

HEAT SHOCK PROTEIN

TECHNOLOGY



ANTIGENICS' PATENTED FLAGSHIP TECHNOLOGY UTILIZES HEAT SHOCK PROTEINS (HSPs), A UBIQUITOUS CLASS OF MOLECULES THAT PLAY KEY ROLES IN IMMUNE RESPONSE. BECAUSE HSPs ASSOCIATE WITH VIRTUALLY ALL OF A CELL'S PEPTIDES (PIECES OF PROTEINS), A PARTICULAR CANCER'S 'FINGERPRINT' MAY BE CAPTURED BY ISOLATING HSP-PEPTIDE COMPLEXES FROM THE CANCER CELLS.

ANTIGENICS' INVESTIGATIONAL, PATIENT-SPECIFIC THERAPEUTIC CANCER VACCINE ONCOPHAGE® (VITESPEN; FORMERLY HSPPC-96) IS DESIGNED TO CAPTURE THIS FINGERPRINT AND USE IT TO TRIGGER THE BODY'S IMMUNE SYSTEM TO ATTACK A PATIENT'S SPECIFIC CANCER. THIS PRECISION IS INTENDED TO LEAVE HEALTHY TISSUE UNAFFECTED, AND IS DESIGNED TO LIMIT THE TOXICITIES ASSOCIATED WITH TRADITIONAL BROADER-ACTING CANCER TREATMENTS.

ANTIGENICS IS ALSO WORKING TO DEVELOP INFECTIOUS DISEASE TREATMENTS USING HSP TECHNOLOGY. AG-707 IS AN INVESTIGATIONAL THERAPEUTIC VACCINE PROGRAM FOR THE TREATMENT OF GENITAL HERPES THAT REPRESENTS THE COMPANY'S FIRST NON-PATIENT-SPECIFIC APPLICATION OF ITS HSP TECHNOLOGY.

WHAT ARE HEAT SHOCK PROTEINS? Heat shock proteins are a class of proteins that appear to exist in all cells and in all life forms, and are induced when a cell undergoes environmental stress such as heat or oxygen deprivation. Under normal conditions, these proteins act as 'chaperones' to ensure that the cell's other proteins are in the right shape and in the right place at the right time. For example, HSPs help other proteins fold into shape, transport them within the cell, and escort old ones to be broken down.

VACCINATING AGAINST CANCER For decades it has been known that animals can be 'vaccinated' against cancer. This is how it works: weakened cells from a tumor are used to vaccinate a mouse. If the mouse is then injected with full-strength cells from that same tumor, the mouse rejects the cells and does not develop cancer. Conversely, if a mouse has not been vaccinated in this manner, the tumor cells will cause the mouse to develop cancer. About 25 years ago Antigenics' founding scientist, Pramod Srivastava, PhD, began a series of experiments that identified heat shock proteins as the element responsible for protecting the mice from cancer, and his pioneering work with HSPs continues today.

HSPs & IMMUNE RESPONSE HSPs trigger immune response through a variety of intracellular and extracellular activities. Because HSPs are normally found inside cells, extracellular HSPs can indicate that a cell became so sick that it has died and spilled out all of its contents. This type of messy, unplanned death (called necrosis) typically occurs only when something is very wrong with the cell. Because of this, extracellular HSPs are one of the most powerful ways of sending a 'danger signal' to the immune system to generate a response that can help eliminate infection or disease.

HOW IT WORKS Antigenics' founding technology is based on the fact that the human body's immune system has the inherent ability to fight every single type of disease – past, present or future – as long as it is able to recognize it as a threat. Built on more than 20 years' worth of research, the company's heat shock protein

technology was developed to help improve the immune system's ability to recognize friend from foe by taking advantage of the body's HSP-mediated immune response. Injecting purified HSP-peptide complexes is designed to introduce the antigenic peptides directly to antigen-presenting cells (APCs) – a process that mimics and amplifies the 'danger signal' believed to be naturally triggered by HSPs. The APCs pick up the complexes, then alert the immune system by displaying antigenic peptides on their cell surfaces, which then activates 'killer' T cells to target and destroy the diseased cells.

WIDESPREAD APPLICATION The company's investigational HSP-based cancer vaccine Oncophage is autologous, meaning it is derived directly from – and created specifically for – each individual patient. This patient-specific approach is designed to treat with extreme precision an enormously variable disease that differs not only from cancer to cancer, but also from person to person. By isolating HSP complexes from a patient's tumor, the vaccines are meant to capture the specific cancer's 'fingerprint' in order to program the immune system to target any cells – and only those cells – that bear this fingerprint.

Antigenics is also evaluating HSP technology in nonautologous applications. By complexing recombinantly derived HSPs and common viral proteins, Antigenics' AG-707 genital herpes immunotherapeutic product is intended to target only infected cells, which bear these viral proteins. HSP technology was designed to allow extreme specificity in cancer and infectious disease treatment, thereby preserving healthy tissue.