Targeting the minor subset of melanoma stem cells eradicates established melanoma lesions

P. Schmidt¹, C. Kopecky¹, A.A. Hombach¹, P. Zingrino¹, C. Mauch¹, H. Abken¹

Abstract

Current paradigms in cancer therapy attempt to eliminate all malignant cells of a tumor lesion. The cancer stem cell (CSC) paradigm, however, predicts that tumors are initiated by a minor subset of cancer initiating cells and are maintained by a few, so far less identified cancer maintaining cells. In this contribution, however, we demonstrate that specific elimination of a less than a 2% subset of melanoma maintaining cells eradicates established melanoma lesions without targeting the tumor cell mass. The tumor stem cell subset is selectively eliminated from tumor lesions by adoptive transfer of cytotoxic T cells redirected by an engineered chimeric antigen receptor. Targeted elimination of the minority of tumor cells which co-express HMW-MAA (MCSP) and CD20 eradicated established melanoma lesions in long-term despite the bulk of tumor cells. Targeting of any random cancer cell subset was not effective. HMW-MAA+CD20+ melanoma subset cells were found in about 4 out of 5 melanoma biopsies of different histology and clinical grade. Our data provide first evidence that progressing melanoma is maintained by a minority of cells, the targeted elimination of which results in tumor eradication.