

## Adoptive cell therapy of autoimmune diseases employing genetically T- regulatory cells with redirected antibody specificity

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Regulatory T cells (Treg) are known for their ability to suppress inflammatory responses, however, the scarcity of antigen-specific Treg impedes their clinical application. To study whether Tregs can be genetically modified by ectopic chimeric antibody-type receptor (CAR) and maintain their suppressive function, we have generated “Treg-T bodies” specific to synthetic or natural antigens and tested their ability to alleviate acute, transient and chronic colitis. We have demonstrated that small numbers of isolated CD4<sup>+</sup>CD25<sup>+</sup>Foxp3<sup>+</sup> Treg T-bodies expressing the relevant CAR could protect and alleviate different symptoms of colitis and even rescue mice from death to acute colitis. The adoptively transferred Treg T-bodies migrated to and accumulated in the inflamed colon where they underwent specific stimulation to secrete their suppressive cytokines (e.g. TGFβ). Both in-vitro and at the site of inflammation, these cytokines suppress Teff cells in non-antigen specific manner. Consequently, we could demonstrate a bystander effect in which Treg redirected to a non-pathogenic naïve colon antigen could be attracted to the inflamed site and suppress ongoing colitis. In another system, we took advantage of the fact that CEA is over-expressed in colitic gut tissue and have established a model of chronic colitis in CEA transgenic mice by the adoptive transfer of CEA-specific CD4<sup>+</sup> Teff cells. In this model, that is more relevant to the human disease, the CEA-specific Treg T-bodies specifically alleviated the disease to a large degree. Finally, we expended the scope of Treg T-body potential by showing their ability to suppress the development and growth of inflammation-induced cancers.

### 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 Eshhar has published more than 210 research articles.

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