Linda McPhail, Ph.D.

In a research career spanning over 40 years, Dr. McPhail's laboratory focused on the biochemistry underlying the respiratory burst of neutrophils. She began her career as a graduate student in the laboratory of Dr. Larry DeChatelet, where her work showed that the enzyme activated in neutrophils by invading microorganisms was a membrane-associated NADPH oxidase. During a postdoctoral fellowship with Dr. Richard Johnston, Jr. and her first faculty position with Dr. Ralph Snyderman, she established the concept that activation of NADPH oxidase used stimulus-dependent second messenger pathways, involving signaling lipids and calcium. This led to the development of a cell-free system for NADPH oxidase activation, using anionic signaling lipids, such as arachidonic acid and phosphatidic acid. This cell-free system was an invaluable tool that ultimately allowed the identification of NADPH oxidase as a multi-component system, consisting of both cytosolic and membrane proteins, which assembled in the membrane to form an active enzyme. Her laboratory at Wake Forest University School of Medicine (formerly Bowman Gray School of Medicine) continued the study of signaling pathways responsible for NADPH oxidase activation. She and her collaborators discovered that a phospholipase D was stimulated in neutrophils during the respiratory burst. Further, her work showed that the product of phospholipase D, phosphatidic acid, and another signaling lipid, diacylglycerol, directly interacted with NADPH oxidase components to induce conformational changes and enzyme activation. Her most recent work found that $p22^{phox}$, the small subunit of the NADPH oxidase membrane component, flavocytochrome b_{559}, is regulated by phosphorylation of a specific Threonine residue, Thr 147, and the phosphorylation promotes binding of the cytosolic component $p47^{phox}$. Her work would not have been possible without her many collaborations with colleagues and the contributions of her students and postdoctoral fellows. She is now enjoying retirement, but she is still enthralled by the NADPH oxidase family of enzymes.