Targeting Gene Therapy - A Reality?

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Layout and Goals
Sessions:
I. Cancer Gene Therapy – I
II. Cancer Gene Therapy – II
III. Cancer Immunotherapy
IV. Targeting and Vectors

Everyone has heard of gene therapy, this is going to revolutionize medicine and bring untold benefits to us all. This is the message we read in the press, but what is the truth? Has any gene therapy trial in patients with cancer produced a single response? The data is not very impressive in 1998, but a great deal of work remains and it is very early days. The ideas behind the majority of gene therapies are developed by scientists, and applied by clinicians. A Forum to bring together the believers and the non-believers in the future of gene therapy should allow a full and frank discourse between these parties and hopefully lead to the instigation of trials which can resolve some of the pertinent issues. In addition, the Forum should serve as an ideal opportunity for scientist and clinician to review the problems each encounters in developing novel strategies based on gene therapy. An appreciation of the problems encountered by each group should speed the development of effective trials. The annual Forum is an ideal environment for such interchanges.
Outcome Report

This was a very exciting and stimulating meeting devoted to basic and clinical research advances in gene therapy for the treatment of cancer. Despite the recent unfortunate death due to gene therapy (of a patient without cancer) that has been widely discussed in the lay press the Forbeck meeting gave a very useful perspective on the current state of the art of this field. From the results presented at this meeting it is possible to estimate that around 1,000 people in the world with cancer have received some form of gene therapy. We can also conservatively estimate that 5-15% of these people have derived some benefit from this therapy. A likely guess is that around 10 people have died possibly related to gene therapy (1% rate) and tests of other new therapies often have mortality rates of 5-10%. While we obviously don’t want anyone harmed by gene therapy, these estimates tell us gene therapy is well within the range for possible benefits and side effects encountered in the development of other types of new cancer therapies. Many different tumor types are being tested and these trials are mainly occurring in adults with children’s trials to come later.

A variety of approaches were discussed. One is to replace the damaged gene (much like fixing the brakes on one’s car). Amazingly we learned you only need to do this in some cells. There is a ‘bystander’ effect where getting the gene into some tumor cells leads to the death of surrounding tumor cells. Also discussed were ways to target genes to tumors and to put genes into tumors to make them more sensitive to standard therapies such as chemotherapy and radiotherapy. There was discussion of putting genes for drug resistance into bone marrow stem cells to allow us to give more chemotherapy. Gene therapy is also being used to stimulate an immune response against cancer cells. This includes making tumors more immunogenic, and also genetically ‘fix’ or engineer killer T cells to more efficiently kill tumor cells. Finally, genetic vaccination with a patient’s own tumor antigen encoded in DNA was presented as an exciting new approach to tumor immunotherapy.

In all of these presentations we realize that ultimately we need to use standard clinical endpoints such as time to progression, survival and the relief of symptoms to monitor the effectiveness of gene therapy. We need to develop collaborations with industry and avoid conflicts of interest in the finances and reporting of the gene therapy results. Most importantly, we as scientists and physicians need to educate both individual patients and their families about the realistic benefits of gene therapy trials, and also the general public, media, congress, political leaders, and patient advocates about this work. It is essential to have truthful, open discussion as was exemplified by the outstanding discussion and new ideas that came out of this year’s Forbeck Symposium on Cancer Gene Therapy.

Quotes from Participants

“Best scientific meeting in gene therapy I have ever attended ... perhaps the ideal format for an in-depth scientific meeting.”
- Robert Martuza, MD, Georgetown University Medical Center, Washington, DC

“I am very grateful for the opportunity to participate in the Gene Therapy forum. Both professionally and socially this was an exceptional experience. You can only suspect how effective this forum was, in large part due to the unusual format used.”
- Eli Gilboa, Ph.D., Duke University Medical Center, Durham, NC
“This was a thoroughly enjoyable meeting in a delightful environment. The amount of discussion during presentations and during ‘off time’ promotes identification of novel approaches to ‘old’ problems.”
- Phil Greenburg, University of Washington, Seattle, WA

“The intimate gathering of exceptional scientists is unparalleled. It is like the ultimate in high powered journal clubs. I will be establishing collaboration; I already have a commitment to receive reagents for testing. Also, I had a number of new ideas of how to redirect my research.”
- Tim Cripe, MD, Scientific Guest