Cancer Immunology Research

Table of Contents

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MASTERS OF IMMUNOLOGY

CANCER IMMUNOLOGY AT THE CROSSROADS: COMPLEMENTARY THERAPEUTIC MODALITIES

MEETING REPORT

CANCER IMMUNOLOGY MINIATURES

PRIORITY BRIEF

RESEARCH ARTICLE

COMMENTARY

RESEARCH ARTICLES

Table of Contents

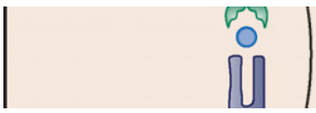

Table of Contents

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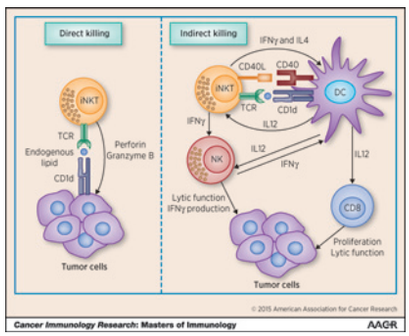
Table of Contents

ABOUT THE COVER



Invariant natural killer T (iNKT) cells are a unique population of T lymphocytes that lies at the interface between the innate and adaptive immune systems, and they are important mediators of immune responses and tumor surveillance. iNKT cells can recognize endogenous lipids presented by CD1d molecules on tumor cells and release Perforin and Granzyme B to lyse tumor cells directly. In the absence of CD1d expression on tumor cells, iNKT cells may become activated in response to CD1d-expressing or Toll-like receptor (TLR)-activated antigen-presenting cells (APC). The bidirectional activation of iNKT cells and APCs promotes the activation of NK-cell and tumor-specific T-cell responses, thereby mediating tumor-cell killing indirectly. This figure was created by Rosanna M. McEwen-Smith of the Weatherall Institute of Molecular Medicine and the University of Oxford. For details, see the Masters of Immunology article by Cerundolo and colleagues that begins on page 425 of this issue.

ABOUT THE MASTER

Vincenzo Cerundolo, MD, PhD, is the director of the United Kingdom Medical Research Council (MRC UK) Human Immunology Unit and professor of immunology at the Weatherall Institute of Molecular Medicine, University of Oxford, UK. In the early 1990s Dr. Cerundolo made key discoveries characterizing the cellular mechanisms involved in the presentation of intracellular peptides to MHC class I–restricted T lymphocytes, which have had a great impact on the field. In particular, he was instrumental in the identification of genes within the MHC locus that are critical for the generation of peptides presented by MHC class I molecules. Dr. Cerundolo described the first human antigen processing-deficient cells, leading to the cloning and characterization of the transporter associated with antigen-processing 1 and 2 (TAP1, TAP2) genes and the identification of several families of TAP1/2-deficient patients with necrotizing granulomatous skin lesions and small vessel vasculitis. He was the first to determine the relationship between the length of peptides and their binding affinity to MHC class I molecules, hence explaining the homogenous length of peptides isolated from MHC class I molecules. He showed the proteasome-dependent processing of defined melanoma antigenic proteins into epitopes for antitumor T cells and thus the direct role of immunoproteasomes in cross-presentation of exogenous proteins.

Dr. Cerundolo demonstrated how the length and saturation of lipid antigens contained within the CD1d binding site modulate their affinity of binding to invariant NKT cells (iNKT cells), hence explaining how lipid-specific lymphocytes are capable of recognizing both the group head and the length of lipid antigens, ensuring greater specificity of antigen recognition. His seminal findings on the processing and presentation of peptide and lipid antigens made fundamental advances to the field of antigen presentation to MHC class I–restricted T cells and CD1d-restricted iNKT cells. His demonstration that iNKT cells enhance both antigen-specific antibody and T-cell responses has had a major influence on the development of new vaccines and has opened up new therapeutic strategies to enhance immune responses against cancer and infectious pathogens.

Dr. Cerundolo was born in Lecce, Italy. He was a graduate in medicine and completed his PhD in immunology at the University of Padua, Italy, where he also received training in clinical and experimental oncology. He moved to the UK as an EMBO Fellow in 1988 to work with Professor Alain Townsend. Dr. Cerundolo was appointed professor of immunology at the University of Oxford in 2000, director of the MRC Human Immunology Unit in 2010, and head of the Investigative Medicine Division of the Radcliffe Department of Medicine in 2012. Dr. Cerundolo enjoys running and is a member of one of the Oxford Road Runner Clubs. He is a fellow of Merton College at the University of Oxford, the Academy of Medical Sciences, UK, and the Royal College of Pathologists, and is the Batsheva Fellow of the Israeli Academy of Medical Sciences. He serves on the scientific advisory boards of numerous institutions and charitable organizations, and on the editorial boards of leading peer-reviewed journals.

Current research in the Cerundolo laboratory focuses on gaining a better understanding of the mechanisms that control the cell–cell interplay required for optimal expansion and activation of tumor-specific T-cell populations, and to apply this knowledge to the development of better treatment strategies in cancer patients.

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3 (5)

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