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Biosketch

Dr. Paul B. Watkins is director of the University of North Carolina Institute for Drug Safety Sciences. He is also Professor of Medicine, Pharmacy, and Public Health at the University of North Carolina, Chapel Hill. Dr. Watkins is a trained clinical hepatologist and also an accomplished basic and translational investigator in the fields of drug metabolism and hepatotoxicity. He serves as the chair of both the Steering and Genetics Committees for the U.S. Drug-Induced Liver Injury Network (DILIN) (U01DK065201). He also directs the DILIsim Initiative, which is a public-private partnership involving scientists from 13 major pharmaceutical companies and the FDA. Dr. Watkins is one of the most frequently cited authors in the field of pharmacology according to *www.ISIhighlycited.com.* He is the recipient of numerous honors and awards including the 2009 Therapeutic Frontiers Award from the American College of Clinical Pharmacy, the 2013 Agilent Thought Leader Award, and the 2015 Rawls-Palmer Award for Progress in Medicine from the American Society for Clinical Pharmacology and Therapeutics.

Abstract: Application of novel biomarkers to assess liver safety in clinical trials

The most problematic form of DILI is the delayed and sudden onset of hepatocellular injury that appears to often involve an adaptive immune attack on the liver. It is now believed that there are a series of steps that must occur to "prime" the liver for an adaptive immune attack due to a drug. These steps include stress or death of hepatocytes, creation of a neoantigen on the surface of hepatocytes, release of damage associated molecular patterns (DAMPS) within the liver, and activation of innate immune cells (e.g. Kupffer cells). There are now blood-based biomarkers that show great promise to identify several of these steps when they occur in subjects in clinical trials, including distinguishing hepatocyte apoptosis from necrosis, detecting release of DAMPS, and detecting activation of innate immune cells. These new biomarkers are now being applied to early clinical trials of new drug candidates and data obtained with these biomarkers have been used in regulatory submissions.