

Tech Brief: Cancer and Infectious Disease Vaccines

Camouflaged as harmless, home-grown cells, cancer cells multiply uncontrollably and invade and damage normal tissues without the immune system recognizing the disease. Recently, however, researchers at Roswell Park Cancer Institute (RPCI) have been working on a novel, vaccine-centered strategy for blowing the whistle on tumors and activating the body's natural immune defenses against them.

Why don't our bodies attack cancer as they would an ordinary infection? As smart as the immune system seems to be — repulsing countless new microorganisms that attack us every day — it can be fooled. That gullibility works in our favor when we use vaccines to trick the immune system into pumping out antibodies that arm us against full-scale infections like tetanus or polio. But since cancers originate inside the body, their antigens (surface molecules that trigger immune responses) “look” normal to the immune system.

Unmasking those malignant cells and alarming the immune system to their antigens has proven to be difficult — one of the reasons why medicine does not yet have a vaccine that consistently induces tumor regression or improves patient survival. But RPCI researchers have found a way to use certain naturally occurring molecules called heat shock proteins (HSPs) to alert the immune system that all may not be what it seems.

HSPs are present in all living cells, where they offer protection against many environmental stresses while also playing an essential part in the routine processing, folding, and assembly of other cellular proteins. To do this, HSPs possess the unusual ability to bind to and hold other cellular proteins and to correctly install them into numerous cellular pathways that are the basic processes necessary for life. However, new research shows that some of these cellular proteins in cancer cells that HSPs bind to can be cancer antigens. Researchers at RPCI have shown that these HSP-cancer antigen complexes can be recreated in the test tube using synthetically made tumor antigens. They have also shown that

the HSPs bind to specific receptors on antigen presenting cells, the sentinel cells or triggers of the immune system that activate a strong immune response. Thus HSPs can bind to both cancer antigens and the specific immune cells that activate the immune system. When the HSP is binding a cancer antigen, the resulting immune response aggressively attacks that antigen on cancer cells, killing the cancer cells while leaving the rest of the body unharmed.

Promising developments

Autologous HSP tumor vaccines could change our ideas about immunotherapy. Until now, cancer vaccines have been limited to prevention, rather than cure, and to a limited range of conditions. The U.S. Food and Drug Administration has licensed only two preventive vaccines. One is aimed at the hepatitis B virus, which is associated with liver cancer; the other at the human papillomavirus that causes cervical cancer. An extensive amount of pre-clinical research has already been completed by RPCI scientists and published in major journals such as **Cancer Research** and the **Journal of Immunology**. These studies show a remarkable level of effectiveness of these synthetic HSP vaccines in treating melanoma and breast cancer, a level of effectiveness far greater than previously used vaccine technologies such as those employing Complete Freund's Adjuvant. In addition to melanoma and breast cancer, these vaccines have been prepared at RPCI against renal cell, prostate, and lung cancers. Further, using the ability of the HSP to deliver protein antigen to and activate the immune system, this technology is also applicable to infectious diseases, such as tuberculosis (TB), which is responsible for about two million deaths each year. HSP-TB vaccines have been prepared at RPCI and await clinical evaluation. Indeed, any disease for which one or more antigens have been identified is a candidate for this new HSP technology. Since they are synthetic, these vaccines can be prepared in unlimited quantities and stored for use whenever needed.

*Roswell Park Cancer Institute is a pioneer in the study of thermal therapy and heat shock proteins. Our expertise and research also extend into photodynamic therapy; tumor hypoxia and oxidative stress; radiation and oxidative DNA damage and repair; and membrane biophysics. For more information on vaccines, contact **Richard Matner, PhD, MBA, Tech Transfer Director**, at Richard.Matner@roswellpark.org.*