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Epigenetic mechanisms in pharmacological drug discovery and toxicity studies to predict the pathogenesis of human diseases in the era of Precision Medicine and of the global metabolic disease crisis

'ithin global concerns of "metabolic diseases", exposures to radiations, chemicals and microbial agents, the ineffective toxicological tests, the costly animal tests, governmental restrictions on animals for drug discovery and toxicity testing, new strategies are needed to reduce and treat these acute and chronic diseases. There is no universally acceptance of the mechanisms by which radiations, chemicals and microbial agents might contribute to the pathogenesis, prevention and treatment of human diseases. Moreover, the emphasis on "Precision" or "Personalized" Medicine, together with the availability of sophisticated molecular technologies, is starting to generate tons of data, only to be analyzed by non-biologically-based algorisms. When humans are exposed to any pharmacological or toxic agent, there are only three mechanisms of responses: (a) mutagenesis by either "errors of DNA repair" or "error of DNA replication"; (b) cytotoxicity by necrosis, apoptosis, autophagy; and (c) epigenetic alteration of gene expression at the transcriptional, translational or posttranslational levels. While mutagenesis can affect human health, only UV radiation is an effective point mutagen, while ionizing radiation is a powerful chromosomal mutagen and viruses can be insertion mutagens. One needs to realize that there are three different cell types: stem cells, their progenitors and the terminally differentiated cells, each with different responses to these agents. While very controversial, it will be postulated that, even though many chemicals can



induce oxidative stress, most natural and synthetic chemicals, that contribute to birth defects, cancer, cardiovascularimmunological-reproductive or neurological diseases, act as epigenetic toxicants. Those drugs and chemo preventive agents seem to act epigenetically to prevent or treat various diseases.

The current use of human adult, organ specific stem cells, grown in 3-dimension, will be shown to discover new drugs and to test for toxicities, based on their upstream epigenetic effects on either secreted- or gap junctional -intercellular communication.

## **Speaker Biography**

James E Trosko has completed his PhD at the age of 25 from Michigan State University, USA. He is a Distinguished Emeritus Professor at Michigan State University. He spent 3 years as a postdoctoral fellow at Oak Ridge National Laboratory under Ernest Chu; Sheldon Wolff and Richard Setlow. After joining Michigan State University, he obtained an NCI- Career Development award; spent one year at the McArdle Lab for Cancer Research at the University of Wisconsin under Van R. Potter. Later he was Chief of Research at the Radiation Effects Research Foundation for two years in Hiroshima and Nagasaki, Japan. He spent 2 years at Seoul National University as a Korean "World Class University Professor". He also spent one year at the ARNAS-Civico-Regional Cancer Hospital in Palermo, Sicily. He has over 450 publications that have been cited over 17,000 times, and his publication H-index is 62.

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