142 ENHANCED ANTITUMORAL ACTIVITY OF HER2-CAR-TS IN COMPARISON TO TRASTUZUMAB IN A LIVE CELL IMAGING SUPPORTED 3D ASSAY

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Background Although most breast cancer patients are treated these days with a curative intention, there are still many patients progressing to metastatic disease. The advent of anti-HER2 therapy has prominently prolonged the time of disease progression and survival for those patients, where a decent proportion is suffering from a HER2+ tumor. Beside classical approaches via antibodies against HER2, the use of Chimeric Antigen Receptor T (CAR-T) cells also in a solid cancer context is getting more and more attention.

Methods In our study we evaluated the efficacy of Trastuzumab and HER2+ targeting CAR-T cells in a panel of human cancer cell lines (SK-OV3, Hs578T and JIMT-1) with different HER2 expression levels. The tumor cells were seeded in the presence or absence of different immune cells (PBMC, monocytes, NK cells or T cells) and cultured as 3D spheroids in a matrix-based system. The tumor growth and if applicable the invasion of the immune cells was measured via fluorescence-based live cell imaging. On the last experiment day, a metabolic read-out (CellTiter-Glo, CTG assay) was performed.

Results Trastuzumab inhibited the tumor growth in a dose-dependent manner in the HER2+ cell line SK-OV3. The efficacy was increased specifically when NK cells were added to the culture. The HER2 positive cell line JIMT-1 was resistant to Trastuzumab treatment, which is in line with published data. The model was derived from a Trastuzumab-refractory patient. Interestingly, the addition of NK cells induced a marked increase of activity in this model as well. The HER2 targeted CART cells eradicated the 3D spheroids of SK-OV3 as well as JIMT-1 in a dose-dependent manner. The untransduced control T cells did not influence the tumor growth at all. The HER2- cell line Hs578T served as a negative control in the Trastuzumab as well as in the CAR-T cell experiments, and proved to be resistant to any treatment in this study. Taken together the 3D live cell imaging platform proved to be a feasible tool for efficacy testing of biologics as well as cellular therapies.

Conclusions Our in house developed HER2 CAR-T cells proved to be specific and effective in eradicating the targeted cancer cells. The mechanism behind the modulated sensitivity of the HER2+ JIMT-1 cells against HER2-targeted treatment will help to shed some light in possible resistance mechanism and hopefully have some translational value for patients suffering from this disease.

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