



American Society for Investigative Pathology

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Rouse-Whipple Award - 1999

Francis V. Chisari



Francis V. Chisari, M.D., Professor and Head of the Division of Experimental Pathology at the Scripps Research Institute, is the winner of the 1999 Rous-Whipple Award from the Association for Investigative Pathology. This award, for investigators over age 50 who have had a distinguished career in research who are continuing to contribute to the field is one of the most prestigious honors in the field of experimental pathology.

Dr. Chisari is the author of a series of landmark papers illuminating the immunobiology and pathogenesis of hepatitis B and C virus infections. His group was the first to define the CD4 and CD8 T-cell responses to HBV in infected patients, and to demonstrate that viral clearance occurs in the context of a vigorous multispecific T cell response while a weak or narrowly focused T cell response to the viral antigens leads to viral persistence. This series of studies provided critical insight into the immunological basis of viral clearance and persistence during HBV infection, and it established the scientific basis for development of specific immunotherapy for chronic hepatitis.

Dr. Chisari developed the first transgenic mouse models for a human viral pathogen, *i.e.* the hepatitis B virus. Applying transgenesis to other studies, his lab made the seminal discovery that overproduction of HBV large envelope polypeptide recapitulates many of the hepatotoxic hallmarks of the human disease, including hepatocellular carcinoma. Using his transgenic mouse models, Dr. Chisari demonstrated the immunopathogenetic basis for viral hepatitis and he proved that immune mediated chronic hepatitis is sufficient to cause hepatocellular carcinoma. He recently showed that autologous activated dendritic cells can break tolerance to HBV at the cytotoxic T-lymphocyte (CTL) level in these animals, suggesting another approach to enhance the specific immune response and terminate chronic hepatitis B. Importantly, in a recent series of landmark papers, his group discovered that HBV replication in the liver is abolished noncytopathologically by inflammatory cytokines secreted by CTLs following antigen recognition. This seminal discovery reveals that the immune response may clear certain infections by "curing" as well as by killing infected cells.

Dr. Mark L. Tykocinski, Chairman of the Department of Pathology and Laboratory Medicine at the University of Pennsylvania Health System calls Rous-Whipple laureate "an outstanding scientist ... at the cutting edge of Experimental Pathology" whose work "embodies and defines the best of his discipline." Dr. Peter M. Howley, Chairman of the Department of Pathology at Harvard Medical School says Dr. Chisari "has made, and continues to make, fundamental contributions to our understanding of the pathogenesis of hepatitis B virus infections" and calls him "one of the leading scientists in the world in viral pathogenesis." Letters of support for his nomination also came from Dr. Michael B.A. Oldstone and Dr. Thomas S. Edgington at Scripps, and from Dr. R.M. Zinkernagel at the Department of Pathology/Institute of Experimental Immunology at the University Hospital of Zurich.

Dr. Chisari was born in New York, NY and graduated in 1968 from the Cornell University Medical College. He did his postdoctoral training at Cornell, Dartmouth, NIH, the Mayo Clinic and the Institut Pasteur. He has been at Scripps since 1973. As winner of the 1999 Rous-Whipple Award, Dr. Chisari will receive a monetary award and a plaque, and has been invited to present a lecture at ASIP's Annual Meeting in April, 1999 in Washington, D.C.