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Adoptive cell therapy of cancer and autoimmune diseases employing genetically T cells with redirected antibody specificity

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Tcells specifically respond to their target through the TCR that recognize a complex composed of its self-MHC and peptide derived from the target antigen. To endow T cells with non-MHC restricted (nor individual-specific) restricted recognition we have designed and engineered chimeric receptor whose antigen binding unit is made of single chain Fv of a given antibody and intracellular domains of stimulating and co-stimulating molecules. Upon transduction of T-cells with such chimeric antibody-based receptor (CAR) we have demonstrated that the resulting cells (nick-named T-bodies) could function in effector T and NK cells (Teff). Using CAR specific to tumor associated antigens we created T-bodies that specifically discriminated between malignant and healthy tissues and efficiently eradicate well-established primary and disseminated tumors. We have studied different modes of adoptive cell therapy in various murine models including orthotopic grafted human prostatic, pancreatic and mammary adenocarcinoma xenografts in SCID mice as well as transgenic mice spontaneously developing mammary, or inflammation induced colorectal tumors. In all these model adoptive transfer of the tumor specific T-bodies following to mild lympho-depleting treatment yielded very pronounced antitumor responses. For complete responses and cure repeated systemic of T-bodies administration was required. In certain cases of accessible primary solid tumors direct intratumor injection of T-bodies (e.g. breast cancer) or through endoscopy (pancreatic cancer) or colonoscopy (colorectal cancer) yielded very efficient tumor eradication. Recently, we have developed a protocol to generate a universal Teff by creating time-window that allows non-matched T-bodies to cure tumor-bearing mice without causing GvH. Presently, The T-body approach found curative in pilot clinical trials.

Biography

Zelig Eshhar has completed his PhD at the Weizmann Institute and post doctoral Studies from Harvard University Medical School. He spent sabbatical years of research at DNAX Institute of Molecular Biology and Stanford University and at the National Cancer Institute at the NIH. He served as the Chairman of the Department of Immunology at the Weizmann Institute and holds the position of Chairman of research in Immunology Tel Aviv Sourasky Medical Center and guest professor at the Faculty of Medicine of Tel Aviv University. Professor Ehhar has published more the 210 research articles.

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