

**Professor Carl Nathan, M.D.**

Carl Nathan, MD is R.A. Rees Pritchett Professor and chairman of the Department of Microbiology and Immunology at Weill Cornell Medical College and co-chair of the Program in Immunology and Microbial Pathogenesis at Weill Graduate School of Medical Sciences of Cornell University. A graduate of Harvard College and Harvard Medical School, he trained in internal medicine and oncology at Massachusetts General Hospital, the National Cancer Institute and Yale before joining the faculty of The Rockefeller University. At Weill Medical College, he has served as founding director of the Tri-Institutional MD-PhD Program, senior associate dean for research and acting dean and presently directs the Milstein Program in Chemical Biology of Infectious Disease. A member of the Institute of Medicine of the National Academies of Sciences, a Fellow of the American Academy of Microbiology, a former Ellison Medical Foundation senior scholar in global infectious diseases and a Trustee of the Hospital for Special Surgery, he also serves as an advisor to the Cambridge University Institute for Medical Research, associate scientific director of the Cancer Research Institute and an editor of the Journal of Experimental Medicine.

Research in Nathan's lab has contributed to an integrated immunologic and biochemical picture of how macrophages protect the host from intracellular microbial pathogens and how some microbes persist. He first established that lymphocyte products activate macrophage bactericidal pathways, identified interferon- $\gamma$  as the first macrophage-activating cytokine in vitro and in humans, helped move it into the clinic, and identified TGF- $\beta$  as the first immunosuppressive cytokine. Simultaneously with Marletta, Nathan's lab discovered the roles of tetrahydrobiopterin, NADPH, O<sub>2</sub>, FAD and FMN in NO synthesis, findings essential for the purification of NO synthases. His lab first purified iNOS, cloned and named iNOS and identified its unprecedented Ca<sup>2+</sup>-independent binding of calmodulin, accounting for its high-output state. Their generation of iNOS-deficient mice allowed recognition of the enzyme's contrasting roles in septic shock and host defense, including control of experimental tuberculosis. Studying patients with tuberculosis, Nathan first documented expression of iNOS in human macrophages. Turning to how *Mycobacterium tuberculosis* persists in the face of immunity, Nathan and colleagues discovered unexpected enzymatic pathways by which the pathogen resists oxidative and nitrosative injury, including the bacterial proteasome, the nucleotide excision repair system and a peroxidase/peroxynitrite reductase that shares subunits with pyruvate dehydrogenase. His lab has developed novel inhibitors of these enzymes, including the first compounds that selectively kill non-replicating bacteria and the first inhibitors selective for a bacterial proteasome.