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Tumors can suppress immune responses. Inhibition of immunosuppression with the IDO inhibitor indoximod improved response to an antitumor vaccine. Combined immunotherapy with anti-OX40 and indoximod led to both increased numbers and improved functionality of vaccine-induced effector T cells.
The Immune Checkpoint Modulator OX40 and Its Ligand OX40L in NK-Cell Immunosurveillance and Acute Myeloid Leukemia

Tina Nuebling, Carla Emilia Schumacher, Martin Hofmann, Ilona Hagelstein, Benjamin Joachim Schmiedel, Stefanie Maurer, Birgit Federmann, Kathrin Rothfelder, Malte Roerden, Daniela Dörfel, Pascal Schneider, Gundram Jung, and Helmut Rainer Salih

The TNFR-family member OX40 is expressed on AML cells, influencing various AML cellular functions as well as immunosurveillance by OX40L-expressing NK cells. These effects should be considered when developing OX40-targeted approaches for cancer immunotherapy.

T-cell Responses in the Microenvironment of Primary Renal Cell Carcinoma—Implications for Adoptive Cell Therapy

Rikke Andersen, Marie Christine Wulff Westergaard, Julie Westerlin Kjeldsen, Anja Müller, Natasja Wulff Pedersen, Sine Reker Hadrup, Özcan Met, Barbara Seliger, Bjarne Kromann-Andersen, Thomas Hasselager, Marco Donia, and Inge Marie Svane

TILs isolated from primary RCC specimens could recognize tumors. However, their immune responses were weaker than TILs from metastatic melanoma and displayed a mono-/oligo-functional pattern. The ability to select and expand poly-functional T cells may improve cell therapy for RCC.

Exosomes Associated with Human Ovarian Tumors Harbor a Reversible Checkpoint of T-cell Responses


Exosomes derived from ovarian cancer tumors repress the function and proliferation of T cells in the tumor microenvironment. T cells can be reactivated after exosomes are removed, which may point to exosomes as a target for checkpoint modulation.

ABOUT THE COVER

Cytotoxic T cells rely on a complex system of checks and balances that modulates their activation, functional capabilities, and survival. One surface protein, SLAMF6, binds to itself in a homotypic fashion. Eisenberg and colleagues created a reagent from the ectodomain of SLAMF6 that interfered with this binding, resulting in increased activation of CD8+ T cells and stronger effector functions, even prolonging the survival of adoptively transferred CD8+ T cells, without the addition of IL2. This work provides evidence that when SLAMF6 is engaged via cell–cell contact it has an inhibitory effect on CD8+ T cells, which is relieved by the competitive binding of its soluble form. Read more in this issue, starting on page 127. The original confocal image is of human T cells activated with anti-CD3, with SLAMF6 (red) clustering at sites of cell–cell contact. Artwork by Lewis Long.