

IS IT SAFE?

This year a section of NHF's 5th Gene Therapy Workshop was devoted specifically to safety considerations. Specific safety concerns have surfaced in two ongoing clinical trials.

the Genstar trial was put on temporary hold after the first treated patient exhibited an immune response to therapy. The degree to which an individual reacts to the virus appears to be somewhat unpredictable, commented Dr. James Wilson of the Institute for Human Gene Therapy and the University of Pennsylvania. While one subject may handle the vector without concern, another may respond severely. This was the case in the gene therapy study two years ago where a young subject died following treatment with a vector for a metabolic disease.

Dr. Mark Sands of Washington University School of Medicine works with adeno-associated virus (AAV)—the vector being used in the Avigen trial—to study lysosomal storage disease. Using mice as a model, Dr. Sands was able to correct the gene defect. However, six of eight animals developed cancerous tumors during the study. Mark Kay of Stanford University was quite concerned when he first heard the revelation, considering his group places much faith in AAV.

When Sands' group reported the results, the Food and Drug Administration (FDA) asked Kay's lab and an additional lab to analyze tissue from the tumors to determine if the foreign genetic material had entered the mouse DNA and possibly turned on a cancer gene. Both Kay's lab and the other group produced identical results in that neither was able to find evidence

of vector DNA in the mouse chromosome. While this doesn't eliminate all possible ways that a genetic vector could cause cancer, it does rule out one of the potential mechanisms. Since AAV has been used extensively by a number of groups and these tumors have never surfaced before, Kay believes that it is unlikely AAV will be implicated in the end.



Mark Kay



Communication between scientists, regulatory agencies and the public is important. It improves the research performed and facilitates the development of a safer treatment. Amy Patterson of the National Institutes of Health (NIH) discussed the advances NIH has made in collaboration with FDA, namely developing a single system for reporting severe side effects caused by a treatment during a clinical trial. (Prior to this, those conducting a study had to make a separate report to each agency.) With a touch of humor, Patterson commented, "The thought that two government agencies might have the same set of guidelines on a single issue is nothing short of a miracle."

Individuals from NHF's Board of Directors shared their views and reactions to the research, yet the same struggle surfaces each year—the desire to embrace the advances while pointing out the drawbacks. "I would be very cautious at this point," Kevin Kelley stated. "We need to be bold and think big, but at the same time safety is a major concern." 🧑🏻‍⚖️

For more information on taking part in a clinical trial, log on to ww.hemophilia.org.

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