

7: Vaccines in Immunology: New Insights and Development

Session Chair

Robert L. Elliott

Burdine Breast Foundation, USA

Session Introduction

Title: Adjuvant breast cancer vaccine improves disease free survival of breast cancer patients with depressed lymphocyte immunity

Robert L. Elliott, Burdine Breast Foundation, USA



Title: Novel vaccination strategies for the delivery of HIV moieties

Toufic Nashar, Tuskegee University, USA



Title: Didecameric keyhole limpet hemocyanin is potent in promoting antigen cross-presentation and inducing antigen-specific cytotoxic T cell activation

Shuguang Bi, University of California, USA



Title: High immunogenic activity of GX301, a telomerase-based, multi-peptide, multi-adjuvant cancer vaccine

Gilberto Filaci, University of Genoa, Italy



Title: Photodynamically inactivated Leishmania as a potential novel carrier for vaccine delivery against infectious and non-infectious diseases

Kwang Poo Chang, Rosalind Franklin University, USA



Title: Vaccines in immunology

Onodu Winifred Uzoamaka, Ministry Of Health Enugu, Nigeria



Adjuvant breast cancer vaccine improves disease free survival of breast cancer patients with depressed lymphocyte immunity

Robert L. Elliott

Burdine Breast Foundation, USA

Breast cancer patients were vaccinated in the adjuvant setting with an autologous, allogeneic whole cell vaccine to evaluate the effect on host lymphocyte immunity and disease free survival. We began preparing whole cell preparations for a vaccine study in 1995. Stage I and II breast cancer patients had host lymphocyte immunity against tumors associated antigens evaluated before and after treatment. Those patients with depressed immunity after therapy determined by a lymphocyte blastogenesis assay (LBA) were offered the whole cell vaccine. Patients were given six intradermal injections (three weekly followed by three monthly). Ten weeks after the last injection the LBA was repeated. Thirty-seven patients were vaccinated in the adjuvant setting with the whole cell autologous, allogeneic vaccine. There were no severe toxicities and the vaccine was well tolerated. Some patients experienced slight pain and swelling at the injection site. There has been a seventeen year follow-up for all vaccinated patients. The survival data of the vaccinated patients with depressed immunity, compared to historic controls of unvaccinated patients with normal and depressed immunity to their tumor associated antigens, strongly suggest an overall improvement in survival of vaccinated patients. This study confirms the importance of maintaining good host lymphocyte immunity after completion of standard therapy and validates the value of cancer immunotherapy especially in the adjuvant setting.

Biography

Elliott completed his M.D. from University of Mississippi and completed an integrated Gen & Thoracic surgery residency. He had a fellowship in anatomy, cell biology, and electron microscopy at Washington University School of Medicine, St. Louis, MO. He has been director of Breast Center for 39 years, and has published many papers and made many presentations at international meetings and societies.

relliott@eehbrestca.com

Novel vaccination strategies for the delivery of HIV moieties

Toufic Nashar
Tuskegee University, USA

HIV infection poses tremendous challenges to the efforts of designing vaccination strategies. Important confounding issues are rapid replication of the virus in the gut, viral load, destruction of helper T cells, and integration of viral nucleic acid into host DNA. To address the complexity of HIV infection, a state of “high readiness” in the host should be adopted to prevent or reduce the impact of viral infection. The latter may be fulfilled by the use of live attenuated recombinant viral or bacterial vectors in conjunction with strong recombinant protein adjuvants, as platforms for the delivery of HIV moieties. Live attenuated coxsackievirus B4 (CVB4) expressing a partial HIV gag p24 protein sequence induced high p-24-specific T helper and T cytotoxic immune responses after oral and intra-peritoneal delivery of CVB4/p24. Co-administration of a class of bacterial proteins shown to have strong immunomodulatory effects on antigen presenting cells and T cells, resulted in apparent enhancement of the cytotoxic T cell response. It is proposed that recombinant forms of these proteins expressing HIV epitopes would be good adjuvant platforms in conjunction with live attenuated recombinant vectors.

Biography

Toufic Nashar has completed his Ph.D from University of Bristol, U.K. and postdoctoral studies at University of Bristol and University of Kent, UK, and Albany Medical College, NY, US. He held the post of Research Affiliate at Wadsworth Research Center, NY, US. He is currently Assistant Professor Immunology/Virology at Tuskegee University, Alabama. He has more than 19 publications including peer-reviewed articles in reputed journals, review articles and book chapters. His research work has focused on immune modulation for vaccine development against viral and bacterial diseases.

tnashar@mytu.tuskegee.edu

Didecameric keyhole limpet hemocyanin is potent in promoting antigen cross-presentation and inducing antigen-specific cytotoxic T cell activation

Shuguang Bi

University of California, USA

Activation of antigen-specific cytotoxic T cells is an essential component of the cellular immune responses that must be induced for therapeutic vaccines against cancers to be effective. Antigen cross-presentation is required for the activation of tumor antigen-specific cytotoxic T cells. Here we report that keyhole limpet hemocyanin (KLH) in its didecameric form is a potent promoter of antigen cross-presentation and the subsequent induction of antigen-specific cytotoxic T cell activation. KLH is a well-established immune stimulant, hapten carrier and vaccine adjuvant with a 50-year record of safety in humans. The KLH protein is extensively glycosylated, existing in its native form as an 8 MDa cylindrical didecamer of 400 KDa subunits. Using ovalbumin as a model antigen, a murine immature dendritic cell line and a murine cytotoxic T cell hybridoma cell line that can be activated specifically by ovalbumin antigen presented by the MHC I molecules on dendritic cells, we found that KLH didecamers promoted antigen cross-presentation and induced antigen-specific cytotoxic T cell activation. In marked contrast, KLH dimers failed to elicit these activities. We also found that KLH didecamers that had lost specific glycosyl moieties during purification or storage lost their ability to promote antigen cross-presentation and could not induce antigen-specific cytotoxic T cell activation. Analyses with endocytosis inhibitors suggest that exposure to intact KLH didecamers may change the pathways of dendritic cell antigen uptake, thereby promoting antigen cross-presentation. Our data thus suggest that intact and fully glycosylated KLH didecamers can serve as a safe and effective adjuvant for vaccines against cancers.

Biography

Shuguang Bi completed his Ph.D in biochemistry from Georgetown University in 2004. He Angeles and University has been doing research on immunology and cancer vaccine in University of California at Los of California at Santa Barbara ever since graduation. He has published more than a dozen papers in reputed journals, including PNAS, JBC and Glycobiology.

shuguang.bi@lifesci.ucsb.edu

High immunogenic activity of GX301, a telomerase-based, multi-peptide, multi-adjuvant cancer vaccine

Gilberto Filaci

University of Genoa, Italy

Vaccination against cancer is a new frontier of oncological treatment but issues related to the weak immunogenicity of tumor antigens hamper its efficacy. In particular, peptide vaccines, although safe, have problems related to HLA restriction and rapid clearance. To overcome these issues, we set a telomerase-based vaccine constituted by four different peptides and two adjuvants. The peptides are promiscuous and able to bind to both HLA class I and class II molecules. The adjuvants, Montanide ISA-51 and Imiquimod, induce efficient innate immune responses strongly activating antigen presenting cells. Moreover, Montanide produces a water-in-oil emulsion with the peptide solution that protects against protease clearance and favors uptake by phagocytes. Overall, this new vaccine is theoretically able to induce telomerase-specific immune responses encompassing the physiological route of immune activation involving both innate and adoptive circuits as well as both Th and CTL lymphocytes. Safety and efficacy of GX301 were tested in a phase I/II clinical trial enrolling stage IV prostate and renal cancer patients resistant to conventional therapies. No grade 3-4 adverse effects were observed. Importantly, 100% of patients showed evidences of efficient immunization against telomerase. Although performed in a very advanced cancer patient population, clinical evaluation showed disease stabilization in 4 cases, as well as prolonged overall survival and progression free survival in patients (8/14) showing a full pattern of vaccine-specific immunological responses. In conclusion, the adoption of a multi-peptide, multi-adjuvant strategy seems to be effective in inducing efficient immune responses against potentially weak immunogenic antigens such as self-tumor antigens.

Biography

Dott. Filaci has a degree in Medicine and a PhD in Experimental Hematology. He is Associate Professor of Internal Medicine at the University of Genoa, Italy. He is the director of the Clinical and Experimental Immunology Operative Unit of the Centre of Excellence for Biomedical Research. He has published more than 65 papers in peer-reviewed journals. He is member of CIS and FOCIS, and served as reviewer for several international journals.

gfilaci@unige.it

Photodynamically inactivated *Leishmania* as a potential novel carrier for vaccine delivery against infectious and non-infectious diseases

Kwang Poo Chang

Rosalind Franklin University, USA

Leishmania are parasitic protozoa, including those, which cause self-limiting and self-healing simple cutaneous leishmaniasis. These parasites can be photodynamically rendered nonviable, but infection-competent for exploitation as an universal vaccine carrier because they are innately endowed with the following exceptionally favorable attributes: [1] Vaccine adjuvanticity, as indicated by the lasting cell-mediated immunity observed after spontaneous cure in human cutaneous leishmaniasis; [2] Large capacity to express multiple vaccines with post-translational modifications by well-established simple transgenic approaches; [3] Tight protection of the vaccine loads due to their naturally acquired resistance to humoral lytic factors in the mammalian hosts; [4] Homing specificity to the desirable site in the very cells for vaccine processing and presentation, i. e. the phagolysosome of the antigen-presenting cells (macrophages and dendritic cells). This combination of advantages compares *Leishmania* favorably against viral, bacterial and particulate constructs to serve as a vaccine carrier. Our research objective is to safely harness the above-mentioned attributes of *Leishmania* for homing vaccines to antigen-presenting cells, thereby enhancing their immune efficacy. *Leishmania* are genetically and chemically modified to facilitate their endogenous induction and exogenous loading with photosensitizers, i. e. porphyrins and novel phthalocyanines, thereby rendering them photosensitive to produce ROS for cytolysis to release vaccines in the ROS-resistant phagolysosomes of antigen-presenting cells. Our current efforts are focused on safety/efficacy evaluation of the available constructs and their optimization *in vitro* and *in vivo* by using ovalbumin as a surrogate vaccine. We plan to optimize the *Leishmania* carrier for photodynamic immuno-therapy and -prophylaxis against infectious and non-infectious diseases.

Biography

Kwang Poo Chang has completed his PhD in his twentieth from a Canadian University and postdoctoral studies from the Rockefeller University. He rose to the position of Associate Professor at Rockefeller University and has been a Professor of Microbiology/Immunology, Chicago Medical School since 1983. He has engaged in basic and translational laboratory research of *Leishmania* and leishmaniasis for >35 years through the support by >20 grant awards from NIH, NSF, WHO, AHA, private Foundations and other sources. He has published >120 papers in reputed journals, served as an editorial board member in 9 different journals and edited/co-edited 4 books/symposium volumes.

KwangPoo.Chang@rosalindfranklin.edu

Vaccines in immunology

Onodu Winifred Uzoamaka
Ministry Of Health Enugu, Nigeria

Vaccines represent one of the greatest triumphs of modern medicine. Since the first mass vaccination against smallpox and its eventual eradication, many more vaccines have been developed based on advances in bacteriology and virology and the use of attenuated live or killed whole pathogens. Immunological discoveries have allowed the development of more refined anti-toxin and conjugate vaccines, while biotechnology provided the tools for rationally designed and genetically engineered vaccines.

Many challenges remain in developing safer and more effective vaccines against the more complex diseases such as rotavirus diarrhoea, pneumococcal disease, tuberculosis and HIV-AIDS, and for the rapid protection against newly emerging pathogens or pathogen strains. These vaccines are likely to require the isolation of the "protective" antigenic molecules from the whole pathogen, as well as ways to deliver these to induce effective immune responses with minimal side effects. It has long been recognized that most antigens require the addition of an adjuvant that triggers the innate immune system and boosts an immune response.

Recent immunological breakthroughs have uncovered that the innate immune system has a much higher degree of complexity than previously thought and can be activated along a wide range of different pathways, depending on the engagement of different innate immune receptors. This in turn determines the type of immune response that will be generated against the vaccine antigens or pathogens. Harvesting the complexity and exquisite specificity of this innate immune system has inspired a new direction in vaccine research, towards the generation of novel adjuvant formulations, tailored to induce defined immune responses effective against specific pathogens. This paper seeks to highlight new insights and development in vaccine research and development against infectious diseases.

Biography

Winifred has Masters Degree in Nursing at the age of 30 years at University of Nigeria Nsukka. Currently the State coordinator of Safe Motherhood at Department of Public Health, Ministry of Health Enugu, Enugu State- Nigeria. I have presented papers in more than five International conferences with about 15 published articles/papers in reputable journal.

delegatesgov@gmail.com