

MI-1. Scientific Abstract. Colorectal cancer is one of the leading causes of cancer deaths in the United States. The major problem is metastatic disease, with liver being the primary site of the metastases. The protocol is designed to determine the toxicity and biologic response of direct administration of the Ad_{GV}CD.10 vector to one hepatic metastasis of a biopsy proven colorectal carcinoma together with systemic administration of the "prodrug" 5-fluorocytosine (5FC). The vector to be used, Ad_{GV}CD.10, is an E1a⁻, partial E1b⁻, partial E3⁻ adenovirus vector based on the Ad5 genome. The vector contains the expression cassette of a cytomegalovirus early/intermediate promoter/enhancer (CMV) driving the *E. Coli* gene coding for the enzyme cytosine deaminase (CD), an enzyme that converts 5FC to the chemotherapeutic agent 5-fluorouracil (5FU). The rationale of this study is that by transferring the CD gene to the metastatic colon cells, the cells will express the CD enzyme which will convert the prodrug 5FC to the toxic therapeutic agent 5FU, thus suppressing tumor growth in the local milieu. A total of 18 individuals will be evaluated. At the conclusion of the study, the following objectives will be met: (1) to determine the dose-dependent toxicity of direct administration of the Ad_{GV}CD.10 vector to hepatic metastases together with oral administration of 5FC; (2) to demonstrate transfer and expression of a therapeutic gene in a human solid tumor in vivo using a replication deficient adenovirus vector; and (3) to demonstrate that direct administration of Ad_{GV}CD.10 and oral administration of 5FC results in biologic changes in hepatic metastases which would be consistent with pursuing this strategy for therapy of colon carcinoma metastases of the liver.