

Joint Event on

World Congress on

BIOCHEMISTRY AND ENZYMOLOGY

&

2nd Global Conference on

TISSUE ENGINEERING AND REGENERATIVE MEDICINE, STEM CELL RESEARCH

March 25-26, 2019 | Amsterdam, Netherlands

WORLD BIOCHEM 2019 & REGENERATIVE MEDICINE 2019



KEYNOTE FORUM DAY 1

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David Capaldi, J Genet Mol Biol 2019, Volume 3



David Capaldi

Rejuva Stem Cell Clinic, USA

BIOGRAPHY

David Capaldi was graduated from St. George's University School of Medicine and completed residencies in general surgery at Nassau University Hospital in New York and diagnostic radiology at John T. Mather Memorial Hospital and Stony Brook University Hospital in New York. Capaldi is currently a licensed physician in the state of Florida and the state of New Jersey. His diverse training also includes a B.S. in pharmacology & toxicology and an MBA in pharmaceutical business from the University of the Sciences in Philadelphia. His education and experience in radiology and surgery, combined with his interest in using stem cell therapy in the treatment of a variety of medical disorders and traumas have led him to join the staff at Rejuva Stem Cell Clinic as the full time provider and he enjoys the active lifestyle of South Florida, especially surfing and golfing.

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HUMAN UMBILICAL CORD BLOOD DERIVED STEM CELLS: REVIEW OF THE SCIENCE, RESEARCH AND CLINICAL APPLICATIONS

Human umbilical cord mesenchymal stem cells, particularly those derived from the cord blood, have become wildly popular with physicians and represents a fast-rising source of stem cells as represented in the research and its use in clinical practice in the United States. MSCs work in a paracrine manner to aid in host endogenous repair. MSCs release growth factors and proteins to communicate and effect neighboring cells. Studies illustrate a host of cytokines, chemokines and growth factors released by MSCs such as VEGF, FGF, PDGF, SCF to name a few. Growth factor release such as that of VEGF helps in the formation of new vascularization or angiogenesis while release of IL-1ra aid in suppressing the pro-inflammatory response of TNF- α . Hence, MSCs work in various methods to aid in healing and natural repair. This presentation will focus on the research and areas of proven benefit and also will reveal areas of need in the research, so we can work toward discovering the full potential of HUCMSC's. Detailed analysis of the HUCMSC product and its contents, method of action, clinical efficacy and safety.



Hasanat MA

Bangabandhu Sheikh Mujib Medical University, Bangladesh

BIOGRAPHY

Hasanat MA working as professor in the Department of Endocrinology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh and he obtained M Phil and MD from Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM), Dhaka, Bangladesh. He has published more than 45 original articles. He achieved best researcher award of BSMMU in 2016. His major research areas are diabetes (including GDM), PCOS and infertility, thyroid diseases and other endocrine problems. His speeches on GDM and thyroid autoimmunity are available in many websites. He is also working as Editor (American Research Journal of Endocrinology, SciFed Obesity Research Journal, International Journal of Diabetes, Global Scientific Research Journals and Clinical Journal of Diabetes Care and Control) and Assoc. editor (Obesity and Diabetes International) of different open access journals.

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MECHANISM OF GESTATIONAL DIABETES: INSULIN RESISTANCE OR SECRETORY FAILURE?

The aim of the project was to obtain a better understanding of the biochemical derangement that leads to hyperglycemia during pregnancy in Bangladeshi women.

Gestational Diabetes Mellitus (GDM) is an emerging issue for health care professionals. It is associated with adverse pregnancy outcome. In Bangladesh, an alarming frequency of GDM has been observed recently. Among the risk factors identified in the literature, ethnicity appears to be the most significant one. The trend toward increased maternal age, the epidemic of obesity and diabetes, decrease in physical activity and adoption of modern lifestyle in developing countries may all contribute to an increase in prevalence of GDM. However, genetic polymorphism seems to be interposed to compound the issue. We have been investigating these issues of GDM in our population. In this context, we have observed progressive increase in insulin resistance (IR) resulting in compensatory increase in insulin secretion as measured by C-peptide but not sufficient to the degree of overcoming resistance. Appearance of many hormones, such as hPL, prolactin, progesterone, cortisol and cytokine like TNF- α particularly during late pregnancy antagonizes the effect of insulin and triggers a state of IR. Among these biomarkers we have found fasting insulin, TNF- α and fibrinogen to be increased significantly in women with GDM especially when associated with overweight compared to pregnancy with normal glucose tolerance (NGT). On the other hand, prolactin, hPL, hs-CRP were not found to differ between GDM and NGT. Apart from these, we also observed higher frequency of single nucleotide polymorphism (SNP) for TC-F7L2 rs7903146 gene in GDM particularly for young and lean mothers. In conclusion, GDM is a constellation of involvement of multiple factors.



Mwafaq Ibdah

Agriculture Research Organization, Israel

BIOGRAPHY

Mwafaq Ibdah has completed his PhD at the age of 32 years from Martin Luther University, Hale/Salle, Germany and postdoctoral studies from Michigan State University and Washington State University. He is tenured researcher at Neve Ya'ar Research Center, The Agriculture Research Organization (ARO), Isarel. He has published more than 20 papers in reputed journals and has been serving as an editorial board member of *repute*.

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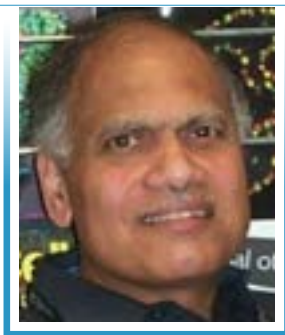
DEVELOPING OF TRILOBATIN DIHYDROCHALCONE AS A NEW-STYLE OF PHYTOCHEMICAL AGENT

The increasing prevalence of several diseases, like Alzheimer's disease, obesity, cancer, and diabetes, in humans in recent decades worldwide, accompanied by rising concern regarding the safety of many synthetic chemistry-based pharmaceuticals, has raised public demand for phytochemical-based medicines. This in turn has led to increasing interest in metabolic engineering as an approach to produce such natural products on an industrial scale, which has the potential to decrease production costs of, eg desired dihydrochalcones.

We note that fruits accumulating high level of phytochemicals including flavonoids and dihydrochalcones that may play a key role in reducing chronic disease risk. We have developed a novel concept to produce a new-style phytochemical agent of benefit for humans by genetic transformation of three characterized genes in plant cells, bacterial, and yeast systems. We have applied a set of molecular and biochemical tools to identified reactions and enzymes leading to the biosynthesis of dihydrochalcones. We recently cloned and biochemically characterized three key enzymes in the dihydrochalcone biosynthesis pathway; a p-coumaroyl-CoA double bond reductase that converts p-coumaroyl-CoA into p-dihydrocoumaroyl-CoA, chalcone synthase that accepted p-dihydrocoumaroyl-CoA, in the presence of malonyl-CoA, leading to production of phloretin, and a specialized phloretin-4'-O-glycosyltransferase which glycosylated phloretin in the presence of UDP-glucose into trilobatin. The production of the phytochemical trilobatin was achieved by overexpression of these genes in microbial cell factory. The proof of our concept have open the possibility for developing new-style of natural phytochemical for a growing market of population suffering from "modern" diseases.

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Mukund J Modak, J Genet Mol Biol 2019, Volume 3



Mukund J Modak

The State University of New Jersey, USA

BIOGRAPHY

Mukund J Modak is professor in Department of Biochemistry and Molecular Biology. He has completed his BSc in 1963 in University of Poona in Maharashtra. He has completed his MSc in 1965 in University of Bombay, Haffkine Institute, India and also completed his PhD in 1965 from university of Bombay Haffkine Institute.

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MOLECULAR INSIGHTS INTO STRAND DISPLACEMENT SYNTHESIS BY DNA POLYMERASE: DISTAL RRRY MOTIF AND TWO 3 HELIX BUNDLE STRUCTURES ARE REQUIRED FOR SDS

Strand displacement synthesis of DNA (SDSD) is an important process that is required in the maturation of Okazaki fragments during the lagging strand DNA synthesis. Using prototype *E.coli* DNA polymerase I (pol I), we have shown that a structural motif consisting of three helix bundle in the fingers subdomain (FS) is required for SDSD. We now show that, in addition to FS, a distal motif consisting of a conserved RRRY sequence spanning positions 821-824, and located at the junction of polymerase and 3'-5' exonuclease domain of pol I, also participates in SDSD. The biochemical results showed that alanine mutations of individual residues reduce DNA binding affinity of enzyme by 5 – 35 – fold. We have previously reported that the Y821 of RRRY motif regulates the proof-reading activity of pol I suggesting at least two functions of RRRY motif. Furthermore, we have identified another 3-helix bundle structure in the 5'-nuclease domain of pol I. This motif is also necessary for efficient catalysis of SDSD. Hence, we conclude that SDSD by pol I requires structural elements from its all three domains. Interestingly, the 3 helix bundle resident tyrosine (Y215) is not required for the 5'-nuclease activity. We further demonstrate that in DNA polymerases, with active 3' exonuclease, further cleavage of displaced strand occurs in coordinated manner using intramolecular mode.

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Jim Engström, J Genet Mol Biol 2019, Volume 3



Jim Engström

Cellink, Sweden

BIOGRAPHY

Jim Engström is a Global Application Specialist at CELLINK, one of the leading 3D Bioprinting companies in the world founded in Gothenburg, Sweden. He holds a Master's degree in Biology from Gothenburg University. Jim has been working in the biotech/med-tech field for the past twelve years. His passion for new innovative technologies led him to a new career at CELLINK in January 2018. Jim works closely with his fellow team members to support and educate customers and potential customers in order to help raise CELLINK's visibility and to connect world renowned researchers around the globe.

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3D BIOPRINTING OF HUMAN SOFT TISSUES

3D Bioprinting has gained attention in tissue engineering due to its ability to spatially control the placement of cells, biomaterials and biological molecules. The development of new hydrogel bioinks with good printability and bioactive properties has made it possible to 3D bioprint and accelerate the maturation of complex 3D tissue-like models. In this talk, we present our recent work in bioink development for 3D bioprinting and culture of healthy tissues such as skin, bone and cartilage, as well as cancer tissues, such as breast cancer and osteosarcoma tissue models.

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KEYNOTE FORUM DAY 2



Ming Pei

West Virginia University, USA

BIOGRAPHY

Ming Pei completed his PhD from Beijing University, China and postdoc training from Harvard-MIT Division of health sciences and Technology, USA. Currently he is a tenured professor and director of stem cell and tissue engineering laboratory in the department of orthopaedics, West Virginia University, USA. He has over 100 publications that have been cited over 3100 times, and his publication H-index is 32 and has been serving as an editorial board member of reputed Journals.

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SITE-DEPENDENT VARIATION OF LINEAGE PREFERENCE FROM ADIPOSE STEM CELLS

Stem cells from subcutaneous adipose tissue (ScASCs) are considered a potential cell source for cartilage regeneration. Unfortunately, the capacity of ScASCs toward chondrogenesis is very limited. Interestingly, recent reports indicate that stem cells from infrapatellar fat pad (IPFSCs), an adipose tissue depot next to knee joints, exhibit an excellent potential to differentiate into cartilage. Despite the fact that some studies have investigated these two kinds of adipose stem cells in chondrogenic differentiation, few reports are available to compare adult stem cells from these two tissues in genome sequencing and protein composition. ScASCs and donor-matched IPFSCs were isolated from four 4-month-old healthy rabbits. Our cell proliferation assay showed that ScASCs proliferated faster than IPFSCs, while IPFSCs exhibited much higher expression of CD146, a marker related to pericytes, stemness, and maybe chondrogenesis. IPFSCs exhibited obvious preference for chondrogenic differentiation based on the expression of *SOX9*, *COL1A1*, *COL2A1*, and *ACAN* ($p < 0.05$), while ScASCs were preferential for adipogenic differentiation based on the expression of *ADIPOQ*, *LPL*, *PPARG*, and *LEP*, and the synthesis of adiponectin ($p < 0.05$). None of them showed priority in osteogenesis based on the expression of *BGLAP*, *RUNX2*, *DCN*, and *SPARC*, and the synthesis of osteocalcin ($p > 0.05$). Expression of stemness and senescence related genes (*NANOG*, *REX1*, *NES*, *SOX2*, *CDKN1A*, *TP53*) indicated that no differences were evident between both groups ($p > 0.05$). Proteomes of IPFSCs and ScASCs are uniquely distinguishable for both the cells and the secreted ECM using both partial least squares discriminant analysis (PLS-DA) and volcano plot. The finding is also consistent with the data from a principal component analysis (PCA) of RNA sequencing. The results demonstrated that, despite similar source from adipose tissue, the preference for differentiation lineage is depot dependent, indicating that local microenvironment might dominate the fate of local stem cells. Our findings suggested that IPFSCs are more suitable for cartilage regeneration while ScASCs tend to differentiate toward adipose tissue.



Ralph Rogers

Rogers Regenerative Medical Group, UK

BIOGRAPHY

Ralph Rogers is a consultant in regenerative orthopaedics & sports medicine. He studied medicine at the University of Leuven (Belgium) and after completion of PhD in Exercise Physiology at the University of Maryland (USA). He was also a research fellow at the National Institute of Health (NIH). Rogers continued his educational pursuit by receiving an MBA from the University of Leicester. He travels extensively to the USA and Europe to explore various regenerative medical techniques and was among the first Physicians in the UK to implement Regenerative orthopaedics in his clinical practice. He is the founder of the Rogers Regenerative Medical Group where the goal is to treat patients and share best practice in the cutting-edge field of regenerative medicine therapies with physicians around the world.

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REGENERATIVE MEDICINE IN NONSURGICAL ORTHOPAEDICS & SPORTS MEDICINE

The number of sports injuries and orthopedic conditions, such as Osteoarthritis of the knee, in the population is considerable. Time loss can vary from a few days to end-of-season or beyond. In addition, many of these conditions represent a significant cost in lost time from work and lost wages. When injured, many musculoskeletal structures do not completely regain their normal structural and biomechanical properties, resulting in the formation of scar tissue, which increase the risk of re-injury. This is due to poor vascularization which reduces the availability of oxygen, growth factors and other nutrients necessary for tissue regeneration which significantly affects the quality and speed of healing response. However, healing may potentially be enhanced and expedited by new non-surgical regenerative medicine treatments using a patient's own growth factors to promote healing. Regenerative medicine is of particular interest as evidence increasingly refute the commonly used patient pathway of rest, anti-inflammatory medications, corticosteroid injections and surgery. There is mounting evidence to suggest that treatments such as platelet rich Plasma (PRP), Lipogems, Alpha 2 Macroglobulin (A2M) and Extracorporeal Shockwave therapy (ESWT) may provide an adjuvant or alternative treatment option for conditions that affect muscle, tendons, ligaments, and cartilage. These techniques are also appealing to patients as they are minimally invasive and are often performed in a relaxed out-patient setting, with little down time. Another major advantage of regenerative medicine is that patients use "their own body tissue" for natural healing process. These treatments are easy to prepare, administer, safe, effective, available immediately at the point of care; and cost-effective compared with surgical options. The promise of regenerative medicine in non-surgical orthopedics and sports injuries is exciting and may prove to be "Game Changer"!

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Anne Rios, J Genet Mol Biol 2019, Volume 3



Anne Rios

Princess Maxima Center of Pediatric Oncology, Netherlands

BIOGRAPHY

Anne Rios obtained her PhD in 2011. Her work represented a novel cell signalling mechanism that triggers the differentiation of a defined subset of cells within a stem pool (Nature, 2011). Then she joined in the laboratory of professors Jane Visvader and Geoff Lindeman focusing on breast cancer. In 2016, she received the Medical Innovation Award (Centenary Institute Lawrence Creative Prize Winner) for her postdoctoral's work (Nature, 2014). In 2017, she was appointed group leader at the Princess Máxima Center and head the Princess Máxima Imaging Centre. She is currently investigating the cellular mechanisms underlying pediatric and adult solid tumor progression using State-of-the-art imaging technologies.

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INVESTIGATING THE CELLULAR DYNAMICS OF ORGANS DEVELOPMENT AND CANCER USING 3D IMAGING

Rios implemented a novel 3D-imaging approach (with 3D glasses) to perform innovative multicoloured lineage tracing studies to follow the development and fate of mammary stem cells (MaSC) and descendant progenitor cells *in vivo* in entire mammary gland. As stem cells divide they produce clones of cells; using this imaging technique the fate of these individual clones could be tracked throughout various stages of mammary gland development, including puberty, pregnancy and normal adult homeostasis. This work provided the first *in vivo* evidence for the existence of bipotent MaSCs, which give rise to the two cell lineages that constitute the mammary ducts, the luminal and the myoepithelial cells, as well as the presence of distinct long-lived unipotent progenitor cells. The cellular dynamics observed at different developmental stages support a model in which both stem and progenitor cells drive morphogenesis during puberty, whereas bipotent MaSCs coordinate ductal homeostasis and remodelling of the adult mouse gland (Nature 2014, Nature Comm. 2016, NCB 2017). We have now specialized this 3D technology combined with the multicolored reporter confetti to detect early aberrant cellular behaviour in models of breast cancer and to visualise how cancerous cells, according to their cell-of-origin, exit normal ductal homeostasis and survive to self-organise into a solid tumour.



Sunita Hooda

University of Delhi, India

BIOGRAPHY

Sunita Hooda obtained her PhD degree in physical chemistry in 1992 from Indian Institute of Technology Delhi, India. She is presently, working as an associate professor in the Department of Chemistry, Acharya Narendra Dev College (University of Delhi). She has expertise in NMR studies of synthesized polymers. She publishes 53 research papers in reputed national and international journals. Her current research area of interest is "Synthesis of Polymeric and Heterocyclic Chemosensors for Cations, Anions and Molecules Recognition".

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CURCUMIN BASED FLUORESCENT CHEMOSENSOR FOR SELECTIVE DETECTION OF Cu^{2+} AND Hg^{2+} IONS IN AQUEOUS MEDIUM AND CELL IMAGING STUDY

Curcumin based fluorescent Schiff base chemosensor L2 (4,4'-((1E,3Z,5E,6E)-3-hydroxy-5-(thiazol-2-ylimino)hepta-1,3,6-triene-1,7-diyl)bis(2-methoxyphenol)) shows notable change in absorbance and emission spectra on screening with some metal ions (Fe^{3+} , Cu^{2+} , Ni^{2+} , Zn^{2+} , Cd^{2+} , Hg^{2+} , Pb^{2+} , Cr^{3+} , Mn^{2+} , Co^{2+} , Ag^{1+} .etc.) in HEPES buffer. Binding constant for L2 + Cu^{2+} ($2.4 \times 10^5 \text{ M}^{-1}$) and L2 + Hg^{2+} ($7.46 \times 10^5 \text{ M}^{-1}$) which indicate good interaction of chemosensor with Cu^{2+} and Hg^{2+} ions. An interesting value of detection limit was observed with Cu^{2+} and Hg^{2+} ions, was to be 2.0 and 1.2 μM , respectively, which further clear the selectivity of the molecular probe towards Cu^{2+} and Hg^{2+} ions respectively. Detection of Cu^{2+} ions by chemosensor L2 in to biological cells was performed by using fluorescence cell-imaging study. Staining cells only with chemosensor exhibited intercellular fluorescence and upon the addition of Cu^{2+} ions the cells lost their fluorescence. The cell imaging studies clearly indicate that chemosensor L2 has good cell permeability and show the formation of L2- Cu^{2+} complex.