Research Interests

Nathan’s research deals with the immunological and biochemical basis of host defense. He established that lymphocyte products activate macrophages, that interferon-gamma is a major macrophage activating factor, and that mechanisms of macrophage antimicrobial activity include induction of the respiratory burst and inducible nitric oxide synthase (iNOS). He and his colleagues purified, cloned, knocked out and characterized iNOS biochemically and functionally, discovered the cofactor role of tetrahydrobiopterin in NOS’s and introduced iNOS as a therapeutic target. Although iNOS helps the host control Mycobacterium tuberculosis, the leading cause of death from bacterial infection, Mtb resists sterilization by host immunity. Nathan’s lab now focuses on the biochemical basis of this resistance. Genetic and chemical screens have identified enzymes that Mtb requires to survive during non-replicative persistence, including the mycobacterial proteasome and components of pyruvate dehydrogenase that serve in peroxynitrite reductase. His group is identifying compounds that kill non-replicating bacteria while testing new collaborative models between academia and industry to help invigorate antibiotic research and development.

References

