TCR-m Antibodies to Intracellular Protein Targets; Epitope Regulation

Nearly all protein targets are inside the cancer cell and are not currently druggable. Human antibodies are designed to react with peptide fragments of oncogenic proteins presented on the cell surface to kill cancer cells.[1][2] Such TCRm can be made into CAR T cells or bispecific antibodies as well. [3] The regulation of antigen presentation and prediction of epitope targets of TCR's is also studied. [4,5,6]

Targeted Alpha Particle Therapy

Alpha particles are short-ranged high-energy radiations capable of killing in a range of 1 to 3 cells. We are attempting to deliver alpha-emitting isotopes to leukemia cells and small solid tumors using engineered cells and antibodies as ligands. Bi-213 and Ac-225 are purified and chelated to the Ig. Biochemistry of the agents, radiobiology, and pharmacology are studied. Model systems under study include myeloid leukemias, prostate cancer, and lymphoma. Several human trials have been initiated. [7]

Innovative Next Generation CAR T cells

Smarter CAR T cells that secrete biologic agents or small molecule drugs or can be selectively controlled or gated are under development.[11] Engineered cells that block host defenses are in development.

Oncogenic Protein Vaccines

The amino acid sequences of overexpressed oncogenic proteins, or mutated sequences, can be used to develop tumor-specific vaccines for treating humans. One such vaccine for treating a variety of cancers and leukemia directed to WT1 was developed by our laboratory and is currently being used to treat patients. We are also examining the use of mutated heteroclitic peptides with higher avidity for the HLA molecule to use as immunogens. [8]

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