IDENTIFICATION OF POTENTIALLY SAFE AND SELECTIVE CAR TARGETS FOR HEAD AND NECK CANCER VIA A PAN-CANCER SINGLE CELL TRANSCRIPTOME ANALYSIS

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Background Chimeric antigen receptor (CAR) T cell therapies have yielded transformative clinical success for patients with blood tumors, but their full potential remains to be unleashed against solid tumors. One challenge is finding selective targets: cell surface proteins that are expressed widely by cancer cells and minimally by healthy cells in the tumor microenvironment and other normal tissues.

Methods Analyzing pan-cancer patient tumor single cell transcriptomics data, we first define and quantify selectivity and safety scores of existing CAR targets for indications in which they are in clinical trials or approved. Selectivity scores are computed by the ability of a given surfaceome gene to classify tumor from nontumor cells in the tumor microenvironment. Safety scores are computed by mining healthy tissue transcriptomics and proteomics atlas data. Second, we identify new candidate cell surface CAR targets that have better selectivity and safety scores than the leading targets among those currently being tested, in an indication-specific manner.

Results Remarkably, in almost all cancer types, we cannot find such better targets, testifying to the overall near optimality of the current target space. However, in HPV-negative head and neck squamous cell carcinoma (HNSC), for which there is currently a dearth of existing CAR targets, we find five new targets that have both superior selectivity and safety scores. Among the HNSC new targets, we find a few that additionally are strongly essentiality in HNSC cell lines.

Conclusions Our analysis may provide new surfaceome targets against which CARs may be engineered to treat HNSC patients more safely and effectively.

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