EuroSciCon

# DAY 1

## Scientific Tracks & Abstracts

Euroscicon Conference on

# MEDICINAL CHEMISTRY AND BIOSIMILARS

March 25-26, 2019 | Budapest, Hungary

# DAY 1

March 25, 2019

## Sessions

Medicinal Chemistry | Drug Design and Drug Development | Pharmaceutical Chemistry | Computer Aided Drug Design (CADD) | Pharmaceutical Sciences | Molecular and Cellular Pharmacology | Novel Target Drugs to the Treatment of Cancer | Biosimilars Development Programme | Monoclonal Antibody Biosimilars | Globalization of Biosimilars

**Session Chair**
**Thomas D Bannister**
The Scripps Research Institute, USA

**Session Co-Chair**
**Soliman Khatib**
MIGAL-Galilee Research Institute, Israel

*Session Introduction*

**Title:** Biomimetic HPLC property measurements to estimate human *in vivo* distribution and tissue binding of drug discovery compounds
**Klara Valko,** Bio-Mimetic Chromatography Ltd, UK

**Title:** SynSpace: A design platform to expand synthetically-enabled scaffold and lead analogue space for medicinal chemistry and AI-assisted drug discovery
**Gergely Makara,** ChemPass Ltd, Hungary

**Title:** Monoclonal antibodies: Their adverse effects and costs
**H Zafer Guney,** Gazi University Medical School, Turkey

**Title:** Reducing cardiovascular disease (CVD) risk using agents which elevate PON1 activity and improve HDL quality
**Soliman Khatib,** MIGAL-Galilee Research Institute, Israel

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Klara Valko, Der Pharmacia Sinica 2019, Volume:10
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# BIOMIMETIC HPLC PROPERTY MEASUREMENTS TO ESTIMATE HUMAN *IN VIVO* DISTRIBUTION AND TISSUE BINDING OF DRUG DISCOVERY COMPOUNDS

**Klara Valko**[1,2]

[1]Bio-Mimetic Chromatography Ltd, UK
[2]UCL School of Pharmacy, UK

**Biomimetic HPLC stationary phases such as immobilized artificial membrane (IAM), human serum albumin (Chiral-HSA) and α-1-glycoprotein (Chiral-AgP) are able to mimic the *in vivo* interactions of the drug molecules to lipids and proteins. The calibrated retention times obtained on the biomimetic HPLC stationary phases can be used to build models for *in vivo* tissue-plasma partition, unbound volume of distribution, drug efficiency, and cellular concentration without using animal experiments. The measurements can be fully automated and large number of compounds can be ranked for further studies for the fraction of the cost of *in vivo* experiments. The methodology can be applied for new modalities in drug discovery such as peptides that would be difficult to characterize by traditional methods such as equilibrium dialysis to estimate their tissue binding and volume of distribution. Comparison of IAM partition and membrane disruption of antibiotic peptides has been investigated in order to predict their interactions with lipids. The chromatographic retention of potential drug molecules on biomimetic stationary phases can mimic their *in vivo* binding to lipids and proteins that was validated using human clinical data of over 150 known drug molecules.**

## Biography

Klara Valko has completed his PhD from Semmelweis University and Postdoctoral studies from Yale University, CT, USA. After working at GSK for 22 years, currenty, she is the Director of Bio-Mimetic Chromatography Ltd, providing consultations and measurement services for biotech companies involved in drug discovery. She is also an Honorary Professor at UCL School of Pharmacy where she teaches the Physchem/ADME module for Drug Discovery and Pharma Management master course. She has published more than 100 papers in reputed journals and has been serving as an Editorial Board Member of ADMET & DMPK journal. She is a Fellow of the Royal Society of Chemistry.

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# SYNSPACE: A DESIGN PLATFORM TO EXPAND SYNTHETICALLY-ENABLED SCAFFOLD AND LEAD ANALOGUE SPACE FOR MEDICINAL CHEMISTRY AND AI-ASSISTED DRUG DISCOVERY

**Gergely Makara, Gabor Pocze, Laszlo Kovacs, Anna Szekely and Istvan Szabo**

ChemPass Ltd, Hungary

**Despite significant advances in our understanding of the biological basis of diseases, pharmaceutical R&D is struggling to sustain the level of productivity and efficiency it reached in the second half of the 20th century. High failure rates and the increasing cost of drug discovery as well as extended research and development timelines hinder the development of medicines. Due to these challenges there has been an increasing need for substantial innovations in the pharmaceutical sector. It has been shown that if the selection of the synthetic targets in lead optimization cycles is supported by QSAR or deep learning methods, the number of compounds synthesized as well as the cycle time for each iteration can be significantly reduced. We have developed a rule-based artificial intelligence technology that can produce a large number of novel and synthetically-enabled lead analogues and scaffold hopping designs around lead structures. Since its introduction, the cloud-based SynSpace software has been found by multiple organizations to generate a larger number of relevant novel ideas around leads than medicinal chemist teams can do. Thus, SynSpace is a valuable addition to the medicinal chemistry toolbox. We have also been developing automated lead analysis tools that-in conjunction with SynSpace-can automatically carries out scaffold hopping and lead analogue idea generation and thereby offer large sets of novel and project specific lead-like structures to advanced AI platforms for selection. These platforms have the biggest impact on a number of key parameters in drug discovery: cycle time, number of discovery cycles, the number of compounds to be synthesized and coverage of IP space. Improvements in these factors can be converted into higher success rates and major resource savings towards a more economical and productive candidate development phase.**

## Biography

Gergely Makara has completed his PhD in medicinal chemistry at SUNY at Buffalo in 1996 and his postdoctoral studies in medicinal chemistry and molecular modelling with Garland Marshall at the Center for Molecular Design at Washington University at St. Louis in 1998. Since then he has spent 20 years in the pharmaceutical industry, most of it in leadership levels at Neogenesis Pharmaceuticals (Boston, USA), Merck & Co. (Rahway, USA), AMRI Hungary (Hungary), ComInnex (Hungary) and ChemPass (Hungary). His expertise includes organic synthesis, medicinal chemistry, fragment-based drug discovery, drug design, and cheminformatics. He has published more than 30 papers in reputed journals and has contributed to 10 patent applications.

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# MONOCLONAL ANTIBODIES: THEIR ADVERSE EFFECTS AND COSTS

## H Zafer Guney, Ozlem Celik Aydin and Demet Kasim

Gazi University Medical School, Turkey

An important way the immune system copes wih foreign substances in the body, is making large numbers of antibodies. Antigens are molecules that are able to stimulate an immune response. Each antigen has distinct surface features, or epitopes, causing specific responses (Goodman&Gilman's The Pharmacological Basis of Therapeutics, 12th Edition). Antibodies (immunoglobins) are proteins produced by B cells of the immune system in response to exposure to antigens. The term monoclonal antibody means that the man-made antibody is synthesized from cloned immune cells, and the identical monoclonal antibody produced binds to one type of antigen. Polyclonal antibodies are synthesized from different immune cells and the antibodies produced bind to multiple antigens. The monoclonal antibodies are present in the market for a long time. Their indications and use are continuing to expand. Since monoclonal antibodies have been approved for the treatment of various diseases like chronic lymphocytic leukemia, ovarian cancer and other solid tumors, rheumatoid arthritis, ovarian cancer, Chron's disease, Plague Psoriasis, Psoriatic Arthritis, Ankylosing Spondilitis etc (www.medicinenet.com, Basic&Clinical Pharmacology, Lange 14th Edition) the incidence of these drugs' adverse effects and the cost is growing. If monoclonal antibodies are compared with chemotherapy drugs, they have fewer serious side effects. As a result, their adverse effects continue to constitute an important problem. I will talk about the prominent side effects and the cost of the therapy. I will also discuss with the audience the future of monoclonal antibody treament.

### Biography

Hakkı Zafer Guney is a medical doctor and professor of pharmacology. He has completed his medical training in Ankara University Medical School, and speciality training in Gazi University Medical School, Ankara. Beyond being a professor of Pharmacology, he is also the president of the society of biotechnological drugs (BIYILDER) in Turkey since 2018. He has a company on drug R&D (RD Consultancy Ltd.) in Ankara. He has several publications and citations in international and national journals. He has also been serving as an Editorial Board Member and referee in several international journals. He is into several fields (clinical trials, pharmacovigilance, pharmacoeconomics) of clinical pharmacology.

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# REDUCING CARDIOVASCULAR DISEASE (CVD) RISK USING AGENTS WHICH ELEVATE PON1 ACTIVITY AND IMPROVE HDL QUALITY

**Soliman Khatib**
MIGAL-Galilee Research Institute, Israel

**Atherosclerosis is a chronic disease that is characterized by accumulation of lipids and oxidized lipids within the intima of the arterial wall. It is the usual cause of heart attacks, strokes, and peripheral vascular which all together called cardiovascular disease (CVD). Lowering low density lipoprotein (LDL) levels in the circulation using statins therapy has become an integral strategy to reduce CVD risk. However, statins reduce CVD event rates by has a central role in atherosclerosis inhibition due to its anti-atherogenic properties such as, reverse cholesterol transport (RCT), antioxidant, anti-inflammatory and endothelial function improvement. Epidemiological data, animal studies and clinical trials supports HDL as the next target to reduce CVD risk. However, some findings have called into question the hypothesis that pharmacological increase in HDL-cholesterol levels is necessarily promoting reduction of CVD events. Instead, recent studies indicate that the focus should be on improving HDL functions (HDL quality), which truly reflect its actual beneficial effects, rather than increasing HDL-C levels (HDL-C quantity). Our hypothesis is that natural agents with the potential to alter HDL proteomics and lipidomics can improve the atheroprotective effects and functions of HDL and may reduce CVD risk. In our laboratory a promising active compound from an ethanol–water (70:30%) extract of Nannochloropsis sp. Microalgae was isolated. The structure of the compound was determined to be lyso-DGTS lipid. Lyso-DGTS interacts with HDL proteins, enhances paraxonase 1 (PON1), protein that contribute to many of the atheroprotective effects of HDL and elevate many of the HDL activities such as, HDL mediated cholesterol efflux from macrophages, HDL ability to induce nitric oxide release from endothelial cells and HDL antioxidant and anti-inflammatory properties. Our findings suggest a beneficial effect of lyso-DGTS on improving HDL quality which may reduce atherosclerotic risk.**

## Biography

Soliman Khatib has completed his PhD from the Technion institute, Natural Science, Chemistry in 1996-2000. He has completed his BSC from Ben-Gurion University, Natural Science, Chemistry 1993-1995. Now he is a Researcher in the laboratory of oxidative stress, Migal-Galilee Research institute and a Senior Lecturer at Department of Biotechnology, Tel-Hai academic collage. His research focus on understanding the relationship between oxidative stress and diseases related to oxidative stress, identifying volatile organic compounds (VOCs) as early biomarkers for diseases related to oxidative stress; Isolation and identification of natural compounds for treating and preventing diseases related to oxidative stress such as, atherosclerosis, Parkinson and Alzheimer diseases. He has published more than 50 papers in reputed journals.

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