Meet Our Editorial Board Member

Olivier Boutaud, Ph. D.

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Dr. Boutaud got his PhD in Molecular Pharmacology at the Université Louis Pasteur, Strasbourg, France. He moved to Vanderbilt University for a post-doc in 1994 and became a Faculty in the Department of Pharmacology at Vanderbilt in 1998. He is now Research Associate Professor of Pharmacology.

His research area includes the mechanism by which prostanoids, small molecules generated by enzymes called cyclooxygenases, are involved in pathological processes.

Dr. Boutaud demonstrated for the first time that γ -ketoaldehydes are generated by the cyclooxygenases during their normal catalytic cycle [1, 2]. Dr. Boutaud further led the effort in characterizing the structure of DNA adducts [3] and demonstrated that the formation of γ -ketoaldehyde adducts on histones led to destabilization of the histone-DNA interactions [4]. Dr. Boutaud discovered that the formation of covalent adducts between γ -ketoaldehydes and amyloid β leads to increased amyloid β oligomerization [5] and formation of neurotoxic oligomers [6]. Because of the implication of this discovery for Alzheimer's disease, he showed that the levels of γ -ketoaldehydes in hippocampus from patients with AD were significantly increased compared to healthy aged-matched patients [7]. In collaboration with another group, Dr. Boutaud has developed scavengers of γ -ketoaldehydes that do not inhibit the cyclooxygenases [9]. I also have characterized pharmacokinetic in rodents for two of them [10, 11]. This work provides evidence supporting the use of reactive aldehydes' scavengers to treat diseases associated with oxidative stress/inflammation.

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Another field of interest for Dr. Boutaud is the study of acetaminophen mechanism of action. He characterized the molecular mechanism by which acetaminophen inhibits the cyclooxygenases. His first publication in this field demonstrated that acetaminophen works not as an inhibitor of the cyclooxygenase site, as do most of the other NSAIDs, but as a reductant of the heme in the peroxidase site [12]. This discovery was key for understanding the pharmacological profile of this drug and initiated a series of papers demonstrated that the peroxide tone in the environment of the enzymes also affected how salicylate and aspirin work [13]. This work culminated in showing that in metabolic syndrome patients with diabetes, a condition with high oxidative stress, aspirin was much less effective in inhibiting platelet function than in subjects with lower oxidative stress [14]. His work on myoglobin was the basis for showing that acetaminophen protects the kidney from injury following rhabdomyolysis *in vivo* [15]. Following this line of thoughts, he has also shown that cytochrome c-catalyzed oxidation of mitochondrial cardiolipin is inhibited by acetaminophen [16]. This work led to the concept that hemeprotein reductants could be used *in vivo* to treat conditions associated with preoxidase-dependent lipid peroxidation, such as rhabdomyolysis, malaria, sickle cell disease, *etc.* For this reason, Dr. Boutaud has developed analogs of acetaminophen that are more efficacious and less toxic [17]. This work also led Dr. Boutaud to make the seminal discovery that cardiolipin fatty acid composition regulates electron entry in the respiratory chain in the mitochondria [18].

He characterized that the inhibitory phenotype was determined by the PGE₂ receptor subtype 4 and that the potentiating phenotype was determined by the PGE₂ receptor subtype 3 [19, 20].

SELECTED PUBLICATIONS

Over 70 research article, reviews and book chapters.

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