



# 17<sup>th</sup> EURO BIOTECHNOLOGY CONGRESS

September 25-27, 2017 Berlin, Germany

# Keynote Forum Day 1

Euro Biotechnology 2017

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## Denis Spitzer

*French-German Research Institute of Saint-Louis, France*

### **Spray flash evaporation for the continuous production of high performance nano-drugs: New challenges for a new disruptive process**

NS3E laboratory developed the Spray Flash Evaporation (SFE) for preparing drug nanoparticles at industrial scale. The process was several times patented up to now. The solution is kept in a pressurized tank separated from a vacuum chamber by a hollow cone nozzle, used both to heat and spray the liquid. The instantaneous evaporation of the solvent originates from the combination of the abrupt pressure drop and the high energy stored by the overheated solvent prior to nebulisation. The flash evaporation leads to small crystallites with narrow size distribution. The nanoparticles may be composed of single compounds, mixtures of several substances or co-crystals. In the domain of medicaments, co-crystals are of critical importance as they enhance bioavailability and up-take by the human body of Active Pharmaceutical Ingredients (API). Up to now, most used techniques are of batch nature and are not able to give access in big amounts to nano-sized crystals or co-crystals of therapeutic interest. The SFE permits the continuous manufacturing of nano-sized co-crystals, in large amounts with a kinetic complying with the pharmaceutical industry's requirements. The efficiency of SFE is shown by the manufacturing of pure nano-medicaments but also of nano-co-crystals such as resveratrol/4-aminobenzamide (1/1), caffeine/oxalic acid (2/1) and caffeine/glutaric acid (1/1), with a mean particle size of between 30 and 100 nm. After showing the possibility to continuously nano-crystallize medicaments, the presentation will focus on different main challenges to further enhance the production capacity and also to understand the SFE process itself. Among different techniques and metrologies used or specially developed such as phase Doppler interferometry (Figure) and AFM-TERS spectroscopies, the presentation will also focus on different crystallization configurations used.

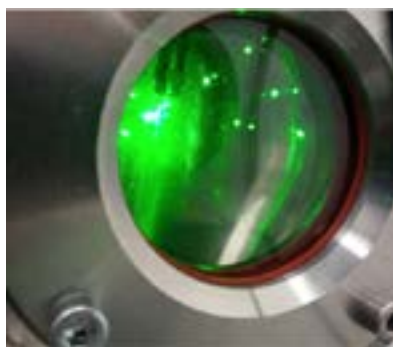


Figure: Phase Doppler interferometry for the on-line metrology

### **Biography**

Denis Spitzer received his PhD in Physical Chemistry in 1993 at University Louis Pasteur of Strasbourg. He is the founding and current Director of the NS3E Research Laboratory UMR 3208 ISL/CNRS/UNISTRA. He conducts research in continuous nano-crystallization processes of organic nanomaterials such as model medicaments and energetic materials. He is the inventor of the SFE process. He is the author of more than 150 publications and scientific reports.

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## *Elizabeth E Hood*<sup>1,2</sup>

<sup>1</sup>Arkansas State University, USA

<sup>2</sup>Infinite Enzymes, LLC, USA

### **Production of industrial enzymes in maize**

Industrial enzymes are excellent technologies to apply in manufacturing to alleviate environmental pollution. Using plant-based materials allows manufacturing of goods from renewable resources. My laboratory and company are engaged in producing enzymes for industrial applications using the plant seed system. The advantages of the seed system are that the production costs can be quite low because scaling-up just involves planting more acres, the seed can be stored for years, and the enzymes are extremely stable in the seed. We use maize grain to express enzyme genes from fungal and bacterial sources that have specific applications in biofuels, bioproducts and waste water remediation. Genes for these enzymes are partially codon optimized and their expression is driven by either an embryo or an endosperm promoter and targeted to one of three subcellular locations—the cell wall, the endoplasmic reticulum or the vacuole. Expressed enzymes include three cellulases, a phospholipase, a Mn peroxidase, and a laccase. Once the gene is expressed and a high-expressing event chosen, breeding into elite inbred germplasm commences. Applications of the various enzymes will be discussed along with regulatory considerations.

### **Biography**

Elizabeth E Hood has 35 years of experience in Biology. She is Distinguished Professor of Agriculture at Arkansas State University and; CEO of two biotechnology start-up companies—Infinite Enzymes, LLC and Infinite Eversole Strategic Crop Services, LLC. Previously, she was an Associate Vice Chancellor for Research and Technology Transfer at ASU; Program Director in Molecular and Cellular Biosciences at the National Science Foundation; Leader in forming one of the world's foremost transgenic plant research groups at ProdiGene, a plant biotechnology company. She has completed his PhD in Plant Biology at Washington University and MS in Botany awarded by Oklahoma State University.

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## Anli Geng<sup>1, 2</sup>

<sup>1</sup>BioEnergy Society of Singapore, Singapore

<sup>2</sup>Ngee Ann Polytechnic, Singapore

### Industrial biotechnology application in fuel and chemical production

Industrial biotechnology is a set of practices that use living cells (such as bacteria, yeast, algae) or component of cells like enzymes, to generate industrial products and processes. This presentation focuses on the application of industrial biotechnology in technology development for fuel and chemical production. The talk will cover industrial biotechnology application in the development of cellulolytic enzymes and metabolic engineering of yeast for the conversion of lignocellulosic biomass to fuels and chemicals. The conversion of oil palm empty fruit bunch, the main biomass resource in Southeast Asia, will be particularly discussed.

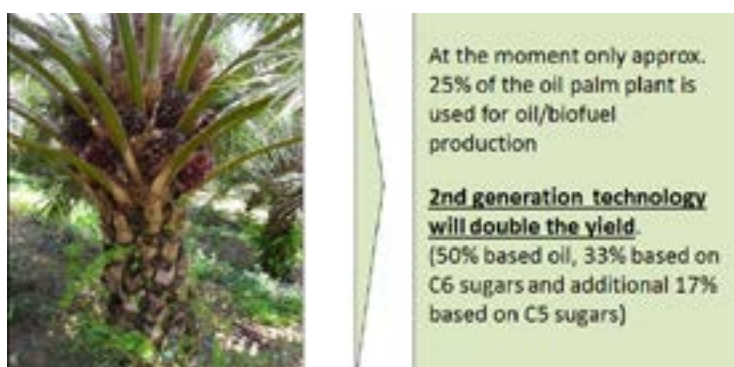


Figure 1: Utilization of oil palm biomass for fuel and chemical production

### Biography

Anli Geng is currently the Assistant Director of Life Sciences and Chemical Technology of Ngee Ann Polytechnic. She currently holds the President position at BioEnergy Society of Singapore (BESS) and she is also the Co-founder and Director of Sunvisiae Biotech Pte Ltd, a Singapore-based industrial biotechnology company. Prior to joining Ngee Ann Polytechnic, she was working at Institute of Environmental Science and Engineering (IESE) as a Research Scientist. She has more than 25 years of R&D experience, working extensively on environmental biotechnology, green energy technology and industrial biotechnology. She has more than 30 journal publications and her work has been presented in many international conferences. Her current research focus at Ngee Ann Polytechnic is developing novel microorganisms to produce industrial enzymes, chemicals and fuels, novel nutraceuticals and cosmetics ingredients. She obtained Ngee Ann Polytechnic Staff Excellence Award and IChemE Award on Sustainable Technology in 2012.

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### Notes:



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## Keynote Forum Day 2

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## Fuad Fares

University of Haifa, Israel

### Novel methods for designing long acting agonists and antagonists of glycoprotein hormones

One major issue regarding the clinical use of many peptides is their short half-life due to the rapid clearance from the circulation. To overcome this problem, we succeeded to ligate the signal sequence of *O*-linked oligosaccharides to the coding sequence of the hormones. The cassette gene that has been used contains the sequence of the carboxyl-terminal peptide of human chorionic gonadotropin  $\beta$  subunit. The CTP contains 28 amino acids with four *O*-linked oligosaccharide recognition sites. It was postulated that *O*-linked oligosaccharides add flexibility, hydrophilicity and stability to the protein. On the other hand, it was suggested that the four *O*-linked oligosaccharides play a significant role in preventing plasma clearance and thus increasing the half-life of the protein in circulation. Using this strategy, we succeeded to ligate the CTP to the coding sequence of follitropin, thyrotropin, erythropoietin, growth hormone and thus to increase the longevity and bioactivity of these proteins *in-vivo*. Interestingly, the new analogs of FSH and GH were found not immunogenic in human and it is already passed successfully clinical trials phase III and phase II respectively. Moreover, FSH long acting (ELONVA) was approved by the European Commission for treatment of fertility since 2010. In addition, our results indicated that long acting GH is not toxic in monkeys and the results from clinical trials phase I and phase II seem to be promising. Designing long acting peptides will diminish the cost of these drugs and perhaps reduce the number of injections in the clinical protocols. On the other hand, we found that deletion of N-linked oligosaccharides from hTSH subunits resulted in significant decreased in the bioactivity. Moreover, de-glycosylated variants of TSH compete with normal hTSH and human thyroid stimulating immunoglobulin in a dose dependent manner. Thus, this variant, behaves as potential antagonist, that may offer a novel therapeutic strategy in the treatment of Grave's disease, the most generic form of hyperthyroidism. In conclusion, it was found that addition of *O*-linked oligosaccharides or deletion of N-linked oligosaccharides could be interesting strategy for designing new analogs of glycoprotein hormones.

### Biography

Fuad Fares has completed his MSc and DSc studies at the Faculty of Medicine, Technion-Israel Institute of Technology, and Postdoctoral studies in Department of Molecular Biology and Pharmacology, School of Medicine, Washington University, St. Louis Missouri. He developed the Department of Molecular Genetics at Carmel Medical Center. He is an Associate Professor in Department of Human Biology, University of Haifa and Head of the Laboratory of Molecular Genetics. He has published more than 90 manuscripts in reputed journals and serving as a member of the Israel Council for Higher Education from last 14 years. He is the inventor of designing long-acting recombinant proteins and the initiator of Prolor Biotech Ltd.

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## Dong-Hun Woo

NEXEL Co. Ltd., South Korea

### Drug screening and discovery using human pluripotent stem cell derived cells

Drug-induced toxicity is a main reason for withdrawals of new drugs in late clinical phases and post-launch of the drugs. Thus, development of predictive *in vitro* assay for early toxicity evaluation is important for drug discovery process. Here, we show various kind of cells derived from human pluripotent stem cells (hPSCs) that could be used for early toxicity evaluation of drug candidates. From our inducing differentiation technology, we have routinely produced highly pure population ( $\geq 98\%$ ) of hepatocytes and cardiomyocytes from human embryonic stem cells (hESCs) and human induced pluripotent stem cells (hiPSCs). Furthermore, we optimized a culture condition of hPSC-derived functional cells suitable for toxicity tests *in vitro*, and we demonstrated the efficacy of our optimized hPSC-derived cell model for predicting toxicity against the several drugs. In conclusion, our hPSC-derived cell model could be a good alternative cell source for pre-clinical study such as predicting toxicity and efficacy test for the drugs, and translational research of disease cure.

### Biography

Dong-Hun Woo is a Chief Technology Officer (CTO) at NEXEL Co., Ltd. He received his PhD in Stem Cell Biology from Korea University. During this time, he worked on tissue regeneration through directed differentiation of human pluripotent stem cells into target cell types of the liver, pancreas, and brain. After PhD course, he initially extended his research into cancer stem cells, studying the molecular mechanisms underlying tumorigenicity of cancer stem cells in glioblastoma at the Lerner Research Institute of Cleveland Clinic in Cleveland, OH, USA. Then, he has his expertise in stem cell biology human pluripotent cell fate specification by bringing genome editing strategies to bear on induced pluripotent stem (iPS) cell models of human genetic diseases at the University of Pennsylvania, PA, USA. His current project involves the generation of functional cells from human pluripotent stem cells for drug screening and toxicity tests as Head of research programs at NEXEL Co., Ltd.

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