

Bright future ahead for antibody cancer therapy

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Antibodies, once touted as the "magic bullets" of cancer care, are now fulfilling that promise and more advances are on the way, say cancer researchers at the Georgetown Lombardi Comprehensive Cancer Center

In a review article posted online March 16 in *Cell*, the researchers say that refinements and modifications of monoclonal antibody drugs -- several of which have already revolutionized the care of breast and [colon cancer](#) --are now being tested in most tumor types.

These modifications allow antibody drugs to bind to more than one target on a cell, and to directly stimulate the body's immune response to promote vaccine-like antitumor effects. Others have been designed to boost their killing power by carrying a payload of radiation, toxins, or other chemicals.

'We are heading into an era where [antibodies](#) will not just be components of an effective [therapeutic strategy](#), they will be at the core of an oncologist's treatment plan for patients," says the review's lead author, Louis M. Weiner, M.D., director of Georgetown Lombardi Comprehensive Cancer Center, an internationally recognized expert in immunotherapy research.

"Advancement in antibody [cancer treatment](#) is not a minor advance or a trivial victory. This is big time stuff," Weiner said in an interview.

His co-authors on the review are Joseph Murray and Casey W.

Shuptrine, both graduate students in the Tumor Biology Training Program at Georgetown Lombardi.

A good example of the new class of antibody-based therapies is [ipilimumab](#), a drug approved in 2011 to treat patients with metastatic melanoma, says Weiner. Ipilimumab is a fully [human antibody](#) which binds to an immune antigen (CTLA-4) on cancer cells that transmits a signal inhibiting other [immune cells](#) from destroying the tumor. Ipilimumab blocks CTLA-4, thereby inducing an active immune response.

"This agent turns off the brakes of an immune response against melanoma, liberating the body to set up long term protection against the cancer," Weiner says. "About 10 percent of patients with metastatic melanoma who use it go into long-term remission, and may well be cured."

Antigens are substances, often a cell surface receptor, which causes the immune system to produce an antibody against it, as a way to target and kill the cell. Therefore, antibody agents targeted to a receptor on a cancer cell have the unique capacity to target and kill cancer cells while activating an [immune response](#). A monoclonal antibody (mAb) is an artificially produced antibody designed to bind to a specific cancer antigen, and currently 11 mAbs are approved for use in oncology, Most of these were approved in the last decade. The most commonly used are trastuzumab (Herceptin) to treat HER2-positive breast cancer and rituximab (Rituxan) for specific forms of lymphoma and leukemia.

Advanced antibody engineering techniques are being used to create more effective treatments, Weiner says. One group, known as bispecific antibodies (bsAbs) can bind to two different tumor antigens, or to a tumor antigen and another target in the tumor microenvironment, such as an immune system killer cell. Other mAbs are being designed as

"conjugates" to carry a toxic payload, which can be a radionuclide, other drugs, toxins, or enzymes. Researchers are also now increasing the capacity of antibodies to be absorbed by [cancer cells](#) so that they can bind to antigens inside the cell – not just on the outside of the cell surface.

"The field of cancer antibodies is definitely maturing. There are scores of new cancer antibody agents now being tested in virtually every kind of solid [cancer](#), and oncologists, researchers and pharmaceutical companies are excited about their promise," Weiner says. "To me this is like watching a child grow up and do well -- very well -- in young adulthood."

Provided by Georgetown University Medical Center

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