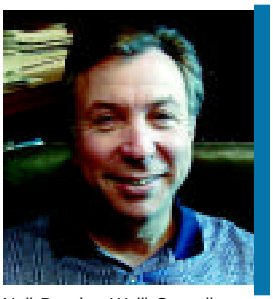
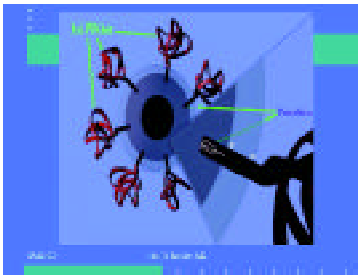
Millennium Develops Cornell Antibody Therapies Against Key Target in Prostate Cancer

Therapeutics Targeting Prostate Specific Membrane Antigen Currently in Clinical Trials



Neil Bander, Weill Cornell Medical College



PSMA is a type II transmembrane protein. The first antibody to PSMA (ProstaScint®, approved for prostate cancer imaging in some patients) binds to a site on PSMA that is hidden within the cell cytoplasm. As a result, ProstaScint® detects only tumor sites that have dead or dying cells where the membrane has been disrupted, allowing contact of the antibody and the antigen (PSMA). Bander's group developed the first antibodies that target a site on PSMA, which is on the exterior ($PSMA_{ext}$) of the cell thereby allowing the antibody to target living cancer cells.

BZL Biologics entered into a sublicense agreement with Millennium Pharmaceuticals, Inc. (Nasdaq: MLNM) to develop and commercialize antibody-based therapeutics targeting Prostate Specific Membrane Antigen (PSMA). BZL is a privately owned company that licensed the antibody therapeutics from the Cornell Research Foundation, Inc. (CRF). The technology was developed in the laboratory of Neil Bander, Bernard and Josephine Chaus Professor of Urological Oncology and Professor of Urology at the Joan and Sanford I. Weill Medical College of Cornell University.

PSMA is believed to be the best-established, prostate-associated, cell surface molecule currently known. It is expressed by virtually every prostate tumor (both primary and metastatic) and the level of expression increases with tumor progression. The primary indication for products targeting PSMA is prostate cancer, although there is strong evidence to suggest that PSMA may also be a relevant therapeutic target in other solid tumors.

Under its license from CRF, BZL has developed commercial-grade products, including humanization of the original murine antibody, and it has completed pre-clinical testing and a Phase I clinical trial on the lead antibody therapeutic. Additional clinical trials are currently underway at New York Presbyterian Hospital–Weill Medical College of Cornell University with additional sites to open trials in the near future. The initial development plan under the sublicense includes programs for both immunotoxin and radiolabeled products. Millennium has access to certain cytotoxic compounds that are ideal conjugates for further development of anti-PSMA therapies.

"We are very excited about our collaboration with Millennium, a dynamic and visionary biopharmaceutical company that is extremely aggressive in bringing products through development," says Dr. Bander. "We view this alliance as a welcome opportunity to develop and market a product for the treatment of prostate cancer, a disease which currently has tremendous unmet medical need. In addition, we look forward to further examining the potential for anti-PSMA therapeutics to play an efficacious role in the treatment of other cancers. Millennium's scientific know-how will be key to exploring these broad new applications."

The humanized J591 antibody, directed toward the extracellular domain of PSMA, is the most advanced anti-PSMA antibody in development. In animal models of prostate cancer, J591 has demonstrated profound efficacy. The antibody has been shown to be well tolerated in Phase I clinical studies and has been used successfully as an imaging agent for primary and metastatic tumors in patients with prostate and other cancers. A radiolabeled version of J591 is currently in Phase I studies in advanced prostate cancer patients.

Antibodies are naturally occurring proteins produced by the immune system in response to substances, known as antigens, that appear to be foreign to the body. Each of the millions of antibodies produced in the body has the ability to single out the presence of a specific antigen, or target, and then trigger its destruction. If the antigen is produced only by diseased cells, these cells can be killed without harming healthy neighboring cells. A monoclonal antibody is one derived from a single cell. Monoclonal antibodies can be produced in quantity, and can be used to treat a variety of diseases ranging from cancer to cardiovascular disease. Because of their high specificity and biological nature, monoclonal antibodies may significantly reduce the side effects experienced with traditional therapies. Monoclonal antibodies are currently the fastest growing therapeutic drug class.

According to the American Cancer Society, approximately 180,400 new cases of prostate cancer will be diagnosed in the United States this year. Of these new cases, 31,900 will result in death. The five-year survival rate of men with prostate cancer is 89 percent with this number rising to 100 percent if the cancer is found before it metastasizes (spreads to another area of the body). There is a tremendous unmet medical need for treating the disease; no therapies are currently available for end-state or hormone-refractory prostate cancer patients. The exact cause of prostate cancer is not yet known, however, scientists have identified certain risk factors, including family history of the disease, age, diet, and race. The majority (greater than 80 percent) of prostate cancer patients are more than 65 years old. Early detection is important, and it is recommended that men over the age of 50 have a prostate specific antigen (PSA) blood test every year and men over the age of 40 be tested annually if there is a family history. Coupled with a digital rectal exam (DRE), the PSA is a very useful test for determining which men need further evaluation.

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