On Demand Talks: Combination Therapy

**06** EXPRESSION OF ANTI-APOPTOTIC GENE CFLIP TO ENHANCE PERSISTENCE IN CAR T CELLS

GMY Tan*, SMAR Hosseini, A Poudel, AD Mclellan. University of Otago, North Dunedin, New Zealand

Background CAR T cell therapy has been successful for targeting blood cancers, but treatment of solid cancers has been limited due to the heterogenous nature of tumour-associated antigen expression on solid cancers, and the suppressive tumour microenvironment.1 Another major obstacle to CAR T cell therapy is activation-induced cell death (AICD) of the CAR T cells.2 In this study, we expressed the anti-apoptotic cFLIP (long form) regulates CD8+ T cell activation through caspase-8-dependent pathways in the melanoma TME. Ultimately, this model could be used as a novel in vitro tool for preclinical testing of immune modulatory therapeutic agents.


**07** A BISPECIFIC VHH APPROACH TO LEVERAGE THE POTENT AND WIDELY APPLICABLE TUMOR CYTOLYTIC CAPACITY OF Vγ9Vδ2 T CELLS

1LA King*, 2R Lameris, 2RC Roovers, 2PP Parren, 1TD de Gruijl, 1HJ van der Vliet. 1AUMC – Cancer Centre Amsterdam, Amsterdam, Netherlands; 2LAVA Therapeutics, Utrecht, Netherlands

Vγ9Vδ2-T cells include a unique and potent subset of T cells which play an important role in tumor defense. Vγ9Vδ2-T cells recognize and can lyse butyrophilin 3A1-expressing target cells with elevated levels of non-peptide phosphoantigens (pAg), induced by cell stress or malignancy. To date, Vγ9Vδ2-T cell based cancer immunotherapeutic approaches were well tolerated and in some cases capable of inducing relevant clinical responses. In an effort to improve the efficacy and consistency of Vγ9Vδ2-T cell based cancer immunotherapy, we designed a bispecific VHH that binds to both Vγ9Vδ2-T cells and EGFR expressed by tumor cells and results in the targeted-specific activation of Vγ9Vδ2-T cells and subsequent lysis of colorectal cancer cell lines and primary colorectal cancer samples both in vitro and in an in vivo mouse xenograft model. Of note, tumor cell lysis was independent of mutations in KRAS and BRAF that are known to impair the efficacy of clinically registered anti-EGFR monoclonal antibodies as well.