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Dr. Esther H. Chang currently serves as a Professor in the Departments of Oncology and Otolaryngology at Georgetown University Medical Center, and a Consultant Professor in the Department of Surgery at Stanford University. Before joining Georgetown University, Dr. Chang held positions as a cancer expert for the National Cancer Institute, as a Professor in the Departments of Pathology and Surgery at the Uniformed Services University of the Health Sciences, and as a Professor in the Department of Surgery at Stanford University. Dr. Chang's research effort focuses primarily on the molecular mechanisms of carcinogenesis. Dr. Chang's contributions are evident in her 100-plus publications and her current and past appointments to a number of scientific advisory boards for the National Cancer Institute, NASA, and the Department of Energy. Her scientific findings have been published in prominent journals including *Nature, Science, Cell, Cancer Research, PNAS, J. Virology*, and *J. Biological Chemistry.*

Systemic Delivery of Tumor-Targeted p53 Gene Therapy Results in Chemo/Radiosensitization

Loss of normal p53 function has been associated with resistance to both chemotherapy and radiotherapy. Introduction of wild-type (wt) p53 by means of adenoviral vectors has been shown to inhibit, both in vitro and in mouse xenograft models, the growth of various types of tumors. We have shown that restoration of wt p53 led to sensitization of an otherwise radiation-resistant squamous cell carcinoma of the head and neck (SCCHN) to radiation. In the mouse xenograft model, the combination of wt p53 restoration and radiation treatment resulted in complete elimination of the tumors.

A ligand-liposome system was optimized in our laboratory to deliver the wt p53 gene efficiently, both in vitro and in vivo. The ability of the introduced wt p53 to sensitize the transfected SCCHN cells to ionizing radiation was demonstrated in vitro. We also demonstrated that, in vivo when the ligand-liposome encapsulated wt p53 was injected I.V., preexisting SCCHN and prostate cancer xenografts completely regressed after radiotherapy. In addition, we observed chemosensitization mediated by wt p53 replacement in SCCHN, breast cancer, and prostate cancer cells both in vitro and in vivo. More recently, in a metastatic mouse melanoma model, B_{16}/F_{10}, we have observed elimination of the lung metastases, when the targeted wt p53 liposomes were systemically delivered in combination with cisplatin. Tail vein injection, as well as intratumoral injection, of the ligand-liposomes with a reporter gene in nude mice bearing human breast cancer or SCCHN xenografts, resulted in a significantly higher percentage of transfected tumor cells when compared with those injected with liposome-DNA or plasmid alone. This new gene delivery system is relatively tumor-specific since we found that the cells in organs such as liver, lung, muscle, bone marrow, and intestinal crypts were not transfected. These results indicate that the combination of wt p53 gene replacement, mediated by the tumor-specific, liposome-based systemic delivery in combination, with conventional ionizing radiation or chemotherapy may provide more effective cancer treatment modalities.