In certain embodiments, the β chain constant region comprises an amino acid sequence that is about 80%, about 81%, about 82%, about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98%, or about 99% homologous or identical to the amino acid sequence set forth in SEQ ID NO: 55, SEQ ID NO: 56, or SEQ ID NO: 57. In certain embodiments, the β chain constant region comprises the amino acid sequence set forth in SEQ ID NO: 55, SEQ ID NO: 56, or SEQ ID NO: 57.

The presently disclosed subject matter provides a recombinant T cell receptor (TCR) comprising an extracellular domain that binds to a RAS peptide comprising a G12 mutation, wherein the extracellular domain comprises an α chain comprising an α chain variable region and α chain constant region, and a β chain comprising a β chain variable region and a β chain constant region, wherein: a) the α chain variable region comprises a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 4, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 5,; and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 6; and the β chain variable region comprises a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 7, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 8, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 9; b) the α chain variable region comprises a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 14, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 15, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 16; and the β chain variable region comprises a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 17, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 18, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 19; c) the α chain variable region comprises a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 24, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 15, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 25; and the β chain variable region comprises a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 26, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 27, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 28; d) the α chain variable region comprises a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 33, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 34, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 35; and the β chain

variable region comprises a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 36, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 37, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 38; or e) the α chain variable region comprises a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 43, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 44, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 45; and the β chain variable region comprises a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 58, a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 46, and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 47.

The presently disclosed subject matter provides nucleic acids encoding the TCRs disclosed herein. The presently disclosed subject matter further provides cells comprising the TCR disclosed herein or the nucleic acids disclosed herein. In certain embodiments, the cell is transduced with the TCR. In certain embodiments, the TCR is constitutively expressed on the surface of the cell. In certain embodiments, the cell is an immunoresponsive cell. In certain embodiments, the cell is selected from the group consisting of a T cell, and a pluripotent stem cell from which a lymphoid cell may be differentiated. In certain embodiments, the cell is a T cell. In certain embodiments, the T cell is selected from the group consisting of a cytotoxic T lymphocyte (CTL), a regulatory T cell, a γδ T cell, a Natural Killer-T cell (NK-T), a stem cell memory T cell (T_{SCM}), a central memory T cell (T_{CM}), and an effector memory T cell (T_{EM}). In certain embodiments, the T cell is a γδ T cell. In certain embodiments, the T cell is a NK-T cell. In certain embodiments, the TCR or nucleic acid is integrated at a locus within the genome of the cell (e.g., T cell). In certain embodiments, the locus is selected from a *TRAC* locus, a *TRBC* locus, a *TRDC* locus, and a *TRGC* locus. In certain embodiments, the locus is a *TRAC* locus or a *TRBC* locus.

The presently disclosed subject matter also provides compositions comprising the cells disclosed herein. In certain embodiments, the composition is a pharmaceutical composition further comprising a pharmaceutically acceptable carrier.

Furthermore, the presently disclosed subject matter provides vectors comprising the nucleic acids disclosed herein. In certain embodiments, the vector is a γ-retroviral vector.

Additionally, the presently disclosed subject matter provides methods for producing a cell that binds to a RAS peptide that comprises a G12 mutation. In certain

HLA-A*31, HLA-A*33, HLA-A*66, HLA-A*68 and HLA-A*74. In certain embodiments, the HLA-A*03 superfamily member is HLA-A*11.

The presently disclosed subject matter provides a use of the cell or the composition as disclosed herein in the manufacture of a medicament for treating and/or preventing a tumor associated with a RAS mutation in a subject, optionally wherein the RAS mutation is a G12D mutation.

The presently disclosed subject matter provides the cell or composition as disclosed herein for use in therapy.

4. BRIEF DESCRIPTION OF THE FIGURES

The following Detailed Description, given by way of example but not intended to limit the invention to specific embodiments described, may be understood in conjunction with the accompanying drawings.

Figures 1A-1C depict a functional screen to elucidate the HLA-restricted immunopeptidome of endogenously processed and presented shared, or "public", neoantigens (NeoAgs) resulting from mutant KRAS proteins. Figure 1A shows a schematic overview of the HLA immune-precipitation (IP) / tandem mass spectrometry (MS/MS) screen using COS-7 as an artificial antigen presenting cell (aAPC). Figure 1B shows a validation MS "mirror" plot for an eluted HLA-A*11:01-restricted KRAS(G12D) peptide from the surface of PANC1, a pancreatic cancer cell line that physiologically expresses HLA-A*11:01 and *KRAS*(G12D) (top panel). A synthetic peptide was run as a control (bottom panel). Figure 1C shows a measurement of the relative stability of the neopeptide/HLA complex on the cell surface of *TAP1/2*-deficient T2 cells electroporated with *in vitro* transcribed RNA encoding HLA-A*11:01. **X** = preferred HLA anchor residue; **X** = location of hotspot mutation. SEQ ID NOs: 1-3 are represented.

Figure 2 depicts a graphical comparison of the amino acid sequence homology and location of hotspot mutations in the RAS family of oncoproteins. * = location of hotspot mutations; vertical bar = site of sequence variation between RAS family members. Zoom area shows the sequence of the hypervariable region of all four RAS proteins (SEQ ID NOs: 143 – 146).

Figures 3A and 3B depict the discovery and varibale chain description of a panel ofHLA-A*11:01-restricted mutant RAS-specific TCR gene sequences. Figure 3A shows T cells derived from either a HLA-A*11:01$^+$ healthy-donors (HD) or HLA-A*11:01$^+$

patients with a history of a *KRAS*(G12D) cancer stimulated *in vitro* with autologous antigen presenting cells presenting *KRAS*(G12D). Individual cultures were screened for the presence of mutant RAS-specific T cells using a higher-order peptide/HLA-I reagent loaded with the mass-spec identified mutant 10mer epitope (SEQ ID NO: 2). Positive wells were labeled with barcoded-dextramers and subjected to single-cell V(D)J sequencing to retrieve the paired αβTCR gene sequences of mutant RAS-specific T cell