate with each other and how is their malfunction connected with particular diseases? How do chronic diseases such as cancer or Alzheimer's disease develop?

Antibodies lie at the heart of the various laboratory techniques used to address these questions. They are powerful tools in basic research because they recognize their antigens with outstanding specificity. This allows researchers to identify molecules that cannot be seen with the naked eye, and, by manipulating these molecules, to draw conclusions about the function of proteins of interest.

Antibodies are also routinely used for verification in various areas of diagnostics and analysis. Common applications include the detection of viral or other types of infection, recognition of allergies, and measurement of hormone levels in blood. They are also used in environmental analysis to provide evidence of contamination or the presence of harmful chemical substances.

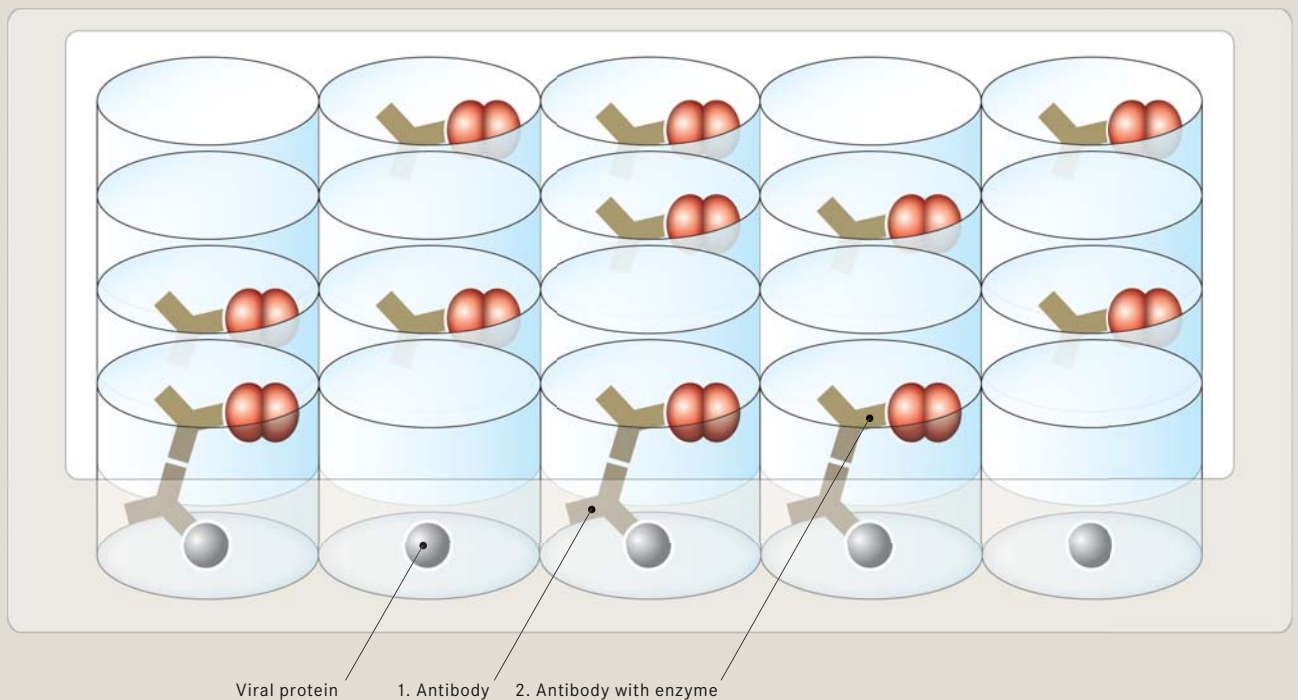
Antibodies to Fight Disease

Antibodies are an essential component of the human immune system. Using antibodies to fight disease is a logical extension of their natural role, and researchers have been working on such applications for decades. All therapeutic applications of antibodies are based on their ability to recognize specific target molecules. For example, antibodies use a variety of methods to recognize and attack tumors.



Antibodies Help to Recognize Illnesses

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Testing for infections is often performed by testing for antibodies produced in response to an infectious agent, rather than by testing directly for the infectious agent. An example of such antibody-based diagnostic tests is the ELISA (Enzyme-Linked Immunosorbent Assay), which is used in the study of HIV and other viral infections. The base

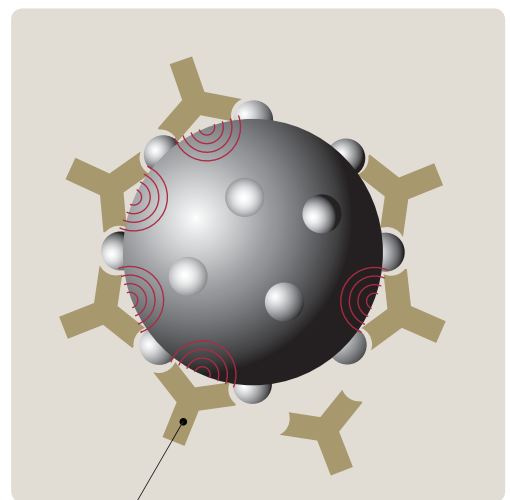
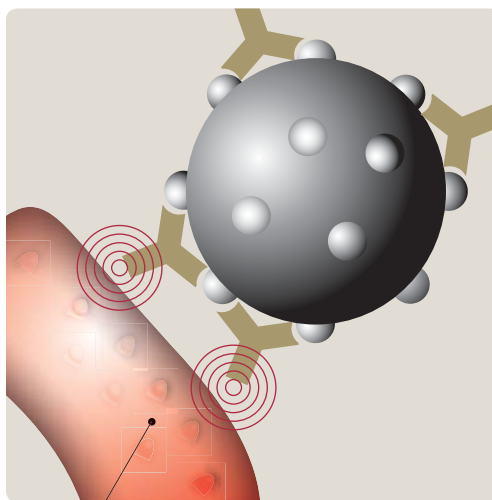
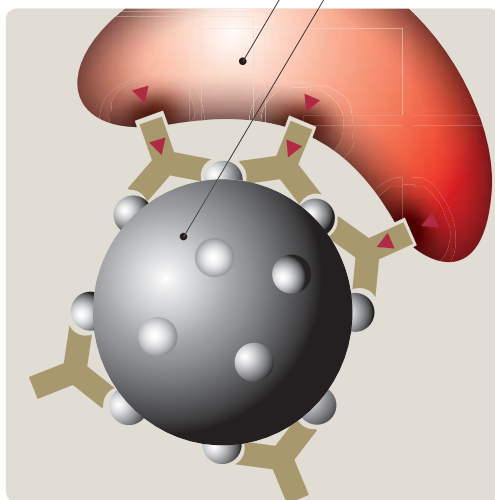
of a reaction vessel is coated with viral protein and the blood of the patient is tested. After several washing steps, antibodies only remain behind in samples from infected patients. These antibodies are detected using a second antibody, which is linked to an enzyme detection system that produces color in the final reaction step.

How Therapeutic Antibodies Work



Effector cell
Target cell

Antibodies use different strategies for fighting disease.



Reactive cell

Cross-Linking

Basic research has shown that it is often possible to identify malignant cells through molecules on their surface, known as target molecules. Antibodies can be used to recognize and attack cells that carry characteristic target molecules. MorphoSys is able to identify a target-specific antibody with this ability of the HuCAL GOLD antibody library. To fight cancer, therapeutic antibodies are carried in the bloodstream to the tumors and bind their target molecules. The fact that they bind labels the tumor cells as unhealthy, and this stimulates other components of the immune system, such as phagocytes, to attack these cells. An example of this type of therapeutic antibody is the MOR202 anticancer antibody from MorphoSys.

Many diseases arise not from an individual unhealthy cell, but from an undesired interaction among cells or from misguided communication, which is normally mediated by messenger molecules. Drugs based on antibodies can also attack these types of disease by inhibiting, or blocking, the interaction between molecules or cells.

Another mechanism exploits the characteristic surface antigens displayed on the surfaces of unhealthy cells in a different manner. Antibodies bind and link these surface antigens together. This process triggers the cells to die or self-destruct, and they undergo processes known as necrosis, programmed cell death or apoptosis. The HuCAL antibody 1D90C3, developed in collaboration with GPC Biotech, is used in an application of this type.



The applications of therapeutic antibodies can be expanded by “arming” the antibodies. Antibodies can be armed by being coupled to a second entity, such as a radioactive molecule or a cytotoxic agent. Examples of armed antibodies include the anticancer antibodies Zevalin® and Bexxar®, which are coupled to radioisotopes. The antibodies act as messengers that transport the radioactive material to the target cells, which in this case are B cells that have undergone genetic alterations

and thus became tumor cells. The amount of radioactivity used is carefully regulated and minimized, which also minimizes the exposure of other healthy tissues to radioactivity. A similar mechanism is applied in the antibody Mylotarg®, which is directed against lymphoma cells and is coupled to a chemotherapeutic agent. The antibody binds the surface protein of a cancer cell and enters the cell’s interior. The chemotherapeutic agent acts here and the unhealthy cell is destroyed.

Antibodies Explain the Basis of Life

Fluorescence microscopy is a frequently used scientific technique that uses antibodies to visualize proteins in cells or even in whole tissues (immunohistochemistry). The technique is performed using very thin slices of a tissue sample or even single cells, which the antibodies can penetrate. The antibodies are coupled with a fluorescent dye, which can be excited by a laser and visualized under a specialized microscope. In this figure, the antibodies are binding to and labeling the cellular cytoskeleton.

