Infectious disease researchers develop basis for experimental melanoma treatment

December 7 2006

While investigating a fungus known to cause an infection in people with AIDS, two grantees of the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH), unexpectedly discovered a potential strategy for treating metastatic melanoma, one of the deadliest forms of skin cancer. The treatment approach, which involves combining an antibody with radiation, has since been further developed and is expected to enter early-stage human clinical studies in 2007.

"This is an excellent example of how scientific research in one discipline may have payoffs in a completely unpredictable way," says NIAID Director Anthony S. Fauci, M.D. "This important AIDS-related research has led to the development of a promising therapeutic strategy for a terrible cancer that affects thousands of people each year."

Arturo Casadevall, M.D., Ph.D., of the Albert Einstein College of Medicine at Yeshiva University, in New York City, and his research team began studying the biology of the skin pigment melanin to better understand why its synthesis plays a role in the process whereby certain yeast-like fungi, specifically Cryptococcus neoformans, cause disease in some people. C. neoformans can cause cryptococcosis, a potentially fatal fungal infection that can lead to inflammation of the brain and death in people with AIDS and other immunocompromised individuals.

The researchers created an infection-fighting antibody, known as a monoclonal antibody, that binds to melanin based on scientific evidence

suggesting that when melanin is synthesized, it causes the immune system to react in a way that might create antibodies to fend off C. neoformans infection. Based on this finding, Dr. Casadevall theorized that melanomas might contain melanin that would allow the monoclonal antibody to deliver radiation to tumor cells. Dr. Casadevall then teamed with his colleague Ekaterina Dadachova, Ph.D., an expert in nuclear medicine and fellow NIAID grantee, to investigate whether the melanin-binding antibody could be converted into an anti-tumor drug.

In a study published in October 2004, Dr. Casadevall and Dr. Dadachova, the study's lead author, combined the C. neoformans monoclonal antibodies with radiation to create radiolabeled antibodies. They then tested these radiolabeled antibodies in mice to determine their effectiveness in attacking melanoma tumors. Initially, the mice had melanoma tumors ranging from 0.6 to 1.0 centimeters (cm) in diameter. After receiving a single dose of the radiolabeled antibodies, tumor growth was completely inhibited and near total tumor regression occurred in those animals with smaller tumors (0.6 to 0.7 cm in diameter). Further, the treated mice showed no signs of kidney or other organ damage and none died during the 30-day study. Conversely, tumors continued to aggressively grow in the untreated control group and by day 20, all but one of the eight untreated mice had died.

In November 2006, Pain Therapeutics, Inc., a San Francisco-based biopharmaceutical company, licensed the radiolabeled monoclonal antibody technology from the Albert Einstein College of Medicine. The company intends to begin testing it as a metastatic melanoma treatment in small human clinical trials in 2007. According to the American Cancer Society, melanoma accounts for approximately five percent of all skin cancers but causes roughly 75 percent of all skin cancer-related deaths.

Dr. Casadevall credits his promising discovery to luck and a hunch that

paid off. "Scientific breakthroughs often occur completely through serendipity, and this is just one of those instances," says Dr. Casadevall. "We're still working on cryptococcosis and developing a general strategy for using radiolabeled monoclonal antibodies to fight infectious diseases."

His laboratory continues to examine the underlying causes of cryptococcosis, and in continued collaboration with Dr. Dadachova, is exploring the use of radiolabeled monoclonal antibodies to treat infectious diseases.

Source: NIH/National Institute of Allergy and Infectious Diseases