ABSTRACT

The present disclosure describes compositions and methods for treating solid tumors expressing mesothelin (MSLN) using chimeric antigen receptor (CAR) T cell therapy. The compositions comprise CARs with an extracellular domain that specifically binds MSLN. The extracellular domain comprises a single variable domain (VHH) antibody that targets MSLN. Polynucleotides encoding the anti-MSLN CAR constructs are provided. Pharmaceutical compositions comprising CAR T cells expressing the anti-MSLN CARs are also described. The CAR T cells demonstrate cytotoxicity against MSLN-expressing tumor cells in vitro and anti-tumor activity in vivo. Methods are provided for generating the CAR T cells by transfecting T cells with lentiviral or retroviral vectors carrying anti-MSLN CAR encoding sequences. The anti-MSLN CAR T cell therapy described herein provides an effective approach for treating solid tumors expressing MSLN, such as mesothelioma, ovarian cancer, pancreatic cancer, and lung cancer.