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Research Interests:

Dr. Wood's laboratory is studying cholesterol regulation in brain, the role of cholesterol in cell structure and function, its involvement in neurodegenerative diseases, and mechanisms of neuroprotection afforded by cholesterol lowering drugs. Cholesterol plays many roles in brain and it is required for optimal functioning. As with cholesterol outside of brain, regulation of this molecule in brain can go awry as demonstrated most pointedly in human malformation syndromes of inborn errors of cholesterol synthesis and Niemann-Pick type C disease. Furthermore, there is evidence suggestive of cholesterol being a factor in neurodegenerative diseases such as Huntington's disease, Alzheimer's disease, and pathophysiology occurring with increasing age. Innovative findings from this lab have been on the regulation of cholesterol membrane domains, cholesterol trafficking, and transcriptional regulation of the cholesterol transport protein apoE. Regarding neuroprotection, a major discovery of this lab was that the cholesterol/isoprenoid lowering drugs statins stimulated gene expression and protein levels of Bcl-2, an anti-apoptotic gene/protein. Ironically, this effect of statins did not involve isoprenoids or cholesterol but instead was induced by endothelin-1 and the transcription factor NFATc3. Our statin studies lead to the realization that while much discussion had occurred regarding isoprenoids there were no reliable data on levels or their regulation in brain. We made the novel discovery that farnesyl pyrophosphate (FPP), a major player in the HMG-CoA reductase pathway and a precursor of cholesterol was increased in brain tissue of Alzheimer's disease patients as was gene expression of FPP synthase whose product is directly involved in FPP synthesis. This work has generated the hypothesis that FPP is independently regulated from cholesterol and that FPP upregulation can increase protein prenylation resulting in loss of synaptic plasticity, a key feature of neurodegenerative diseases including Alzheimer's disease. Dr. Wood's group uses several different approaches (e.g., molecular and cellular biology, transgenic animal and cell lines) in understanding the impact of cholesterol and its family members on normal and pathological brain function.

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