New Cancer Therapy Targeting Tumor Associated Carbohydrate Neoantigens (Ramot)

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Major limitations in current immunotherapy success are low antigenicity of targeting antigen and tumor heterogeneity. Hence there is an unmet need for novel antigen targets that could potentially be expressed on many tumor types. Cancer express aberrant cell surface glycosylation patterns compared to normal cells. These tumor-associated carbohydrate-neoantigens can be targeted for tumor cell killing by antibodies and cytotoxic immune cells.

OUR SOLUTION

Sialic acids cover cell surface glycans and frequently have altered expression on many types of carcinoma cells and correlate with cancer progression and/or metastasis. We focus on targeting sialic acid containing carbohydrate-neoantigens using the chimeric antigen receptor T cell (CAR-T) immunotherapy approach. Current clinical CAR-T cells target mostly soluble tumors using CD19, BCMA and other non-cancer specific antigens that often suffer toxicity and side effects. Our universal anti-carbohydrate CAR-T approach could target many types of carcinomas with high specificity and safety, and could potentially reach patients rapidly.

CURRENT DEVELOPMENT STAGE

We have established a pipeline to obtain different CAR-T and currently have several clones at different stages. We identified several potential antigens and have a platform to generate antibodies of high specificity and affinity, selected clones are then expressed and further characterized by FACS, glycan microarray and SPR. We validate selected antibodies in vitro tumor cells binding, specificity and killing potential. Then, selected antibodies are cloned as single chain constructs into CAR that are then used to generate and transduce CAR-T cells and investigate their safety, binding and killing potential in vitro and in vivo, in both immune-incompetent and immunocompetent mouse models. Validated CAR-T will be submitted for human clinical trial approval.

NOVELTY

Current clinical trials using CAR T cells target specific antigens as CD19 and BCMA, and some against non-specific antigens (existing also on other tissues, i.e. ErbB2 or mesothelin), where toxicity and side effects are common. Cost wise, production of viruses to transduce T cells against each specific target is expensive. In addition, the FDA-approved CD19-CAR T cell therapy is effective for hematological malignancies, but treatment of solid tumors, especially carcinomas, is yet to be achieved. So far, most efforts focused on searching mutant peptide neoantigens overlooking tumor-associated glycosylation changes that could potentially serve as potent carbohydrate-neoantigens targets for immunotherapy. We have the technologies and knowledge to design immunotherapies that would target aberrant glycosylation in cancer. Our universal anti-carbohydrate CAR-T approach could target many types of carcinomas with high specificity and safety, and could potentially reach patients rapidly.

PATENTS

Two provisional patents are pending submission. Each new antigen target and validated CAR-T clone will also be submitted for patent protection.

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