Keynote Forum
November 01, 2017

Toxicology Conference 2017

International Conference on

Toxicology and Pharmacology

November 01-02, 2017 | Toronto, Canada

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Manuela G Neuman

University of Toronto, Canada

Drugs of misuse and therapeutics a deadly combination

Alcohol consumption remains a significant risk factor for the development of liver damage in patients being treated with pegylated interferon (PEG-IFN-α), in the presence or absence of ribavirin as well the protease inhibitors for viral hepatitis B, C (HBV, HCV) and human immunodeficiency viral infections (HIV) or HCV-HIV. The daily alcohol consumption of >60 mg/day provides a significant risk factor for the development of cirrhosis, hepatocellular carcinoma and the increased risk of mortality. This applies to treatments that used a variety of the non-nucleoside reverse transcriptase inhibitor class. Severe hepatotoxicity [defined as AST or ALT being at >5 upper limit of normal] is also seen in patients who are co-infected HIV/HCV and are being treated with indinavir, nelfinavir, ritonavir, saquinavir, or ritonavir plus saquinavir. In highly active antiretroviral therapies (HAART) that included PI-based, NNRTI-based, and PI- plus NNRTI-based therapies, alcohol abuse is an identified risk factor for the drug-induced liver injury (DILI). Alcohol misuse and over the counter drugs (sulphonamides, antipyreticsor anti-inflammatory) may lead to DILI and liver transplant. Also misuse of illicit drugs in the presence or absence of alcohol lead to drug-induced liver injury.

Speaker Biography

Manuela G Neuman is Adjunct Professor of Pharmacology and Toxicology, Associated Global Health at the University of Toronto, and a Professor at the Carol Davila University of Medicine and Pharmacy (UMF), Bucharest. She is the Founder and CEO of In Vitro Drug Safety and Biotechnology, Toronto. She holds an MSc in Biology from University of Bucharest, a Post-doctoral Fellowship from the Institute of Inframicrobiology, Faculty of Medicine, Bucharest, PhD in Physiology and Pharmacology from Tel-Aviv University. She also completed her Post-doctoral fellowship in Clinical Chemistry, Hepatology, Immunology, Gastroenterology and Clinical Pharmacology at the University of Toronto, Toronto, Canada. Her research was in the Department of Biochemistry and in the Chemotherapy Institute, while she acted as a Biochemist at the "Victor Babes" Hospital in Bucharest. In these positions of pharmaceuticals, she had "hands on" daily routine, as well as, acting as a Laboratory Scientific Director making liaison between the laboratory and drug discovery platforms and translational research. She has published extensively in the areas of therapeutic and drug of (use and misuse) monitoring, new biologic and their monitoring in clinical practice, pharmacogenetic and immunopharmacogentic clinical applications, drug-induced liver and skin adverse reactions, liver immunology, hepatocellular carcinoma and inflammatory bowel disease. Since 1992, she is a member of the IATDMCT.

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M Reza Khorramizadeh

Tehran University of Medical Sciences, Iran

Assessment of inhibitory effects of Ficin-hydrolyzed gelatin derived from squid (*Uroteuthis duvauceli*) on breast cancer cell lines and animal model

Marine novel natural products have been applied for cancer therapies. Enzyme-digested gelatin hydrolysates have proven to serve as promising sources of potent biologically active peptides. Potential anti-breast cancer properties of the extracted Ficin-digested gelatin hydrolysate from Indian squid (*Uroteuthis duvauceli*) extensively characterized by cellular and animal models. Gelatin was extracted from squid skin, hydrolyzed by Ficin, and characterized by standard physio-chemical methods. Ficin-digested gelatin hydrolysate was used at various doses of 0-0.1 mg/mL for treatments of MCF-7 and MDA-MB-231 breast cancer cells versus HUVEC normal cells. Cytotoxicity, phase-contrast morphological examination, apoptosis/necrosis, clonal-growth, cell-migration, Matrix-metalloproteinases (MMPs) zymography, and Western blotting were used for cellular assessments. For animal studies, breast tumor-induced BALB/c mice received hydrolyzed gelatin regimen, followed by tumor size/growth and immune-histochemical analyses. Significant inhibition of MCF-7 and MDA-MB-231 with no cytotoxicity on HUVEC cells was detected. Apoptosis was increased in cancer cells, as revealed by elevated ratio of cleaved caspase-3 and PARP. MMP-2 and MMP-9 activities in both cancer cells were dramatically diminished. In mice, gelatin hydrolysate prevented weight loss, decreased tumor size, induced p53, and down-regulated Ki67 levels. These findings suggest that Ficin-digested gelatin hydrolysate could be a beneficial candidate for novel breast cancer therapies.

Speaker Biography

M Reza Khorramizadeh, is a Full Professor at Tehran University of Medical Sciences (TUMS), directs Biosensor Research Center and newly instituted Zebra fish Core Lab at Endocrinology and Metabolic Molecular-Cellular Sciences Institute. Concurrently, he is a 2nd affiliation to the Dept. of Medical Biotechnology, School of Advanced Technology in Medicine, TUMS.

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November 02, 2017

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Beatrice Setnik

INC Research, Canada

First-in-human studies – An examination of the evolving regulatory and clinical practices to ensure subject safety

First-in-human studies are a key milestone in drug development. In such studies, a drug already tested in a preclinical setting (*in vitro*, animals) is tested in humans for the first time. Study participants, who are often healthy volunteers, face an element of risk as the ability to predict the effects in humans is limited. In recent history, albeit in rare cases, study subjects have experienced serious harm in such trials. Regulatory guidelines have evolved following such events to ensure the safety and well-being of study subjects, and most recently in 2017 the European Medicines Agency (EMA) has revised its guidance on first-in-human trials. The revised guidance includes additional strategies to mitigate and mange risks for study subjects, including guidance for the calculation of the starting dose, rules for subsequent dose escalation and the criteria for establishing the maximum dose. The guidance also provides criteria to stop a study, review emerging data and handling of adverse events in relation to the study stopping rules. Over recent years, first-in-human studies have become increasingly complex and include multiple parts such as single-dose ascension, multiple-dose ascension, food interactions, different age groups or gender, proof of concept, or relative bioavailability of different formulations. As such data generated during the course of the trial should be carefully reviewed and used to inform the decision to initiate a subsequent study part or to inform the selection of the doses to be evaluated. This session will discuss the evolving requirements for conducting first-in-human studies and will focus on the key regulatory and clinical considerations in ensuring subject safety.

Speaker Biography

Beatrice Setnik has been working in the area of CNS research, clinical drug development and abuse potential assessment for over 16 years and is an expert in the area of abuse liability evaluation. She is currently the Vice President of Scientific and Medical Affairs at INC Early Phase and an Adjunct Professor with the Department of Pharmacology and Toxicology at the University of Toronto. She earned her Doctorate degree in Pharmacology and the Collaborative Program in Neuroscience from the University of Toronto in 2005.

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Rui Wang

Laurentian University, Canada

To live or to die – H_2S causes the both

Known as a rotten egg gas, hydrogen sulfide (H_2S) can cause human intoxication and death at high concentrations, which is a major life-threatening risk for oilers or city sewage workers. Catastrophically accumulated H_2S gas was also responsible for the biggest life extinction on Earth that killed 95% of all life species on Earth, the end-Permian extinction. Research conducted by my team as well as others over last decades has revealed, however, the critical importance of H_2S to the homeostatic regulation of human health. In this talk, I will highlight some most promising and intriguing discoveries in H_2S toxicology and biology, including the toxicological profile of H_2S, the roles of H_2S in the regulation of blood pressure, ion channel functions, and mitochondrial bioenergetics. H_2S is a silent killer whereas in the meantime we cannot live without it.

Speaker Biography

Rui Wang has completed his MD in China and PhD in Canada. He was the Vice-President of Research of Lake Head University, Canada from 2004-2014. He has served Laurentian University as Vice-President Research since 2015. He has published 267 peer-reviewed papers on the studies of gasotransmitters, including hydrogen sulfide and carbon monoxide that have been cited over 20,100 times. He has also served on the expert panel for toxicological profile for hydrogen sulfide and carbonyl sulfide for US Department of Health and Human Services, Public Health Service, and Agency for Toxic Substances and Disease Registry in 2013.

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