

TWO NOVEL MURINE CELL LINES EXPRESS FUNCTIONAL HLA-A2/K^b

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HLA-A2/K^b transgenic mice have been powerful tools for studying HLA-A2-restricted anti-tumor immunity. Two tumor lines were established from an aged HLA-A2/K^b transgenic mouse that developed spontaneous tumors in the right limb and lung. Histopathologic analysis of the tumor was consistent with an osteosarcoma that had metastasized to the lung. The cells from the primary tumor and the lung metastasis were adapted to culture and are designated Ag201P and Ag201M, respectively. Both Ag201P and Ag201M induced tumors in mice, indicating that the established cell lines are tumorigenic. Both tumor lines expressed HLA-A2/K^b as assessed by RT-PCR and immunofluorescence analysis. Furthermore, the HLA-A2/K^b molecules were functional on both tumor lines as demonstrated by their ability to present exogenously-loaded HLA-A2-restricted peptides to human HLA-A2-restricted T cells. More importantly, endogenously-expressed HLA-A2-restricted epitopes were processed and presented in the context of HLA-A2/K^b in Ag201P and Ag201M cells to human HLA-A2-restricted T cells. Tumor-infiltrating lymphocyte (TIL) cultures that were established from enzyme-digested Ag201P tumor produced murine interferon- γ specifically in response to Ag201P, but not Ag201M or an MHC-mismatched control. Thus, Ag201P and Ag201M are two new murine tumor lines that express functional HLA-A2/K^b, and represent invaluable tools to study HLA-A2-restricted anti-tumor immunity in mice.