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Application of Omics biomarkers for assessing cellular toxicity: Integration of *In vivo* and *In vitro* data

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Abstract

Humans are exposed to combinations of chemicals and drugs on a daily basis and toxic interactions between these agents are a common phenomenon. Challenges to the toxicology community are to predict possible interactions at an early stage so that toxic events may be avoided or attenuated using rapid cost –effective methods. Molecular (omic) biomarkers provide a useful approach but validation measures are required for interpretation and computer modeling methods are needed to integrate omic biomarker data across the various levels of biological organization so that these data may be reasonably used for human risk assessment purposes. This presentation will focus on addressing these issues using the binary semiconductor compounds gallium arsenide (GaAs) and indium arsenide (InAs) as model test compounds under in vivo exposure conditions of hamsters. In vitro exposure studies were conducted kidney cells of both male and female hamsters and humans. Proteomic biomarkers were evaluated by 2-D gel electrophoresis (2-DGE). Overall the results of these studies indicated that InAs was more toxic than GaAs by 2-DGE of hamster urinary protein patterns visualized by silver staining. Computerized image analysis of proteomic responses of kidney cells following in vivo exposure of hamsters and in vitro exposure studiesshowed marked response differences between males and females for both human and hamster kidney cells. Taken together, these data suggest an approach for early identification of cell injury that could be integrated into human risk assessments by identifying gender differences in responsiveness at equal exposure levels of chemicals or doses of pharmaceuticals on an individual or mixture basis. Further computerized extrapolation modeling of these types of data should facilitate improved animal-human and in vitro – in vivo mode of action risk assessment extrapolations for humans.

Biography

B.S. degree in Fisheries (Marine Biology) from the University of Washington in 1968 and a Ph.D. in Pathology from the University ofOregon Medical School in 1972. He was a staff scientist at the National Institute of Environmental Health Sciences from 1972 until 1987 when he became Director of the University of Maryland System -wide Program in Toxicology and Professor at the University Of Maryland School Of Medicine. He was a Senior Research Advisor to the Agency for Toxic Substances and Diseases Registry (ATSDR) in the Division of Toxicology 2002-2003 and Associate Director for Science in the Division of Toxicology and Environmental Medicine at ATSDR 2003-2011. He joined ICF International in 2011 as a Senior Fellow. Dr. Fowler is an internationally recognized expert on the toxicology of metals and chemical mixtures including persistent organic pollutants such as the dioxins. He has served on a number of State, National and International Committees in his areas of expertise including those of the NAS/NRC, WHO and IARC and has been a Fellow of the Japanese Society for the Promotion of Science, a Fulbright Scholar and Swedish Medical Research Council Visiting Professor at the Karolinska Institute, Stockholm, Sweden. He is a Fellow of the Academy of Toxicological Sciences and a member of the AAAS Recruitment and Screening Committee for the Court Appointed Scientific Experts (CASE) Demonstration Project. Dr. Fowler is the author of over 200 research papers / book chapters and editor/co-editor of 7 books dealing with molecular mechanisms of toxicity and molecular biomarkers for early detection of chemical-induced cell injury and cell death. Most recently, he has focused on the application of computational toxicology methods for risk assessment.