

POINTS TO CONSIDER

NON-TECHNICAL ABSTRACT

A number of genes code for proteins, such as interleukin-2 (IL-2) that help to activate the immune system. If these genes are put into tumor cells, they cause the malignant cell to stimulate an immune response to the tumor as a whole. In mouse models, this effect helps slow down tumor growth and may even get rid of the tumor. We have been testing this approach in patients with relapsed neuroblastoma, a common childhood tumor, by giving them tumor cells containing the IL-2 gene. Although the results have shown that this treatment can help the patients make an immune response against the tumor, we have had difficulties in putting the gene into the tumor cells. This has hampered our evaluation of the clinical value of the technique. The reason for our problem is that we have been using retroviral vectors to insert the IL-2 gene. This only works if the tumor cells grow in culture; most neuroblastoma cells do not. We now propose to substitute a different type of gene transfer vector, derived from an adenovirus. A related vector has been employed in previous human gene therapy studies. The adenovirus vector efficiently transfers the IL-2 gene into freshly isolated tumor cells. By this change in technique, therefore, we should be able to treat a higher proportion of eligible patients and more rapidly learn whether this approach is worthy of further pursuit.