DNA VACCINES 2004
THE GENE VACCINE CONFERENCE

ANTI-IDIOTYPIC CDR3 VACCINATION AGAINST CHRONIC B-CELL LYMPHOMA: CRITICAL COMPONENTS OF A DNA VACCINES AGAINST A TUMOR ANTIGEN

M. Rinaldi[1], E. Signori[1,2], S. Iurescia[1,3], D. Fioretti[1,3], S. Calì[4], G. Volpe[5], C. Casnici[6], P. Pierimarchi[1], O. Marelli[6], G. Saglio[5], G. Tonon[4] and V.M. Fazio[1,2,3]

[1]Institute of Neurobiology and Molecular Medicine, Molecular Medicine Section, CNR, Rome, Italy; [2]CIR, Section of Molecular Medicine and Biotechnology, University "Campus Bio-Medico", Rome, Italy; [3]Laboratory for Gene Therapy and Oncology, IRCCS H. "Casa Sollievo della Sofferenza", San Giovanni Rotondo (FG), Italy; [4]Department of Biotechnology, Keryos S.p.A., San Donato Milanese, Milan, Italy; [5]Department of Clinical and Biological Sciences of the University of Turin, San Luigi Hospital, Orbassano-Turin, Italy; [6]Department of Pharmacology, Chemotherapy and Medical Tossicology, University of Milan, Italy

B-cell lymphomas express tumor-specific immunoglobulin, the variable regions of which [idiotype (Id)] can be regarded as tumor-specific antigens and targets for vaccine immunotherapy. Promising results have been obtained in clinical studies of Id vaccination using Id proteins or naked DNA Id vaccines. Several reports have indicated that the immunodominant epitopes of the clone-specific Ig lie mainly in the CDR3. Our group has previously demonstrated the possibility of using the short peptide encompassing the CDR3 of immunoglobulin heavy chain (VH-CDR3) as a target for eliciting a tumor specific immune response via DNA-based vaccination. DNA immunization of outbred mice with different patient-derived VH-CDR3 peptides elicited antibodies able to recognize native antigens on individual patient's tumor cells. Therefore, we evaluated the humoral and cellular immune response recruited by VL-CDR3-directed DNA vaccines using the murine 38C13 B-cell lymphoma tumor as a model system. The nucleic acid sequence of the idiotypic IgM (38C-Id) light chain was analyzed and the region corresponding to the CDR3 sequence was chosen for the production of a synthetic mini-gene. A high-level expression bicistronic plasmid DNA vaccine was designed to express both the short VL-CDR3 and the mouse IL-2 sequences. IL-2 was chosen as immunomodulating cytokine to enhance T cell-mediated immune response, to improve antigen-specific T cell proliferation, differentiation and Ig secretion of antigen-activated B cells. Vaccination of syngenic C3H/HeN mice with the described plasmid DNA vaccine was found to generate an immune response to the 38C13 tumor, inducing both specific circulating antibodies and specific cytotoxic T-cell (CTL) activity. In view of these findings, we have recently explored multiple complementary strategies to enhance the potency of a CDR3-based DNA vaccine, in term of efficient in vivo antigen expression, presentation and immunogenicity. To increase plasmid DNA vaccine delivery and expression, thus improving the antigen dose achievable *in vivo*, the new DNA constructs were improved by inclusion of a DNA nuclear targeting sequence (NTS) and were delivered by *in vivo* electroporation and hyaluronidase pre-treatment. By using a computer algorithm, one epitope within murine 38C13 B-cell lymphoma heavy-chain variable region was selected and "enhanced". A restricted pathogen-derived sequence was fused to the tumor antigen sequence to create a DNA fusion vaccine, or, alternatively, was fused to the tumor antigen sequence via the amino acid linker Ala-Ala-Tyr as a spacer. Here we show that intramuscular vaccination with CDR3-based DNA vaccines using *in vivo* electroporation protects vaccinated mice against a lethal tumor challenge.

CONFERENCE PROGRAM

DNA Vaccines 2004
The Gene Vaccine Conference
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Advisory Scientific Panel

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Freda Stevenson (Tenovus Laboratory, Southampton, UK)

DNA VACCINES 2004 is the follow-up meeting to the successful *DNA VACCINES 2002* conference held in Edinburgh in October 2002.

From an unproven novelty with limited acceptance in the community, DNA or 'Genetic' vaccines have arrived as a potent means of providing immune responses or protective immunity against viruses, bacteria and parasites in many species from fish to primates, including human volunteers. DNA vaccines, comprising plasmid DNA encoding proteins from pathogens, allergens, and tumours, are being evaluated as prophylactic vaccines and therapeutic treatments for infectious diseases, allergies and cancer. Plasmids encoding normal human proteins are likewise being tested as vaccines and treatments for autoimmune diseases.

DNA vaccination has become an accepted method in the research community with human trials now in process. The use of DNA as a means of vaccination offers potential benefits in protective efficacy, cross-strain applicability, development speed and manufacturing cost compared with conventional vaccines. DNA vaccines are known to be particularly effective in inducing killer T-cell responses which are an important ingredient in fighting infections.

DNA VACCINES 2004 will follow-up the success of the 2002 Edinburgh meeting in attracting delegates from the cancer and the infectious disease communities to come together to discuss the 'common ground' between these two major groups.

DNA VACCINES 2004 will again be major opportunity for leading researchers to gather and report on the latest cutting edge research currently being undertaken in the progressive field of DNA or Genetic Vaccines.

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