Cancer Immunology Research

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MASTERS OF IMMUNOLOGY

CANCER IMMUNOLOGY AT THE CROSSROADS: COMPLEMENTARY THERAPEUTIC MODALITIES

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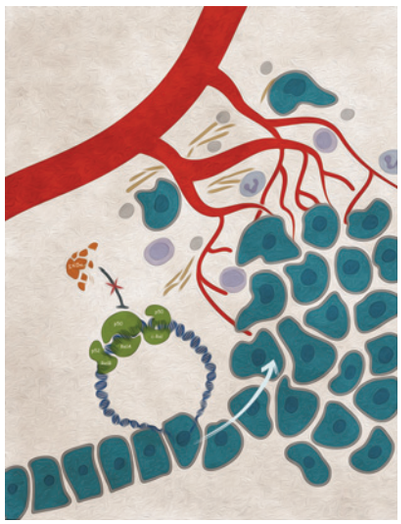
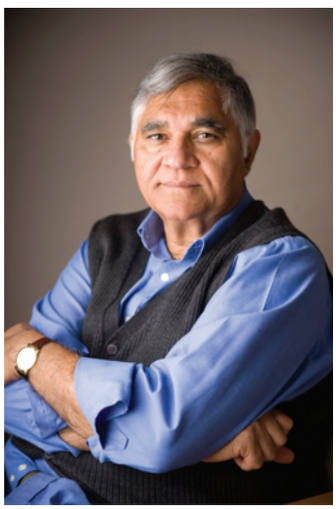


Nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) comprises a family of five transcription factors (NF-κB1/p105/p50, NF-κB2/p100/p52, RelA/p65, RelB, and c-Rel) that form distinct heterodimer or homodimer protein complexes, which bind to consensus DNA sequences at promoter regions of responsive genes. Members of the NF-κB family are involved in signaling pathways controlling vital biologic processes, and stringent regulation of NF-κB activity is indispensable for the integrity of cellular functions. Oncogenic mutations can lead to constitutive and/or elevated NF-κB activity. NF-κB is also activated by cytokines, growth factors, cellular and environmental stresses, and DNA damage. In premalignant lesions with elevated NF-κB activity, the accumulation of proinflammatory cytokines contributes to the protumorigenic microenvironment. NF-κB is the master regulator mediating a cross-talk between inflammation and cancer at multiple levels. NF-κB activity promotes proliferation and angiogenesis, suppresses apoptosis, and induces epithelial–mesenchymal transition, which can lead to distant metastasis. At tumor sites, NF-κB activation may remodel local metabolism and anergize the immune system to favor tumor growth. Suppression of NF-κB in myeloid cells or tumor cells could lead to tumor regression, making the NF-κB pathway a promising therapeutic target. For more details of NF-κB activities in human cancers, see the Masters of Immunology primer by Inder M. Verma and colleagues starting on page 823 of this issue.

ABOUT THE MASTER



Inder Mohan Verma, PhD, is the Irwin and Joan Jacobs Chair Professor in Exemplary Life Science, Professor and Director of the Laboratory of Genetics at The Salk Institute for Biological Sciences (La Jolla, CA), and an American Cancer Society Professor of Molecular Biology. He is also an adjunct professor in the department of biology at the University of California, San Diego, and a distinguished adjunct professor in the Biotechnology Research Group at the King Abdulaziz University (Jeddah, Saudi Arabia). Dr. Verma was educated at the Lucknow University in India, and received his PhD in Biochemistry from the Weizmann Institute of Science (Rehovot, Israel), characterizing mitochondrial ribosomal RNA from the fungus *Aspergillus nidulans*, under the mentorship of Professor Uri Littauer. In 1971 he joined the laboratory of Nobel laureate David Baltimore at the Massachusetts Institute of Technology (Cambridge, MA), where he studied reverse transcriptase from RNA tumor viruses, including avian myeloblastosis virus, mouse leukemia virus, and hamster leukemia virus. Dr. Verma established his independent laboratory at The Salk Institute in 1974, and at the age of 26, he was one of the youngest faculty members.

Dr. Verma's work on RNA tumor viruses and reverse transcriptase led to his identification and/or characterization of several oncogenes, including c-fos, c-rel, and the breast cancer genes (BRCA1, BRCA2). The Verma laboratory has contributed significantly to the delineation of the regulation and expression of c-fos during prenatal and postnatal development, growth, and differentiation. These investigators have characterized the mechanism of BRCA1 tumor suppression. C-rel is a member of the nuclear factor-κB (NF-κB) family of master transcription factors, the subject of this Masters primer. With expertise in molecular biology and retrovirology, Dr. Verma developed viral expression vectors for gene transfer to replace missing or defective cellular proteins, and this work has become the foundation for cell and gene therapy. The Verma laboratory has used the gene therapy technology to generate a mouse model of glioblastoma, from which they have identified neural cancer stem cells, as few as ten of which can induce tumors in immunodeficient mice. They are using the same technique to investigate the initiation and treatment of lung and prostate cancers.

Dr. Verma was born in Sangrur, Punjab, India. He has received many honors, including an Outstanding Investigator Award from the NIH (1988), and he was elected as a member of the Third World Academy of Sciences (1995), the National Academy of Sciences, India (1997), the U.S. National Academy of Sciences (NAS; 1997), the U.S. NAS Institute of Medicine (1999), the American Academy of Arts and Sciences (2000), the European Molecular Biology Organization (1998), and the American Philosophical Society (2006). Dr. Verma was elected as a Foreign Fellow of the Indian National Science Academy (2005). He was awarded the Vilcek Foundation Prize (2008), the ASGT Outstanding Achievement Award (2009), the Spector Prize (2010), and the Pasarow Award in Cancer Research (2010). Dr. Verma now serves as the Editor-in-Chief of the *Proceedings of the National Academy of Science of the United States.*

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