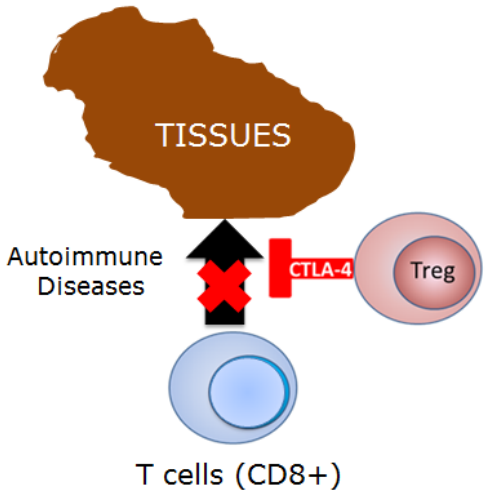
Detection of self-reactive CD8+ T cells with an anergic phenotype in healthy individuals

Immunological tolerance to self requires naturally occurring regulatory T cells. Yet how they stably control autoimmune T cells remains obscure. Here, we show that Treg cells can render self-reactive human CD8+ T cells anergic (i.e., hypoproliferative and cytokine hypoproducing upon antigen restimulation) in vitro, likely by controlling the costimulatory function of antigen-presenting cells. Anergic T cells were naïve in phenotype, lower than activated T cells in T cell receptor affinity for cognate antigen, and expressed several coinhibitory molecules, including cytotoxic T lymphocyte–associated antigen-4 (CTLA-4).

Using these criteria, we detected in healthy individuals anergic T cells reactive with a skin antigen targeted in the autoimmune disease vitiligo. Collectively, our results suggest that cell–mediated induction of anergy in autoimmune T cells is important for maintaining self-tolerance.



Tregs render self-reactive human CD8+ T cells anergic.

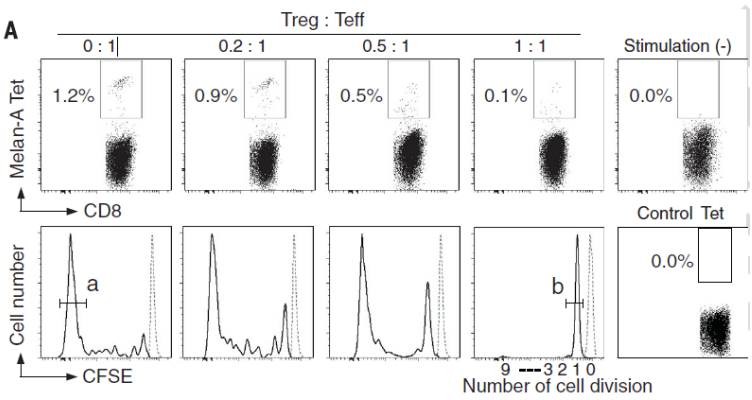
KEYWORDS

Immune Tolerance, Regulatory T cell (Treg), Anergy, Self-reactive CD8+ T cells, CTLA-4（Cyto Cytotoxic T-lymphocyte-associated antigen-4）

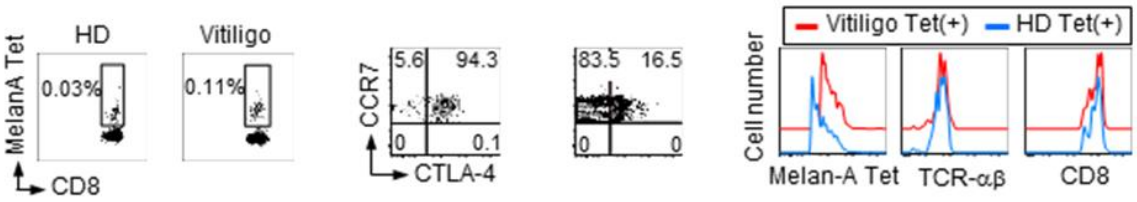
ARTICLE & JOURNAL

Yuka Maeda, Hiroyoshi Nishikawa, Daisuke Sugiyama, Danbee Ha, Masahide Hamaguchi, Takuro Saito, Megumi Nishioka, James B. Wing, Dennis Adeegbe, Ichiro Katayama and Shimon Sakaguchi. Detection of self-reactive CD8+ T cells with an anergic phenotype in healthy individuals. *Science (2014).*

FIGURES



Natural cells render low-affinity self-reactive CD8+ T cells anergic upon antigen stimulation. Melan-A–specific CD8+ T cell induction. CFSE-labeled CD8+ T cells of HLA-A*0201+ healthy individuals were stimulated by Tcell–depleted, g-irradiated, and Melan-A26-35 peptide–pulsed APCs with graded numbers of CD25highCD4+ cells for 10 days. Dotted lines mean Tet–CD8+ cells showing no CFSE dilution. Control tet: NY-ESO-1157-165/HLA-A*0201 tetramer.



Detection of low-affinity anergic self-reactive CTLA-4+CCR7+CD8+ T cells in healthy individuals.

CCR7 and CD45RA expression by Tet+CD8+ T cells in an HD and a vitiligo patient. Tet, TCR-αβ, and CD8 staining intensity of Tet+CD8+ T cells in an HD and a vitiligo patient.