T cells naturally designed and selected to sense and eliminate cancer cells

Hilde Cheroutre

La Jolla Institute for Immunology

Abstract

Cancer immune surveillance is mediated by sensing and eliminating malignant cells. Conventional T cells, which recognize processed antigen peptides presented by classical MHC are pivotal for efficient tumor surveillance. Anti-cancer defenses however, are also met with resistance, immune suppression and dysfunctional T cells. Immune therapies, including checkpoint blockade and adoptive cell therapy, made remarkable advances in overcoming some of these obstacles and engineered CAR-T cells are circumventing limitations imposed by the peptide specificity and MHC restriction of the TCRs expressed by conventional T cells. However, CAR-T cells also engender adverse effects, such as off target elimination of healthy cells, cytokine release syndrome (CRS), neurological toxicity, in addition to time consuming and expensive engineering. Besides conventional CD8 and CD4 T cells, other T lymphocyte types exist that express TCRs that are naturally designed and selected to sense and eliminate unhealthy cells, independently of CD8 or CD4 coreceptor help or detection of processed peptide antigens or restriction by classical MHC. These T cells share common features of innate and adaptive immunity, home to tissues and recognize a wide range of non-polymorphic ligands. Because they do not cause GVHD, or CRS they have been recognized as suitable cell recipients for CARs. However, although the addition of a CAR might enhance their killing potential, it also undermines the natural self-based design and selection of these T cells to specifically eliminate cancer cells but leave healthy cells intact.

Biography

Dr. Hilde Cheroutre received her Ph.D. with “the highest distinction” from the Ghent State University, Belgium, in 1986. After postdoctoral work at the California Institute of Technology (Caltech), she joined UCLA. In 1997, she moved to the La Jolla Institute for Immunology, where she became a Full Professor and Division Head. Her work has covered T cell differentiation, lineage commitment, self-based selection, TCR signaling, T cell memory, and mucosal immunology. Dr. Cheroutre has especially focused on co-receptor-independent T cells, their specificities and specialized functions in anti-cancer- and auto-immunity. She received the NIH Director’s Pioneer Award and is a Distinguished Fellow of the American Association of Immunologists.