Cambridge Healthtech Institute’s Fifth Annual...

ADVANCES IN CANCER VACCINES

August 13-14, 2008 • Royal Sonesta Hotel • Cambridge, Massachusetts

The Advances in Cancer Vaccines meeting is focused specifically on biological therapies that partner with the immune system to fight cancer. Key players in industry, academia, and government will address the progress being made in such challenging areas as humanized monoclonal antibodies, soluble receptors, immunorepressants and tumor treatment.

Join colleagues from around the world to discuss the current challenges and breakthrough successes in the pursuit of an immunotherapeutic approach to attacking cancer, this stealer of lives.

Opportunities and Challenges for Cancer Vaccines
Tibor Keler, Ph.D., Senior Vice President and Chief Scientific Officer, Celldex Therapeutics Inc.

Vaccine, Immunotherapy and the Immunological Constant or Rejection
Francesco M. Marincola, Ph.D., Chief, Infectious Disease and Immunogenetics Section, Department of Transfusion Medicine, Clinical Center, National Institutes of Health

Dendritic Cell Tumor Fusions from the Bench to the Bedside
David Avigan, M.D., Director, Hematological Malignancies/Bone Marrow Transplantation, Beth Israel Deaconess Medical Center, Harvard Medical School

GVAX Immunotherapy for Prostate Cancer
Kristen M. Hege, M.D., Vice President, Clinical Research and Development, Cell Genesys

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This talk describes the development of Targenene’s therapeutic HPV CIN 2/3 vaccine from concept to Phase III. My talk will present an important case study addressing the development path of a cancer vaccine that is about to enter phase III testing.

11:45 Development of Optimized Cryptic Peptides for Tumor Immunotherapy
Kostas Kosmatopoulos, M.D., Ph.D., Dr.Sc., Founder and President and CSO, Vaxon Biotech

Tumor immunotherapy is mainly based on the activation of cytotoxic T lymphocytes (CTL). CTL recognize peptides derived from tumor antigens and presented at the cell surface in association with HLA molecules. Two types of peptides have been described: i) Dominant peptides, which exhibit high HLA affinity, are abundant at the cell surface and are immunogenic; ii) Cryptic peptides, which exhibit low HLA affinity, are weakly presented at the cell surface and are non immunogenic. Dominant peptides appeared to be attractive candidates for tumor immunotherapy and had, therefore, been targeted in all clinical trials performed to date with results not as encouraging as expected. This relative ineffectiveness seems to be due to T cell tolerance to tumor antigens which are proteins expressed by tumor and also by normal cells. Tolerance results in the deletion or inactivation of CTLs specific for dominant peptides. We have shown that CTLs specific for cryptic peptides escape tolerance mechanisms, suggesting that cryptic peptides would be better than dominant peptides for cancer vaccination – provided they can be rendered immunogenic (Gross et al., 2004). Cryptic peptides, which have low HLA affinity, have to be “optimized” by altering their amino acid sequence, thereby transforming them into high affinity peptides capable of stimulating a T cell response. We have developed a method for optimizing cryptic peptides presented in association with HLA-A2. It consists of substituting the amino acid in position 1 by a tyrosine (Y). This modification increases HLA affinity, and has been shown to render immunogenic 90% of cryptic peptides so far studied (Touzon et al., 2000; Scardino et al., 2000). More importantly, immunization of HLA-A2 expressing HHD mice with optimized TERT-derived cryptic peptides protected them against tumor growth in vivo (Gross et al., 2004). Optimized cryptic peptides are, therefore, more promising than dominant peptides for tumor immunotherapy.

12:15 pm Lunch on Your Own (Lunch Workshop Sponsorship Available)

TARGETING T CELLS

1:40 Chairperson’s Remarks

1:45 Antigens Recognized by Cytolytic and Helper T Cells with Vaccine Potential for Cancer Patients
Dorothee Herlyn, D.V.M., D.Sc., Professor, The Wistar Institute

A melanoma and a colon cancer antigen recognized by cytolytic T lymphocytes (CTL) were cloned using the COS cell cDNA library expression approach and identified as RNA isopentyltransferase 1 (TRIT-1)-related protein and nucleophosmin (NPM, B23, nutrin), or N038, respectively. TRIT-1 has been described as a tumor suppressor in lung carcinoma. Nucleophosmin has oncogetic activity, is expressed by lymphomas and upregulated by colon carcinomas, hepatomas, bladder carcinomas, and melanomas. A melanoma antigen recognized by helper T (Th) cells was cloned using a novel phage display approach which offers several advantages over the previously used invarian chain fusion approach. The antigen was identified as ribosomal protein (RP) L8. RPL8 is expressed by melanomas, gliomas and breast carcinomas. Mutated Braf (V600E mutation) is a tumor-specific epitope expressed by approximately 70% of melanomas derived from different patients. Peptides of mutated BRAF induced CTL in melanoma patients’ lymphocytes. This study shows for the first time that TRIT-1-related protein, nucleophosmin, RPL8 and BAF-V600E are recognized by patients’ T cells. The antigens express numerous epitopes potentially associating with different class I and II human lymphocyte antigens (HLA) and therefore they may induce CTL and Th cells in patients expressing various HLA types. These antigens also have potential as vaccines for patients with tumors of various histological types.

2:15 Enhancing the Efficacy of Cancer Immunotherapeutics and Vaccines by Suppressing the Induction of Regulatory T Cells
Kingston Mills, Ph.D., Professor, Experimental Immunology and Head of Immunology, School of Biochemistry and Immunology, Trinity College Dublin

A major obstacle to the development of therapeutic vaccines against cancer is the immune suppressive environment of the growing tumor, including the induction of regulatory dendritic cells and T cells which suppress the development of protective effector T cell responses. This can be compounded by the use of TLR ligands as adjuvants or immunotherapeutics. A problem with TLR agonists that has not been fully appreciated is that they can generate suppressive as well as inflammatory responses in innate immune cells and can generate regulatory as well as effector T cells. This is part of a normal mechanism for limiting collateral damage during infection or sterile inflammation, but can constrain their ability to induce protective anti-tumor immunity in the immune suppressed environment of the tumor. However, the TLR-activated innate immune responses to selectively block the suppressive arm may hold the key to enhancing their efficacy as tumor immunotherapeutics and as adjuvants for cancer vaccines. (see 127.Conroy, Marshall and Mills, 2008, Oncogene, 27(2):168-80)

2:45 Technology Trends (Sponsorship Available)

3:15 Networking Refreshment Break (Sponsorship Available)
Cancer therapy is hindered, in part, by a lack of suitable target antigens. This is particularly relevant in tumors derived from mucosal tissues, in which antigens that are sufficiently immunogenic, tumor-restricted and shared among patients are lacking. We have explored a novel class of tumor-associated antigens fulfilling these criteria by exploiting immune compartmentalization, which restricts cross-talk between systemic and mucosal immune compartments. This compartmentalization limits systemic tolerance to mucosa-restricted self-antigens and shields mucosa from systemic autoimmune responses. Therefore, a novel paradigm suggests that targeting self-antigens expressed by normal mucosal tissues and by derivative neoplasms, should permit effective immunotherapy against systemic metastases, without inducing autoimmune in normal mucosa. We have recently explored targeting the first of these antigens, termed cancer mucosa antigens, in animal models of metastatic cancer (Snook et al, JNCI submitted). Viral vector vaccines were generated containing guanylyl cyclase C (GCC), expressed in normal intestinal epithelium and in all primary and metastatic human colorectal cancer (CRC) specimens. Immunization elicited CD8+ T cell responses in multiple strains of mice. Moreover, responses effectively prevented development of lung and liver CRC metastases and treated established lung CRC metastases. This occurred in the absence of autoimmunity against normal GCC-expressing intestinal tissue. These results suggest the utility of GCC-specific immunotherapy for gastrointestinal malignancies, as well as the potential for CMA-targeted immunotherapy for malignancies of other mucosal tissues and by derivative neoplasms, should permit effective immunotherapy against systemic CRC metastases. This occurred in the absence of autoimmunity against the target antigen as resides in the inoculum. The MVT promises to be the missing vaccination methodology for dealing with endogenous cancers.

5:00 Specific Lytic Antibody Production Against Myeloma Cell Associated CD38 Antigen by the Modified Vaccination Technique

Arpad Z. Barabas, Ph.D., Research Scientist, Surgery, University of Calgary

I have developed a new vaccination methodology called Modified Vaccination Technique (MVT) (patent pending). It is able to redirect the immune response outcome specifically without causing side effects. The method was utilized with 100% success to terminate an experimental autoimmune disease and with equal effectiveness to produce lytic antibodies against a CD38 bearing human myeloma cell line. The vaccine is composed of two components: a specific antigen against which a desired immune response is sought and a specific antibody against the target antigen. (In case of myeloma: CD38 antigen was combined with specific antibody directed against CD38 antigen at slight antigen excess). Injection of the immune complex into animals produced the same class of antibody with the same specificity against the target antigen as resident in the inoculum. The MVT promises to be the missing vaccination methodology for dealing with endogenous antigen induced disorders such as cancer.

5:30 Happy Hour in the Exhibit Hall

6:30 End of Day One
11:45  Overcoming Challenges in Manufacturing and Commercializing an HSP-based Autologous Cancer Immunotherapeutic  
Stephen Monks, Ph.D., Vice President of Manufacturing, Process & Analytical Technologies,  
Antigenics

Oncophage (vitespen) is a novel, patient-specific, autologous immunotherapeutic that has been  
evaluated clinically in a number of cancer indications. It is a peptide-heat shock protein complex  
that when administered intradermally, delivers tumor-specific antigens to antigen-presenting cells,  
leading to the stimulation of powerful T cell-mediated antitumor immune responses. Following  
surgery, frozen tumor is shipped to Antigenics, where Oncophage is prepared individually for  
each patient by a rapid small-scale purification process. Product quality is ensured by application  
of release assays focusing on key biochemical and biological attributes of the molecule. These  
assays allow the resulting non-renewable vaccine to be released in a timeframe suitable for  
patients to begin immunotherapy. The challenges inherent in the manufacture, logistics and  
release of an autologous product, along with the various developmental & regulatory hurdles facing  
this unique therapy, will be presented.

12:15pm  Lunch on Your Own (Lunch Workshop Sponsorship Available)

PLENARY SESSION – FOCUS ON ADJUVANTS

1:40  Chairperson’s Remarks  
William Egan, Ph.D., Executive Director, PharmaNet Consulting

1:50  Plenary Keynote Presentation  
A CBER Perspective on the Use of Novel Adjuvants in Vaccines: Challenges and Opportunities  
Norman W. Baylor, Ph.D., Director, Office of Vaccine, CBER, FDA

2:30  KEYNOTE PRESENTATION  
Unique Vaccine Adjuvant Efficacy of Toll-like Receptor 8 (TLR8) Agonists that Activate Human Antigen-Presenting Cell  
Ofer Levy, M.D., Ph.D., Staff Physician, Infectious Diseases and Principal Investigator, Harvard Medical School/Children’s Hospital Boston

Activation of antigen-presenting cells is a key feature of effective vaccine adjuvants. Our group  
has discovered that uniquely among the many TLR agonists, a novel family of compounds called  
imidazolquinolines that activate cells via TLR8 can effectively activate antigen-presenting cells  
from human newborn cord blood, inducing production of Th1-polarizing cytokines (TNF, IL12) and  
upregulation of co-stimulatory molecules (CD40). These observations suggest that these agents  
may have unique vaccine adjuvant activity in infants and newborns.

3:00  FEATURED PRESENTATION  
CpG TLR9 Agonists as Adjuvants for Prophylactic and Therapeutic Vaccines  
Heather Davis, Ph.D., Senior Vice President, Vaccines Research Site Head, Ottawa Research Laboratories, Coyle Pharmaceutical Group, a Pfizer company

Oligodeoxynucleotides containing CpG motifs are activate innate immunity through Toll-like Receptor 9 (TLR9), and when combined with antigens act as potent adjuvants to augment both humoral  
and cell-mediated responses. This talk will review animal and human clinical data testing CpG ODN with a  
variety of antigens.

3:30  Artificial Cells Derived from Biodegradable Materials that Boost the Immune Response  
Tarek Fahmy, Ph.D., Assistant Professor, Biomedical Engineering, Yale University

While dendritic cells (DCs) are the most potent professional antigen-presenting cells,  
their widespread utility in therapeutic approaches involving ex vivo stimulation of T lymphocytes is  
hindered by several practical factors such as generation of autologous DCs, labor and isolation and  
preparation for clinical applications. Thus, artificial antigen-presenting cells (aAPCs) have been proposed  
and tested in the expansion of a number of specific T cells  
for the treatment of a variety of disease states. Here we have developed a novel physiologically compatible  
system of “cell-like” particles for ex vivo and in vivo T cell stimulation using biodegradable polymers.  
Our approach fabricates FDA approved polymers into particles presenting T cell antigens, thus providing the  
multivalent interactions necessary for efficient stimulation of T cells. A key feature of this technology is the  
ability to co-encapsulate cytokines and program their release during and after activation and in a sustained  
fashion, facilitating long-term bioavailability and efficient stimulation of lymphocytes.

4:00  Refreshment Break in the Exhibit Hall

4:45  From “Alchemy” to Agonists of the Innate Immune System - Features and Applications of the Next Generation Vaccine Adjuvants  
Benjamin Wizel, Ph.D., Head, Preclinical R&D, Intercell AG

Several decades ago, adjuvants have entered the vaccine arena in order to facilitate the  
built-up of protective immunity by vaccines. Up till now only a few adjuvants have been formulated into  
registered vaccine products; mostly the salts of aluminum. The mode of action of the existing adjuvants is not  
well understood. Aside of their protection of the antigens against degradation and depot formation at the  
injection site, it’s very little known, how they kick off the immune cascade. The discovery of the Toll-like receptors  
on the surface of dendritic cells that are able to binding to so-called Pathogen Associated Molecular Signals, PAMS,  
has opened a new target to design specific adjuvants that not only induce antibodies, but also cellular immunity,  
thereby broadening the specificity and the quantity of immune responses towards vaccine antigens. At Intercell,  
we have developed a novel adjuvant, IC31, comprising an antibacterial peptide and a Toll-like 9 agonist that is mixed together with the vaccine antigens. I will discuss in my presentation profile and mode of action of IC31 and the promising  
results obtained when the adjuvant was tested in a variety preclinical and clinical settings.

5:15  The Use of SCV-07, a Novel Immune-Stimulating Diptide, as an Enhancer for Vaccines  
Cynthia Tuthill, Ph.D., Senior Vice President and Chief Scientific Officer, SciClone Pharmaceuticals

SCV-07, or y-D-glutamyl-L-tryptophan, is being evaluated for therapeutic use in a number  
of immune-compromised conditions, including hepatitis C, mucositis, and certain cancers. The immune- 
stimulating effects of SCV-07 treatment, including polarization of the immune response towards the Th1 profile,  
suggest that SCV-07 could also be useful for enhancement of responses to certain vaccines. This talk will  
focus on recent data from animal models which have demonstrated improved responses to various vaccines,  
including those for influenza, tuberculosis, and breast cancer.

5:45  Nanoemulsion-Based Vaccines are Safe Adjuvants that Deliver Antigens to Mucosal Surfaces  
Joyce Sutcliffe, Ph.D., Vice President, Research, NanoBio Corporation

Nanoemulsion-based vaccines employ oil-in-water emulsions composed of nanodroplets  
with an average diameter of 400 nm. The nanodroplets can inactivate whole viruses or  
bacteria, incorporating native-like antigenic components into their structure. Alternatively, purified  
antigens can be mixed with the nanoemulsion adjuvant for delivery to mucosal surfaces. The  
composition and particle size of the nanodroplets are designed for preferential uptake by dendritic cells.  
Antigen processing triggers maturation of the dendritic cells and trafficking to secondary lymphoid  
tissues. A robust response to nanoemulsion-based vaccines has been shown for multiple antigens  
and intranasal administration of these vaccines in several animal models has occurred without signs  
of toxicity to the mucosal structure or local irritation.

6:00  Close of “Advances in Cancer Vaccines” meeting

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Enjoy face to face networking with 200+ qualified delegates. Showcase your latest technology or solution and get feedback for senior level scientists and executives.

For more information, please contact
Suzanne Carroll – Manager, Business Development at
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Discounted Room Rate: $199 s/d
Reduced Room Rate Cut-off Date: July 14, 2008

To book your room online, please visit our web site and click on the hotel and travel page, or you may call the hotel directly. Identify yourself as a Cambridge Healthtech Institute conference attendee to receive the reduced room rate. Reservations made after the cut-off date or after the group room block has been filled (whichever comes first) will be accepted on a space-and-rate-availability basis. Rooms are limited, so please book early.

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ADVANCES IN CANCER VACCINES

August 13-14, 2008 • Royal Sonesta Hotel • Cambridge, Massachusetts

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Main Conference Access (August 13 – 15)
Includes access to Novel Vaccines, Advances In Cancer Vaccines, and Clinical Risk Management & Safety For Vaccines.

Please choose which track will be your primary track:

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☑️ $50 Off

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Request a refund minus the cost ($300) of ordering a copy of the CD.

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