

POINTS TO CONSIDER

SCIENTIFIC ABSTRACT

Many different murine tumors including, the C1300 neuroblastoma line, may be rendered immunogenic by transfer of genes encoding cytokines such as interleukin-2 (IL-2). The immune response generated often destroys unmodified (parental) tumor cells, thereby delaying tumor growth and even eradicating pre-existing tumors.

For the past three years, we have been treating children with relapsed neuroblastoma in a Phase I study. The children receive subcutaneous injections of autologous or partially HLA matched allogeneic tumor cells transduced with a retroviral vector encoding IL-2. Eight patients have been treated, and both local and systemic immune responses have been observed, including a rise in the activities of NK and cytotoxic T cells and the development of eosinophilia. Although these results are encouraging, we have been hampered by problems in generating neuroblastoma cell lines in a timely fashion, and by the low efficiency of retroviral transduction. We are now proposing an amendment to the protocol in which an adenovirus IL-2 vector is used to transduce freshly isolated primary tumor cells. We propose to use the same vector backbone as in recent cystic fibrosis protocols, but to perform the gene transfer *ex vivo*. We can consistently transduce fresh neuroblastoma cells, and obtain sufficient IL-2 to produce the same immunomodulatory changes *ex vivo* that are detected when retroviral vectors are used to transduce established neuroblastoma cell lines. Other than the change in vector, therefore, this protocol is identical to that used for our current neuroblastoma IL-2 gene therapy trial.