

PURE VACCINE solutions

An Emergent Technologies, Inc. Company

BETTER IMMUNOLOGY TOOLS FOR BETTER HEALTHCARE

**PURE VACCINE SOLUTIONS, A
SUBSIDIARY OF PURE PROTEIN,
IS FOCUSED ON USING THE
POWER OF OUR SOLUBLE HLA
TECHNOLOGY TO CREATE TOOLS
SPECIFICALLY FOR VACCINE
DEVELOPMENT AND VALIDATION.**

Industry

Life Sciences / Biopharmaceuticals

Objective

Pure Vaccine Solutions seeks collaborative partnerships with industry leaders to develop and commercialize vaccine tools and technology.

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Vaccine and Drug Development

Pure Vaccine Solutions has a patented method of producing substantial amounts of soluble HLA in various human and animal cell lines. This facilitates epitope/protein discovery in various cancerous and pathogen targeted cell lines. As an example, we have identified numerous peptide epitopes unique to HIV infected T cells. This data indicates that particular proteins are unique to the cytosol and surface of infected cells. These proteins are putative drug or vaccine targets. We have patented this epitope/protein discovery process and have developed a battery of tests which validate putative antigens using soluble HLA.

Pure Vaccine Solutions provides a complete system of HLA based vaccine design. At every step in the process, HLA is used to feedback information as to how design decisions will impact epitope presentation and effectiveness. Pure Vaccine Solutions' suite of technologies is superior to conventional vaccine antigen discovery techniques and our battery of validation tests are unique in their efficacy and economy.

The process begins with directly discovering which peptides are presented by the HLA of diseased cells. This discovery technology bypasses several dangerous assumptions on the road to vaccine design. Disease states are marked by altered protein states inside the cell resulting from differential production, routing, or degradation of individual protein entities. Gene expression assays can detect production changes but cannot perceive routing or degradation events. The HLA's job is to present these permutations and report them to the immune system.

Pure Vaccine Solutions has developed an efficient way to harness this natural

system for discovery research. We begin by mapping peptide epitopes that are produced within the cell by HLA molecules. The function of HLA class I proteins is to survey the protein content of the cell. We comparatively survey thousands of proteins in diseased and healthy cells. Once a peptide epitope is uncovered, the entire sequence of the host protein can be revealed by searching genomic databases. This sequence can be coupled to our high throughput binding assay to uncover other potential epitopes. We have produced over 50 varieties of individual HLA types, which represents a very complete panel for use in binding studies or to create T cell staining reagents. One benefit of having a plentiful supply of protein is the ability to easily modify potential epitopes for improved binding or immunogenicity and quickly assess the results of those modifications.

Many companies have created platforms to deliver vaccine antigens. These range from recombinant viral vectors, to DNA based solutions, to professional antigen presenting cells. Pure Protein can ascertain effects of an "empty" vector on a target cell. This technique can also be used to validate that the intended epitope is being presented and can assess vector modifications intended to improve epitope display.

The Role of HLAs in Vaccine Development, Cancer Research, and Pathogen Research

Vaccines: Class I and II polymorphisms pose a challenge to the vaccine architect: given the vast number of diverse HLA molecules in the population, can one design a vaccine that will bind the various class I and II molecules to stimulate a protective immune response? Will a vaccine work in both the A*0201 and A*2404 individual, or do these individuals need separate vaccines? Our laboratory's work has been focused on addressing such questions, and Pure Protein's products provide a unique tool to resolving such questions.

Cancer: HLA molecules target the immune response not only to bacteria and viruses, but also to tumor cells. Class I HLA molecules alert the immune response to the presence of tumor cells, and the cancerous cells are destroyed. HLA molecules therefore play an important role in the elimination of cancerous cells. Pure Protein's HLA product will be used to characterize anti-tumor immune responses and for the development and testing of anti-tumor vaccine.

Pathogens: Human immune responses have evolved eliminate pathogens. Viral and bacterial pathogens are the predominant threats to the health of mankind. There are numerous other examples of pathogens that concern the immune response, including *Plasmodium falciparum* (malaria) and *Borrelia burgdorferi* (Lyme disease). Using its ability to focus, the immune response can quickly and specifically target such pathogens.

Pathogens employ many different strategies. A common virus strategy is to reproduce within the cells of a host. Once inside a host cell, antibodies cannot reach the virus. The immune response therefore alerts cytotoxic T lymphocytes (CTLs) to the presence of the virus, and the infected cells are killed by the CTLs so that the virus inside cannot reproduce and spread.

Conversely, bacteria typically reproduce outside of the host's cells. To target bacteria, the immune response will recruit phagocytic cells and target antibodies to the bacteria. CTL would be inappropriate, even deleterious, because there is not reason to destroy human cells in this instance. Efficient destruction of the various pathogens therefore requires that different, and appropriate, immune responses are activated.

Mobilizing the proper arm of the immune response allows the host to efficiently mark a pathogen for elimination. This is where the HLA class I and class II molecules respond to the presence of a particular type of pathogen. Once the immune response is alerted to the presence of a bacteria or virus, it will mobilize the appropriate immune effector agents. The HLA produced by Pure Protein will serve as a means for understanding how the immune response targets these pathogens and manipulates immune responses. Our product will also be needed to test the efficacy of vaccines designed to protect us from these pathogens.

Pure Protein has developed an algorithm to reduce the size while increasing the power of clinical trials. Some recent trials of CTL eliciting vaccines have not met their intended endpoints but have shown surprising efficacy for subpopulations with specific HLA types.

Summary

Pure Protein is using its unique ability to produce sHLA naturally loaded with endogenous peptides as an epitope discovery and validation tool. Peptide epitopes are discovered by analyzing the soluble HLA epitopes with reverse-phase HPLC and mass-spectrometry. For viral diseases, the emergence/disappearance of epitopes is detected by comparing mass spectrometric maps before and after infection.

Similarly, "healthy" cell lines can be compared to cancerous or cells with an

oncogene. The technology is flexible enough to allow the developer to designate the pathogen/gene and cell line(s). Our discovery procedure provides these developers with data from a proven, repeatable system.

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