Peter E. Fecci

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Peter Fecci MD, PhD, is currently a Professor of Neurosurgery, Pathology, Integrative Immunobiology, and Biomedical Engineering at Duke University, where he also serves as the Director for the Center for Brain and Spine Metastasis, as well as for the Brain Tumor Immunotherapy Program (BTIP). He is likewise the Director of Surgical Neuro-oncology and a Deputy Director for the Preston Robert Tisch Brain Tumor Center at Duke. His NIH-funded laboratory focuses on integrating strategies to reverse cancer-induced T cell dysfunction with current immune-based platforms. He is a recipient of the Cancer Research Institute Lloyd J. Old STAR Award, the Sontag Distinguished Scientist Award and Distinguished Alumni Award, and is an inductee into the American Society for Clinical Investigation (ASCI). Clinically, as a neurosurgeon, he focuses on intrinsic brain tumors (gliomas, metastases) and has likewise built one of the country's largest centers for Laser Interstitial Thermal Therapy as a minimally invasive option for brain tumors.

Topic: A Novel Mechanism of T Cell Antitumor Immunity

The accepted paradigm for both cellular and antitumor immunity relies upon tumor cell kill by CD8+ T cells recognizing cognate antigens presented in the context of target cell major histocompatibility complex class I (MHC I) molecules. Likewise, a classically described mechanism of tumor immune escape is tumor MHC-I downregulation. Here, we report that CD8+ T cells maintain the capacity to kill tumor cells that are entirely devoid of MHC-I expression. This capacity proves to be dependent instead on interactions between T cell NKG2D and tumor NKG2D ligands (NKG2DL), the latter of which are highly expressed on MHC-loss variants. Necessarily, tumor cell kill in these instances is antigen-independent, although prior T cell antigen-specific activation is required and can be furnished by myeloid cells or even neighboring MHC-replete tumor cells. In this manner, adaptive priming can beget innate killing. These mechanisms are active in vivo in mice, as well as in vitro in human tumor systems, and are obviated by NKG2D knockout or blockade. Such findings challenge the traditional model of T cell-mediated tumor cell kill and likewise provide a therapeutic blueprint for licensing immune responses in MHC-loss tumor cell variants.