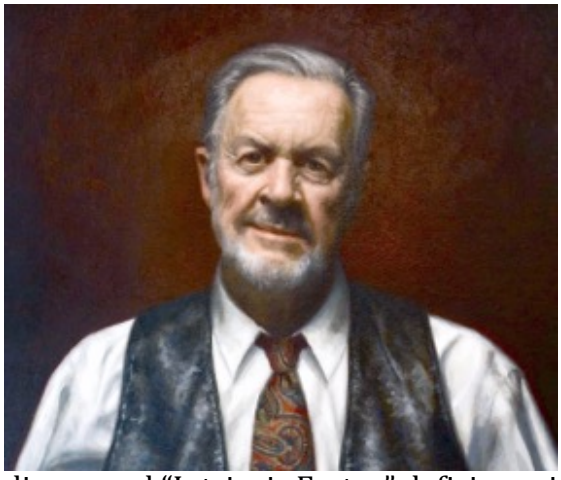
Charles (Cash) McCall, MD. Professor of Internal Medicine, Translational Science, and Microbiology and Immunology, embarked on his now 50th-year of discovery in leukocyte biology and acute inflammation as an Infectious Diseases Fellow with the late Maxwell Finland, Professor of Medicine, Harvard Medical School, and a founder of the Infectious Diseases Society of America. McCall's first publication on leukocytes in 1969 was based on a patient who died of sepsis. "Lysosomal and Ultrastructural Changes in Human 'Toxic' Neutrophils during Infection" was co-authored with his two mentors: Finland and Ramzi Cotran, a pioneer in inflammation research and renowned Mallory Professor of Pathology at Harvard's Brigham and Women's Hospital. These two leaders are his academic career heroes, along with Harvard's renowned hematologist William B. Castle, MD, who discovered "Intrinsic Factor" deficiency in pernicious anemia.



Passionately pursuing leukocyte biology and the molecular basis of acute systemic inflammation, with its scourge of high morbidity and mortality sepsis, Cash has 47 continuous years of NIH RO1 funding. His discoveries began with "toxic" neutrophil microscopy and physiology; the role of neutrophil NADPH oxidase in neutrophil bactericidal function; and how phospholipases and arachidonic acid metabolites 'prime" phagocytes to accentuate inflammation.

He then transitioned to molecular biology, discovering neutrophil gene expression and NFkB p65 and RelB transcriptional reprogramming of endotoxin tolerance. He and his colleagues learned that the NAD+-sensing, nuclear Sirtuins 1 and 6 and mitochondrial Sirtuin 3 coordinate monocyte immunometabolic and bioenergy responses during acute inflammation; this epigenetic and post-translational network is dysregulated during sepsis-associated immune repression and multi-organ failure. Crucially, his research team recently showed that inhibiting Sirtuin 1 during the immune-repressive sepsis state restores immunometabolic homeostasis and rescues mice from death.

Cash now studies two novel concepts about how sepsis might dysregulate the Krebs cycle and its providing reducing agents for mitochondrial respiration fueling; and imbalance the oxidation of cysteine thiols on key inflammation regulators. These two processes rob both failing organs and anabolic pathways needed to restore homeostasis and resolve sepsis. He is planning a clinical trial that aims to restore mitochondrial bioenergetics and balance catabolism and anabolism during sepsis.

Cash received his MD (1961) at Wake Forest Medical School and clinical and research training at the Harvard Medical Services and Thorndike Memorial Laboratory at Boston City Hospital. He has spent his 48-year academic career at Wake Forest, supported by NIH funded for 47 consecutive years. He has mentored many MD and PhD students, post-doctoral trainees, and young faculty. He served as Dean of Research, Interim Chair of Microbiology and Immunology, and Vice-chair for Research in the Department of Internal Medicine. He launched the Sections on Infectious Diseases and Molecular Medicine and was the first Director of the Wake Forest University Translational Science Center. A member of the American Society of Clinical Investigation, American Association of Physicians, Infectious Diseases Society of America, and Society for Leukocyte Biology, he still works full time in research and mentoring at Wake Forest.