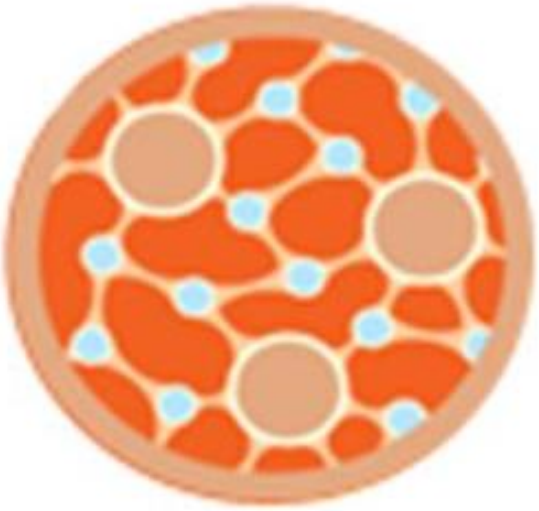
Conference Handbook

TM's 3rd World Molecular & Cell Biology Online Conference

February 25-28, 2014



Dear colleagues

Thank you so much for taking time out of your busy schedule to participate in online conference - **TM's 3rd World Molecular & Cell Biology Online Conference,** which will be held **on February 25-28, 2014.** It will be very helpful to speakers, attendees, and other related people. Target Meeting appreciates your attendances and generous contribution. We hope you will enjoy the difference.

Sincerely Yours

Target Meeting Team in USA

Preparation in advance: USB headset with microphone

Instructions

1. You can receive **all 4 conference track links** before the event. You can participate in all or part of tracks (sessions). It depends on your time or interest.

2. **Double click the track links** at scheduled date & time to join the conference. The conference component software will be downloaded and installed on your computer automatically (about 30 seconds) when you click the track links. If not, please manually download the component software on your computer after you click the track links. Normally the component software will be saved in the download folder, my document, desktop, or somewhere. It depends on your computer. Double click it to run this software (**You must have right to install software on your computer**). Then you will enter the "Conference Room". It is completely secure.

3. Connect USB headset to your computer. If your audio devices are connected correctly, you will see the sound meters in the Control Panel **light up green**. Your USB headset is muted during the conference in case of background noise. If you want to talk with other speakers at the Q&A sessions, please click the icon "**hand**" on the conference control panel. The conference organizer will unmute your headset, then you can discuss with them in real time. The session chair will be unmuted at the beginning and end of each presentation. So the chair can introduce the speakers and organize the Q&A sessions. At the panel discussion sessions, all speakers are unmute.

4. When you give oral presentation, please **open your PowerPoint file (presentation slides) in full screen** on your computer. Conference organizer will pass the Presenter Control Panel to you. Your USB headset will be unmuted automatically. Click **Show My Screen** on the Presenter Control Panel. You can start your presentation after the chair's introduction. Never close the control panel on your computer during the sessions. Please type messages in the control panel and sent it to organizers if you have any questions during the conference. Organizers will reply you in private.

Conference Partners

For more than four decades, LI-COR(R) Biosciences has been helping scientists advance discovery by providing innovative research tools. And with more than twenty years of experience in biotechnology, LI-COR is now a leading manufacturer of near-infrared imaging platforms, analysis software, and IRDye(R) infrared dye reagents. LI-COR pioneered the development of near-infrared fluorescence systems for DNA sequencing, and today provides systems for drug discovery, protein research, small animal imaging, and undergraduate training. These tools provide research solutions for a wide variety of applications, including quantitative Western blotting, small animal imaging, and cell-based assays. Research toward a Cure is part of our ongoing effort to develop research tools and highlight techniques that enhance scientists' technical capabilities to advance cancer research. Currently, thousands of LI-COR systems are being used in laboratories around the world for advanced research and drug development. Our website features published examples of applications and techniques where infrared fluorescence detection contributes to the understanding of cancer and the search for cures. Please visit www.licor.com/cancer for more information. In addition to the biotechnology lines of instruments and reagents, LI-COR instruments for photosynthesis, carbon dioxide analysis, and light measurement are recognized worldwide for standard-setting innovation in plant science research and environmental monitoring. Founded in 1971, the privately held company is based in Lincoln, Nebraska, with subsidiaries in Germany and the United Kingdom. LI-COR systems are used in over 100 countries and are supported by a global network of distributors.

Leica Microsystems is a world leader in microscopes and scientific instruments. Founded as a family business in the nineteenth century, the company's history was marked by unparalleled innovation on its way to becoming a global enterprise. Leica Microsystems' Life Science Division supports the imaging needs of the scientific community with advanced innovation and technical expertise for the visualization, measurement and analysis of microstructures. Our strong focus on understanding scientific applications puts Leica Microsystems' customers at the leading edge of science. Its historically close cooperation with the scientific community is the key to Leica Microsystems' tradition of innovation, which draws on users' ideas and creates solutions tailored to their requirements. At the global level, Leica Microsystems is organized in three divisions, all of which are among the leaders in their respective fields: the Life Science Division, Industry Division, and Medical Division. Leica Microsystems has six manufacturing facilities in five countries, with sales and service organizations in 20 countries. The company is headquartered in Wetzlar, Germany. For current Leica promotions: http://www.leica-microsystems.com/ls-promos.

If you are seeking reliable, top performing, budget friendly laboratory instruments, you've come to the right place. Our Bullet Blender tissue homogenizers, automated blot processors, rockers, and CO2 induction systems are engineered to automate mundane tasks and reduce errors. 4 Reasons to Rely on Next Advance Laboratory Instruments: 1. You'll save time and recognize more accurate and consistent results 2. Our innovative technology and elegant design = superior results at lower costs 3. Product design is driven by the laboratory and budget requirements of biologists 4. Made in the U.S.A., all of our products are reliable, robust and built to last. Please visit http://www.nextadvance.com for more information.

Principal Investigators Association (PIA) is an independent organization created to communicate and promote among scientists in all fields of research best practices and continuing professional development. The information and advice we provide covers such topics as garnering financial support and optimally using monetary, material and personnel resources to increase the scope, efficiency and productivity of your scientific inquiry. PIA offers a variety of product formats designed to fit your busy lives. These include live and on-demand Webinars, grant-writing manuals, funding and lab management executive reports, educational packs and toolkits, free white papers and a free bi-monthly eNewsletter.

Medical News Today is the largest independent medical and health news site on the web - with over 2,500,000 unique monthly users it is ranked number one for medical news on Google and Yahoo!. Medical News Today is used by Blue Chip pharmaceutical and health organizations, advertising agencies, PR companies and vertical ad networks to deliver targeted disease/condition and general health campaigns. For more information, please visit www.medicalnewstoday.com.

F1000Prime is an online tool to help life scientists and clinicians keep on top of current literature. Our peer-nominated global 'Faculty' of over 5000 leading scientists and clinicians identify and write recommendations for the best published research articles across biology and medicine, creating the world's first and largest searchable database of recommendations for over 150,000 life science-related articles. Our Faculty Members and article recommendations are organized into 40 faculties, which are further subdivided into 300 sections. In this way, published literature from every field of biology and medicine is comprehensively and systematically reviewed by an expert panel of scientists and clinicians. At F1000Prime, we pride ourselves on bringing focus to all great research articles, regardless of journal impact factor.

PharmaVOICE magazine, reaching more than 34,000 BPA-qualified life-sciences executives, is the forum that allows business leaders to engage in a candid dialogue on the challenges and trends impacting the industry. PharmaVOICE provides readers with insightful and thought-provoking commentary in a multiple-perspective format through forums, topics, and articles covering a range of issues from molecule through market. PharmaVOICE subscribers are also kept abreast of the latest trends and information through additional media resources, including WebLinx Interactive WebSeminars, Podcasts, Videocasts, White Papers, E-Surveys and e-Alerts. Additionally, PharmaVOICEMarketplace.com provides a comprehensive directory of products, services, and solutions for the life-sciences industry.

Cancer Cell International is an online, open access journal published by BioMed Central. We publish articles on all aspects of cancer cell biology, originating largely from work using cell culture techniques. Much of cancer work relates to biological experiments in which cells are grown in vitro, in two- or three-dimensional systems. Such experiments have provided crucial data in many fields, from the chemoattraction of immune cells or blood vessel endothelial cells (angiogenesis), to measurements of effective doses of drugs, irradiation and other modalities. *Cancer Cell International* considers manuscripts that include animal work (in vivo) only if the work is a logical progression from previous work in vitro. Please visit the website www.cancerci.com for more information or for editorial enquiries please contact editorial@cancerci.com.

20/20 Pharma, published by IMI, is a magazine and website which presents insightful analysis of current events, developments, and trends in the pharmaceutical world.The publication has forged powerful relationships with key industry leaders to provide a platform for decision makers to have the means to procure and plan implementation strategies based on the topics covered.

The heat is on for an online social networking community for nanoscientists. The International Nanoscience Community, TINC, was cooked up by Hungarian chemistry PhD student Andras Paszternak. It now provides a rich menu of communication tools for the international community of scientists working in the growing field of nanoscience and nanotechnology and recently passed the 4900 members mark. The virtual nano community is fully equipped with all the functions one expects from a modern online networking site: personal chat, a scientific forum, more than 95 thematic groups, including microscopy,

nanomedicine, and even a discussion forum on safety and toxicity. http://www.nanopaprika.eu.

World Conference Calendar is a directory publishing information on academic conferences all over the world. Knowledge is really appreciated only when it reached a user. Conferences are one of the best environments that this knowledge is delivered to a large audience. As World Conference Calendar, we are trying to be an effective medium to point out where these exchanges will take place.

Clocate.com is a leading international search engine and directory for worldwide conferences and exhibitions. The events cover the following areas: Industry and manufacturing, Health and medicine, Technology and IT, Business and finance, sciences, education, services (banking, insurance, tourism, Hospitality and more), government, environment, life style and arts. The details for each event include: description, dates, location, address, prices and more.

BioSpectrum Asia is the most influential source of information for life sciences industry and is uniquely positioned as a specialized B2B information platform in Asia Pacific region. The magazine provides comprehensive coverage and useful insights in the areas of pharmaceuticals, biotechnology, medical devices, research & development and policies.

Business with India (www.businesswithindia.in) is a leading portal providing help and assistance to find new business partners and track global business opportunity. Any Product, Any Service, Anywhere in the World.

Biology51 (www.51atgc.com) is a very instructive biological video website. Based on abundant experiences and advantages on biotechnology, the people of this web constructed an expert photographic center in a myria-laminar flow experiment-shooting lab. The expert biotechnological team and photographic team took a lot of operational videos on cell biology, molecular cloning, proteomics, animal models and virology etc. The very huge experimental video libraries could give the unlimited benefits to research people on high-stage experimental technologies, including easily direct observation to all kinds of experiments etc. So she has unique priority to do advertising for biological companies.

Conference Program
(All Times Are New York Time)

Track 1: 8:30AM – 17:30 PM, February 25, 2014

Session 1: **Cell signaling pathways-I**
9:00 AM – 11:00 AM

Session 2: **Cell signaling pathways-II**
11:00 AM – 13:30 PM

Session 3: **Cell signaling pathways-III**
13:30 PM – 15:30 PM

Session 4: **Cell signaling pathways-IV**
15:30 PM – 17:30 PM

Track 2: 8:30 AM – 17:30 PM, February 26, 2014

Session 5: **Molecular Mechanisms of Cancer-I**
9:00 AM – 11:00 AM

Session 6: **RNA biology-I**
11:00 AM – 13:00 PM

Session 7: **RNA biology-II**
13:00 PM – 15:00 PM

Session 8: **Molecular mechanisms of cancer-II**
15:00 PM – 17:30 PM

Track 3: 8:30 AM – 16:30 PM, February 27, 2014

Session 9: **GPCR structure and function**
9:00 AM – 10:30 AM

Session 10: **Cell Death**
10:30 AM – 12:00 PM

Session 11: **Stem cell biology-I**
12:00 PM – 14:30 PM

Session 12: **Cell signaling pathways-V**
14:30 PM – 16:30 PM

Track 4: 8:30 AM – 17:00 PM, February 28, 2014

Session 13: **General biochemistry-I**
9:00 AM – 11:00 AM

Session 14: **General biochemistry-II**
11:00 AM – 13:00 PM

Session 15: **Stem cell biology-II**
13:00 PM – 15:00 PM

Session 16: **General biochemistry-III**
15:00 PM – 17:00 PM

Track 1: 8:30 AM– 17:30 PM, February 25, 2014

8:30 – 9:00 AM
Speakers and attendees can login the online conference.

Session 1: Cell signaling pathways-I
9:00 AM – 11:00 AM
Session Chair: Dr. Vincenza Rita Lo Vasco

9:00 – 9:30 AM
Presentation Title: Slow Regulated Release of H2S Inhibits Oxidative Stress Induced Cell Death by Influencing Certain Key Signaling Molecules.
Aman Shah Abdul Majid, PGDPharm, MD, PhD, Medical Lecturer, Department of Integrative Medicine, Advanced Medical and Dental Institute, USM, Penang, Malaysia.

Q&A Session, presenter answers questions from other speakers or attendees.

9:30 – 10:00 AM
Presentation Title: From molecules to genes.
Amol Patil, Associate Professor, Dept. of Orthodontics and Dentofacial Orthopedics, Bharati Vidyapeeth Dental College and Hospital, Bharati Vidyapeeth Deemed University, India.

Q&A Session, presenter answers questions from other speakers or attendees.

10:00 – 10:30 AM
Presentation Title: Signal transduction in innate immunity - what can we learn from the Caspase Activation Domains (CARDs) of the NLR family members NOD1 and NOD2.
Tom Monie, Researcher, Department of Biochemistry, University of Cambridge, Cambridge, UK.

Q&A Session, presenter answers questions from other speakers or attendees.

10:30 – 11:00 PM
Presentation Title: The involvement of Phosphoinositide signal transduction pathway in angiogenesis.
Vincenza Rita Lo Vasco, MD, PhD, Assistant Professor, Department of Sensitive Organs, Sapienza University of Rome, Rome, Italy.

Q&A Session, presenter answers questions from other speakers or attendees.

Panel Discussion. This session is to provide speakers and attendees with in-depth discussion and networking. You can discuss what you want with other speakers. All speakers are unmuted, so speakers can talk freely during the session.

Session 2: Cell signaling pathways-II

11:00 AM – 13:30 PM
Session Chair: Dr. Dan Cojoc

11:00 – 11:30 PM
Presentation Title: Is it possible to fight influenza by targeting intracellular redox state?
Rossella Sgarbanti, Assistant Professor, Università Telematica San Raffaele, IRCCS San Raffaele Roma, Italy.

Q&A Session, presenter answers questions from other speakers or attendees.

11:30 – 12:00 PM
Presentation Title: Focal stimulation of neuronal cells by optical manipulation.
Dan Cojoc, Senior Scientist, IOM-CNR, Institute of Materials- National Research Council, Italy.

Q&A Session, presenter answers questions from other speakers or attendees.

12:00 – 12:30 PM
Presentation Title: Pax3 and Pax7 reversely interact and regulate the expression and distribution of their target genes in the chicken developing spinal cord.
Juntang Lin, Professor, Department of Life Science and Technology, Xinxiang Medical University, Henan Province, P. R. China; Group leader, Institute of Anatomy I, Klinikum der Friedrich-Schiller-Universität, Germany.

Q&A Session, presenter answers questions from other speakers or attendees.

12:30 – 13:00 PM
Presentation Title: Heme oxygenase ameliorates cardiomyopathy by suppressing markers of heart failure and inflammation in normoglycemic obese rats".
Joseph Fomusi Ndisang, Associate Professor, Department of Physiology, University of Saskatchewan, Canada.

Q&A Session, presenter answers questions from other speakers or attendees.

13:00 – 13:30 PM
Presentation Title: Rethinking the Traditional Western.
John Lyssand, Ph.D., Field Applications Scientist, Biotechnology, LI-COR Biosciences, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

Panel Discussion. This session is to provide speakers and attendees with in-depth discussion and networking. You can discuss what you want with other speakers. All speakers are unmuted, so speakers can talk freely during the session.

Session 3: Cell signaling pathways-III

13:30 PM – 15:30 PM
Session Chair: Dr. Jamil Talukder

13:30 – 14:00 PM
Presentation Title: Signaling Mechanisms Underlying Alcohol Abuse Disorders.
Dorit Ron Ph.D., Professor, Endowed Chair in Cell Biology of Addiction in Neurology, Department of Neurology, University of California, San Francisco, Gallo Research Center Investigator, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

14:00 – 14:30 PM
Presentation Title: Leukotriene activates Ca2+ dependent dephosphorylation of ASCT1 to down regulate Ala transport in IEC-6 cells.
Jamil Talukder, DVM, PhD, Associate Professor, Biology, LeMoyne-Owen College, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

14:30 – 15:00 PM
Presentation Title: Regulation of osteoclast differentiation by Cx37.
Lilian I. Plotkin, PhD, Assistant Professor, Department of Anatomy and Cell Biology, Indiana University School of Medicine, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

15:00 – 15:30 PM
Presentation Title: Pending
Tammy A. Butterick-Peterson, Ph.D., Adjunct Assistant Professor, Minnesota Obesity Neuroscience Lab Group, University of Minnesota, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

Panel Discussion. This session is to provide speakers and attendees with in-depth discussion and networking. You can discuss what you want with other speakers. All speakers are unmuted, so speakers can talk freely during the session.

Session 4: Cell signaling pathways-IV
15:30 PM – 17:30 PM
Session Chair: Dr. Zhen He

15:30 – 16:00 PM
Presentation Title: Development of sexually dimorphic nuclei and the influence of estrogen-like compound exposure.
Zhen He, MD, PhD, Staff Fellow/Neuroanatomist, Division of Neurotoxicology, HFT-132, National Center for Toxicological Research, Food and Drug Administration, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

16:00 – 16:30 PM
Presentation Title: Proline Glutamic acid and Leucine rich Protein1 (PELP1) is a novel coregulator of β-catenin in glioblastoma.
Gangadhara Reddy Sareddy, Researcher, The University of Texas Health Science Center at San Antonio, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

16:30 – 17:00 PM
Presentation Title: Friend or foe: Anti-aging cosmetics on the eye.
Juan Ding, Schepens Eye Research Institute/Massachusetts Eye and Ear, Harvard Medical School, Boston, MA, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

17:00 – 17:30 PM
Presentation Title: The inflammatory factors and their epigenetic regulation in Multiple sclerosis.
Fanglin Zhang, Scientist, Department of Neurology, Multiple Sclerosis Research Center, Vanderbilt University Medical Center, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

Panel Discussion. This session is to provide speakers and attendees with in-depth discussion and networking. You can discuss what you want with other speakers. All speakers are unmuted, so speakers can talk freely during the session.

Track 2: 8:30 AM – 17:30 PM, February 26, 2014

8:30 – 9:00 AM
Speakers and attendees can login the online conference.

Session 5: Molecular Mechanisms of Cancer-I
9:00 AM – 11:00 AM
Session Chair: Dr. Romano Maria Fiammetta

9:00 – 9:30 AM
Presentation Title: Prostate cancer stem cell, midkine protein and lithium chloride.
Mine Erguven, Istanbul Aydın University, Faculty of Health Sciences, Istanbul, Turkey.

Q&A Session, presenter answers questions from other speakers or attendees.

9:30 – 10:00 AM

Presentation Title: NO-releasing doxorubicins: new anthracycline derivatives that overcomes drug-resistance in cancer cells.
Chiara Riganti, MD, Assistant Professor of Biochemistry, Department of Oncology, Turin School of Medicine, University of Turin, Italy.

Q&A Session, presenter answers questions from other speakers or attendees.

10:00 – 10:30 AM
Presentation Title: FKBP51 orchestrates the evil axis EMT/ cancer stemness/drug resistance, in malignant melanoma: a matter of protein/protein interaction.
Romano Maria Fiammetta, Professor & Group leader, Department of Biochemistry and Medical Biotechnology, Federico II University of Naples, Naples, Italy.

Q&A Session, presenter answers questions from other speakers or attendees.

10:30 – 11:00 PM
Presentation Title: Diagnostic yield of primary circulating tumor cells in women with suspicion of breast cancer: Study BEST (Breast Early Screening Test).
Nigel P Murray, Subdivisión de Hematologóa, Hospital de Carabineros, Nuñoa, Santiago, Chile.

Q&A Session, presenter answers questions from other speakers or attendees.

Panel Discussion. This session is to provide speakers and attendees with in-depth discussion and networking. You can discuss what you want with other speakers. All speakers are unmuted, so speakers can talk freely during the session.

Session 6: RNA biology-I
11:00 AM – 13:00 PM
Session Chair: Dr. Erik Wiemer

11:00 – 11:30 AM
Presentation Title: MicroRNAs in the tumor biology of soft tissue sarcomas.
Erik Wiemer Ph.D., Associate Professor, Dept. of Medical Oncology, Erasmus University Medical Center, Netherland.

Q&A Session, presenter answers questions from other speakers or attendees.

11:30 – 12:00 PM
Presentation Title: Regulation of Tissue Factor biology via microRNAs.
Andreas Eisenreich, Charité-Universitätsmedizin Berlin, Campus Benjamin Franklin, Centrum für Herz- und Kreislaufmedizin, 12200 Berlin, Germany.

Q&A Session, presenter answers questions from other speakers or attendees.

12:00 – 12:30 PM

Presentation Title: Functions of p63 and its miR-205 target in cell migration and metastasis.
Paola Tucci, Ph.D., Assistant Professor, Department of Pharmacy, Health and Nutritional Sciences, University of Calabria, Italy.

Q&A Session, presenter answers questions from other speakers or attendees.

12:30 – 13:00 PM
Presentation Title: Sexually dimorphic microRNA expression: a new thought on sex bias of autoimmune diseases.
Rujuan Dai, Assistant Professor, Department of Biomedical Sciences and Pathology, Virginia-Maryland Regional College of Veterinary Medicine, Virginia Tech, Blacksburg, VA24060, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

Panel Discussion. This session is to provide speakers and attendees with in-depth discussion and networking. You can discuss what you want with other speakers. All speakers are unmuted, so speakers can talk freely during the session.

Session 7: RNA biology-II
13:00 PM – 15:00 PM
Session Chair: Dr. Kathleen L. Hefferon

13:00 – 13:30 PM
Presentation Title: Applications of Virus Expression Vectors for Infectious Disease Research.
Kathleen L. Hefferon, Professor, University of Toronto, Canada.

Q&A Session, presenter answers questions from other speakers or attendees.

13:30 – 14:00 PM
Presentation Title: MicroRNAs in the malignant transformation of colon adenoma to Adenocarcinoma.
Subbaya Subramanian, Assistant Professor, Department of Surgery, The University of Minnesota, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

14:00 – 14:30 PM
Presentation Title: lncRNA 7SL represses p53 translation by competing with HuR.
Kotb Abdelmohsen, Senior Scientist, Laboratory of Cellular and Molecular Biology, NIA-IRP, NIH, Baltimore, MD, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

14:30 – 15:00 PM
Presentation Title: Reciprocal regulation of microRNA and long non-coding RNAs in cancer cells.
Yin-Yuan Mo, Professor, Cancer Institute, University of Mississippi Medical Center, Jackson, MS, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

Panel Discussion. This session is to provide speakers and attendees with in-depth discussion and networking. You can discuss what you want with other speakers. All speakers are unmuted, so speakers can talk freely during the session.

Session 8: Molecular mechanisms of cancer-II
15:00 PM – 17:30 PM
Session Chair: Dr. Christina Voelkel-Johnson

15:00 – 15:30 PM
Presentation Title: Tumor-stromal crosstalk in pancreatic cancer pathobiology and chemoresistance.
Ajay Singh, Associate Professor, Department of Oncologic Sciences, Mitchell Cancer Institute, University of South Alabama, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

15:30 – 16:00 PM
Presentation Title: Sphingosine kinase 2 as a novel therapeutic target in prostate cancer.
Christina Voelkel-Johnson. PhD., Associate Professor of Microbiology and Immunology, Department of Microbiology & Immunology, Medical University of South Carolina, Charleston SC, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

16:00 – 16:30 PM
Presentation Title: Cell Directionality as an Indicator of Breast Cancer Progression.
Christina Stuelten, Scientist, Cell and Cancer Biology Branch, National Cancer Institute, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

16:30 – 17:00 PM
Presentation Title: Deficient Aldehyde Dehydrogenase 1A1 Expression In Primary Cells Isolated From Gorlin Syndrome Patients: Implications For Radiation Carcinogenesis and Developmental Defects.
Thomas Weber, Senior Research Scientist, FSD/Cell Biology and Biochemistry, Pacific Northwest National Laboratory, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

17:00 – 17:30 PM
Presentation Title: Vesicular trafficking protein, Rab25 is a conditional oncogene in breast cancer.
Shreya Mitra, Researcher, Department of Systems Biology, University of Texas MD Anderson Cancer Center, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

Panel Discussion. This session is to provide speakers and attendees with in-depth discussion and networking. You can discuss what you want with other speakers. All speakers are unmuted, so speakers can talk freely during the session.

Track 3: 8:30 AM– 16:30 PM, February 27, 2014

8:30 – 9:00 AM
Speakers and attendees can login the online conference.

Session 9: GPCR structure and function
9:00 AM – 10:30 AM
Session Chair: Dr. Anwar Rayan

9:00 – 9:30 AM
Presentation Title: Profiling the Pharmacology of GPCR Complexes
Kevin Pfleger, Associate Professor, Molecular Endocrinology-GPCRs, Western Australian Institute for Medical Research, Australia.

Q&A Session, presenter answers questions from other speakers or attendees.

9:30 – 10:00 AM
Presentation Title: Indexing Chemicals for their Bioactivity on GPCRs by Ligand-Structural Combined Approach.
Anwar Rayan, Head of the Drug Discovery Informatics Lab at the QRC research center – Al Qasemi Academic College & CEO of GeneArrest LTD company, Israel.

Q&A Session, presenter answers questions from other speakers or attendees.

10:00 – 10:30 AM
Presentation Title: Expressioneering Technology accelerates Functional Expression and Crystallization of GPCRs for Drug Discovery.
Saurabh Sen, Senior Scientist, R&D, Lucigen Corp, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

Panel Discussion. This session is to provide speakers and attendees with in-depth

discussion and networking. You can discuss what you want with other speakers. All speakers are unmuted, so speakers can talk freely during the session.

Session 10: Cell death
10:30 AM – 12:00 PM
Session Chair: Dr. Giulia Grisendi

10:30 – 11:00 PM
Presentation Title: Monte Carlo simulation elucidates the type 1/ type 2 choice in apoptosis under death ligand induction.
Subhadip Raychaudhuri, Associate Professor, Indraprastha Institute of Information Technology, India.

Q&A Session, presenter answers questions from other speakers or attendees.

11:00 – 11:30 PM
Presentation Title: Gene modified mesenchymal progenitor cells for cancer gene therapy.
Giulia Grisendi, PhD, Researcher, Department of Medical and Surgical Sciences for Children & Adults, University Hospital of Modena and Reggio Emilia, Italy.

Q&A Session, presenter answers questions from other speakers or attendees.

11:30 – 12:00 PM
Presentation Title: Sharpin plays an important role in the regulation of keratinocyte apoptosis and skin inflammation.
Fumiyo Ikeda, PhD, Group leader, Institute of Molecular Biotechnology (IMBA) Dr. Bohr-Gasse 3, 1030, Vienna, Austria.

Q&A Session, presenter answers questions from other speakers or attendees.

Panel Discussion. This session is to provide speakers and attendees with in-depth discussion and networking. You can discuss what you want with other speakers. All speakers are unmuted, so speakers can talk freely during the session.

Session 11: Stem cell biology-I
12:00 PM – 14:30 PM
Session Chair: Dr. Ming Pei

12:00 – 12:30 PM
Presentation Title: Application of human cardiomyocytes derived from pluripotent stem cells for toxicity testing and disease modeling.
Peter Sartipy, PhD, Vice President Stem Cell Discovery and Senior Principal Scientist, Cellectis AB, Arvid Wallgrens Backe 20, 413 46 Göteborg, Sweden.

Q&A Session, presenter answers questions from other speakers or attendees.

12:30 – 13:00 PM
Presentation Title: Limbal Side Population cells for the treatment of limbal stem cell deficiency.
Bakiah Shaharuddin, M.D, M.MED (Ophth), Institute of Genetic Medicine, Newcastle University, International Centre for Life, Central Parkway, Newcastle Upon Tyne, NE1 3BZ, U.K.

Q&A Session, presenter answers questions from other speakers or attendees.

13:00 – 13:30 PM
Presentation Title: Decellularized stem cell matrix mediated cartilage regeneration and its significance for regenerative medicine
Ming Pei, M.D., Ph.D., Tenured Associate Professor, Director, Stem Cell and Tissue Engineering Laboratory, Department of Orthopaedics, West Virginia University, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

13:30 – 14:00 PM
Presentation Title: Molecular Elucidation and Engineering of the Stem Cell Fate Decisions.
David Schaffer, Ph.D., Professor of Chemical and Biomolecular Engineering, Bioengineering, and the Helen Wills Neuroscience Institute, Director, Berkeley Stem Cell Center, University of California, Berkeley, CA, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

14:00 – 14:30 PM
Presentation Title: Targeting and Tackling the Cancer Stem Cell Niche.
Lynne-Marie Postovit, PhD, the Sawin-Baldwin Chair in Ovarian Cancer and the Dr. Anthony Noujaim Legacy Oncology Chair as well as an associate professor in the Department of Oncology at the University of Alberta and an adjunct professor in the Department of Anatomy and Cell Biology at Western University, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

Panel Discussion. This session is to provide speakers and attendees with in-depth discussion and networking. You can discuss what you want with other speakers. All speakers are unmuted, so speakers can talk freely during the session.

Session 12: Cell signaling pathways-V
14:30 PM – 16:30 PM
Session Chair: Dr. Jianjun Sun

14:30 – 15:00 PM
Presentation Title: Molecular adaptations of mammalian hibernation; regulation

of energy dependent cellular processes during metabolic depression.
Kenneth B. Storey, Ph.D., F.R.S.C., Professor of Biochemistry at Carleton University in Ottawa and holds the Canada Research Chair in Molecular Physiology, Canada. **Michael Wu**, the lab of Dr. Kenneth B. Storey, Carleton University, Canada.

Q&A Session, presenter answers questions from other speakers or attendees.

15:00 – 15:30 PM
Presentation Title: Anti-inflammatory effects of natural extracts enriched with bioactives.
Alexander Gosslau, Visiting Professor, Department of Chemistry and Chemical Biology, Rutgers University, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

15:30 – 16:00 PM
Presentation Title: Pending.
Jianjun Sun, Assistant Professor of Biological Sciences, University of Texas at El Paso, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

16:00 – 16:30 PM
Presentation Title: Pending.
Rahul Saxons, Researcher, Department of Biochemistry and Molecular & Cellular Biology Georgetown University Medical Center, Washington, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

Panel Discussion. This session is to provide speakers and attendees with in-depth discussion and networking. You can discuss what you want with other speakers. All speakers are unmuted, so speakers can talk freely during the session.

Track 4: 8:30 AM– 17:00 PM, February 28, 2014

8:30 – 9:00 AM
Speakers and attendees can login the online conference.

Session 13: General biochemistry-I
9:00 AM – 11:00 AM
Session Chair: Dr. Tiana V. Curry-McCoy

9:00 – 9:30 AM
Presentation Title: Surrogate reporter-based enrichment of cells containing RNA-guided Cas9 nuclease-induced mutations.
Suresh Ramakrishna, Stem Cell Research, College of Medicine, Hanyang University,

Seoul-133-791, South Korea.

Q&A Session, presenter answers questions from other speakers or attendees.

9:30 – 10:00 AM
Presentation Title: Genetic polymorphism of milk proteins and their relationship with milk compositional traits in Indian goat breeds.
Ajoy Mandal, Senior Scientist, Eastern Regional Station, National Dairy Research Institute, India.

Q&A Session, presenter answers questions from other speakers or attendees.

10:00 – 10:30 AM
Presentation Title: Circulating complementary innate IgM originating from ancestral antigen completeness in reduction of O-glycosylations.
Peter Arend, MD, ret. Philipps University of Marburg/Lahn, Germany.

Q&A Session, presenter answers questions from other speakers or attendees.

10:30 – 11:00 PM
Presentation Title: Alcohol: A Glimpse at Direct, and Indirect Organ Damage; With Application to Future Research.
Tiana V. Curry-McCoy Ph.D., Assistant Professor, Medical Laboratory Imaging Radiologic Sciences-Clinical Laboratory Science, College of Allied Health Sciences, Georgia Regents University (MCG&ASU), USA.

Q&A Session, presenter answers questions from other speakers or attendees.

Panel Discussion. This session is to provide speakers and attendees with in-depth discussion and networking. You can discuss what you want with other speakers. All speakers are unmuted, so speakers can talk freely during the session.

Session 14: General biochemistry-II
11:00 AM – 13:00 PM
Session Chair: Dr. Iulia M. Lazar

11:00 – 11:30 PM
Presentation Title: Novel uses of circular variance for macromolecular analyses.
Mihaly Mezei, Director of Molecular Modeling Core (associate professor), Department of Structural and Chemical Biology, Mount Sinai School of Medicine, NYU, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

11:30 – 12:00 PM
Presentation Title: The Role of Proteomics in the Elucidation of Cancer Pathways.
Iulia M. Lazar, Ph.D., Associate Professor, Department of Biological Sciences, Virginia

Polytechnic Institute and State University, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

12:00 – 12:30 PM
Presentation Title: ß-phenylethylamine as a novel inhibitor of E. coli biofilm.
Birgit M. Pruess, Associate Professor, Veterinary and Microbiological Sciences, North Dakota State University, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

12:30 – 13:00 PM
Presentation Title: Modeling the Evolution of Drug Resistance in Malaria.
David Hecht, Professor of chemistry at Southwestern College in Chula Vista, California and an adjunct faculty member, San Diego State University Dept. of Chemistry, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

Panel Discussion. This session is to provide speakers and attendees with in-depth discussion and networking. You can discuss what you want with other speakers. All speakers are unmuted, so speakers can talk freely during the session.

Session 15: Stem cell biology-II
13:00 PM – 15:00 PM
Session Chair: Dr. Devyn M. Smith

13:00 – 13:30 PM
Presentation Title: Leveraging stem cell discoveries to enable drug discovery?
Devyn M. Smith, Chief Operating Officer, Pfizer's Neusentis Research Unit, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

13:30 – 14:00 PM
Presentation Title: Neural Stem Cell Models & Potential Anesthetic-Induced Neurotoxicity.
Cheng Wang, M.D., Ph.D. Senior Scientist at the National Center for Toxicological Research (NCTR)/US Food and Drug Administration (FDA), USA. He is also an Adjunct Faculty member in the Department of Pharmacology and Toxicology, University of Arkansas for Medical Sciences (UAMS), USA.

Q&A Session, presenter answers questions from other speakers or attendees.

14:00 – 14:30 PM
Presentation Title: Cardiomyocyte Differentiation in Human Skeletal Muscle Stem Cells by Biophysical Factors and Post-Transcriptional Regulation.
Jason Tchao, MS, Department of Bioengineering, University of Pittsburgh, USA;

Kimimasa Tobita, M.D. Research Associate Professor, Director of Animal Imaging Core, Rangos Research Center, Children's Hospital of Pittsburgh of UPMC, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

14:30 – 15:00 PM
Presentation Title: Age-related dysfunction in mechano-transduction impairs differentiation of human mammary epithelial progenitors.
Fanny Pelissier, Researcher, Life Science Division, Lawrence Berkeley National Laboratory, Berkeley, California, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

Panel Discussion. This session is to provide speakers and attendees with in-depth discussion and networking. You can discuss what you want with other speakers. All speakers are unmuted, so speakers can talk freely during the session.

Session 16: General biochemistry-III
15:00 PM – 17:00 PM
Session Chair: Dr. Jong Hyun Ham

15:00 – 15:30 PM
Presentation Title: The intercellular signaling systems for the virulence of the rice pathogenic bacterium Burkholderia glumae.
Jong Hyun Ham, Ph. D., Associate Professor, Department of Plant Pathology and Crop Physiology, Louisiana State University Agricultural Center, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

15:30 – 16:00 PM
Presentation Title: Metabolomics, Metaboloepigenomics, Polyomics.
Miroslava Cuperlovic-Culf, Senior Research Officer, National Research Council of Canada, Moncton, Canada.

Q&A Session, presenter answers questions from other speakers or attendees.

16:00 – 16:30 PM
Presentation Title: Methamphetamine increases the levels of dopamine D2 receptor and dopamine transporter in dopaminergic nerve terminals.
Anna Moszczynska, Ph.D., Assistant Professor, Department of Pharmaceutical Sciences, Rm 3142, Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

16:30 – 17:00 PM

Presentation Title: Bioprinted Neocartilage Formation in Poly (ethylene) Glycol and Gelatin Methacrylate Copolymer Using Human Mesenchymal Stem Cells.
Xiaofeng Cui, Ph.D., Senior Research Fellow, Institute of Advanced Study, Technical University of Munich; Director of Research, Stemorgan Therapeutics, New York, USA.

Q&A Session, presenter answers questions from other speakers or attendees.

Panel Discussion. This session is to provide speakers and attendees with in-depth discussion and networking. You can discuss what you want with other speakers. All speakers are unmuted, so speakers can talk freely during the session.

Presentation Summaries (Alphabetical Order)

1 Ajay Singh
2 Ajoy Mandal
3 Alexander Gosslau
4 Aman Shah Abdul Majid
5 Amol Patil
6 Andreas Eisenreich
7 Anna Moszczynska
8 Anwar Rayan
9 Bakiah Shaharuddin
10 Birgit M. Pruess
11 Cheng Wang
12 Chiara Riganti
13 Christina Stuelten
14 Christina Voelkel-Johnson
15 Dan Cojoc
16 David Hecht
17 David Schaffer
18 Devyn M. Smith
19 Dorit Ron
20 Erik Wiemer
21 Fanglin Zhang
22 Fanny Pelissier
23 Fumiyo Ikeda
24 Gangadhara Reddy Sareddy
25 Giulia Grisendi
26 Iulia M. Lazar
27 Jamil Talukder
28 Jianjun Sun
29 John Lyssand
30 Jong Hyun Ham
31 Joseph Fomusi Ndisang
32 Juan Ding
33 Juntang Lin
34 Kathleen L. Hefferon
35 Kenneth B. Storey
36 Kevin Pfleger
37 Kimimasa Tobita
38 Kotb Abdelmohsen
39 Lilian I. Plotkin
40 Lynne-Marie Postovit
41 Marco Colombini
42 Maria Cristina Vinci
43 Mihaly Mezei
44 Mine Erguven

45 Ming Pei
46 Miroslava Cuperlovic-Culf
47 Nigel P Murray
48 Paola Tucci
49 Peter Arend
50 Peter Sartipy
51 Rahul Saxons
52 Romano Maria Fiammetta
53 Rossella Sgarbanti
54 Rujuan Dai
55 Saurabh Sen
56 Shreya Mitra
57 Subbaya Subramanian
58 Subhadip Raychaudhuri
59 Suresh Ramakrishna
60 Tammy A. Butterick-Peterson
61 Thomas Weber
62 Tiana V. Curry-McCoy
63 Tom Monie, Researcher
64 Vincenza Rita Lo Vasco
65 Xiaofeng Cui
66 Yin-Yuan Mo
67 Zhen He

1. Tumor-stromal crosstalk in pancreatic cancer pathobiology and chemoresistance.
Ajay Singh, Department of Oncologic Sciences, Mitchell Cancer Institute, University of South Alabama, USA.
Summary: Pancreatic cancer remains a therapeutic challenge for clinicians and translational researchers. Currently, it is the fourth leading cause of cancer-related death with a rising incidence and unabated mortality. To change this grim scenario, we need to develop an improved understanding of the mechanisms underlying the aggressive and drug-resistant nature of pancreatic cancer. In this regard, we have identified signaling pathways that operate through tumor-stromal interaction and mutually promote growth and chemoresistance of pancreatic cancer. Research is currently ongoing to systematically investigate the therapeutic significance of our observations with a hope that, in due course, it will open up new avenues for effective therapeutic care of pancreatic cancer patients.

2. Genetic polymorphism of milk proteins and their relationship with milk compositional traits in Indian goat breeds.
Ajoy Mandal, Eastern Regional Station, National Dairy Research Institute, A-12 Block, Kalyani- 7412 35, Nadia, West Bengal, India.
Summary: Genetic polymorphisms of milk proteins have received considerable research interests because of possible associations between milk protein genotypes and economically important traits in dairy animals. Genetic polymorphism of milk proteins and their effect on milk composition traits of Indian goat breeds belonging to different agro-climatic regions of India was studied. Milk protein genotyping was carried out by sodium dodecyl sulphate polyacrylamide gel electrophoresis (SDS – PAGE) method at αS1- CN (CSN1S1), β-CN (CSN2), αS2- CN (CSN1S2), κ –CN (CSN3), β-LG and α-LA loci. Milk proteins of different Indian goat breeds viz. Jamunapari, Barbari, Marwari, Sirohi, Jakhrana, Kutchi, Beetal, Ganjam and local goats, contained the four major casein variants i.e. αS1, αS2, β and κ and two types of whey proteins, α-lactalbumin and β-lactoglobulin. Indian goats exhibited αS1- casein A allele in higher frequency in the majority of the breeds except Ganjam and local goats. A total of 16 casein haplotypes were observed in Indian goat breeds and breed specific haplotypes were observed with respect to geographical region. Expected heterozygosity at six different loci demonstrated the genetic diversity and breed differentiation among Indian goat breeds. The variability among goat breeds contributed by αS2- CN (CSN1S2), β-LG and αS1- CN. The Indian goats exhibited αS1- casein A allele in higher frequency in all the breeds indicating the higher casein yield in their milk.

3. Anti-inflammatory effects of natural extracts enriched with bioactives.
Alexander Gosslau, Department of Chemistry and Chemical Biology, Rutgers University, USA.
Summary: Chronic inflammation is widely recognized as a major underlying cause of various degenerative diseases including diabetes, arthritis and cancer. Accumulative effects of tissue destruction caused by electrophilic species coupled with damage induced by proteolytic metalloproteinases lead to pathological conditions which increase with aging. The need for anti-inflammatory therapies is evident and natural products have the potential to fill this therapeutic gap addressing the complexity in the inflammatory

cascade thereby reducing side effects and compensatory reactions requiring secondary treatment. We developed two proprietary extracts such as black tea extract (BTE) enriched with theaflavins and orange peel extract (OPE) enriched with polymethoxyflavones. Effects on inflammation were analyzed by nutrigenomics using a human cell-based TPA-induced monocyte-macrophage differentiation model. BTE and OPE significantly down-regulated the expression of a panel of surrogate genes involved in inflammatory response, including COX-2, TNF-□, ICAM-1, NF□B, IL-1□, Il-6, and IL-8 with an inflammatory index of -0.39 and -0.55 for BTE and OPE, respectively. Down-regulation of inflammatory genes correlated to anti-inflammatory effects of BTE and OPE in different in vivo animal models for inflammation such as skin, ear, and paw edema. In two double blind, randomized, placebo-controlled clinical pilot trials employing LPS-mediated irritation or intensive exercise-induced inflammation, BTE induced attenuation of different cytokines and chemokines as well as reduced inflammatory symptoms such as ROS reduction and delayed onset muscle soreness. In summary, enrichment of phyto extracts such BTE and OPE with specific anti-inflammatory bioactives is a promising strategy to find naturally derived extracts effective against diseases associated with inflammation.

4. Slow Regulated Release of H2S Inhibits Oxidative Stress Induced Cell Death by Influencing Certain Key Signaling Molecules.

Aman Shah Abdul Majid, Department of Integrative Medicine, Advanced Medical and Dental Institute, USM, Penang, Malaysia.

Summary: Hydrogen sulphide (H2S) is one of three gaseous signaling molecules after nitric oxide and carbon monoxide. Various H2S donor compounds have been synthesized to study its physiological function. Among these compounds sodium hydrosulphide (NaHS), a donor of releasing H2S rapidly have shown to be protective in certain neuronal cell line but several in vivo studies have generated conflicting data. Furthermore several slow releasing H2S donors have been shown to have positive effects on cells in culture. The intracellular concentration of H2S and hence its rate of production may be a factor in keeping the balance between its neuroprotective and toxic effects. The present study was undertaken to deduce how a rapid releasing H2S donor (NaHS) as opposed to a slow releasing donor (ADTOH), affect oxidative stress related intracellular components and survival of RGC-5 cells. It was concluded that when RGC-5 cells are exposed to the toxic effects of glutamate in combination with buthionine sulfoxime (Glu/BSO), ADTOH was more efficacious in inhibiting apoptosis, scavenging reactive oxygen species (ROS), stimulation of glutathione (GSH) and gluthathione-S-transferase (GST). Western blot and qPCR analysis showed ADTOH increased the levels of Nrf2, HO-1, PKCα, p-Akt, Bcl-2 and XIAP but caused a decrease of Nfκβ and xCT greater than NaHS. This study is first to compare the efficacy of two H2S donor drugs as potential neuroprotectants and demonstrate that slow regulated release of H2S to cell culture can be more beneficial in inhibiting oxidative stress induced cell death.

5. From molecules to genes.

Amol Patil, Dept. of Orthodontics and Dentofacial Orthopedics, Bharati Vidyapeeth Dental College and Hospital, Bharati Vidyapeeth Deemed University, Pune, Maharashtra, India.

Summary: Pending.

6. Regulation of Tissue Factor biology via microRNAs.
Andreas Eisenreich, Charité-Universitätsmedizin Berlin, Campus Benjamin Franklin, Centrum für Herz- und Kreislaufmedizin, 12200 Berlin, Germany.
Summary: Tissue Factor (TF) is important for the control of several physiologic and patho-physiologic processes, such as thrombogenesis, angiogenesis, and tumorigenesis. Due to the important (patho-)physiologic-relevant role of TF, the expression and biologic function of TF is highly regulated. In recent years, micro (mi)RNAs were shown to be crucial for post-transcriptional expression regulation and functional modulation of TF under physiologic- and patho-physiologic conditions. Here, the latest findings regarding the impact of miRNA on TF biology will be summarized in the context physiologic as well as patho-physiologic-relevant settings, such as vascular haemostasis control or cancer biology.

7. Methamphetamine increases the levels of dopamine D2 receptor and dopamine transporter in dopaminergic nerve terminals.
Anna Moszczynska, Department of Pharmaceutical Sciences, Rm 3142, Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, USA.
Summary: Methamphetamine (METH) is a central nervous system psychostimulant with a high potential for abuse. At high doses, METH causes a selective degeneration of dopaminergic terminals in the striatum. Dopamine D2 receptor antagonists and dopamine transporter (DAT) inhibitors protect against neurotoxicity of the drug by decreasing intracellular dopamine content and, consequently, dopamine autoxidation and production of reactive oxygen species. In vitro and ex vivo, amphetamines regulate D2 receptor and DAT functions via regulation of their intracellular trafficking. Limited data exists on trafficking of both proteins and their protein-protein interactions in vivo. The aim of the present investigation was to examine synaptosomal levels of D2 receptor and DAT after two different regimens of METH and to determine whether METH affects D2 receptor-DAT protein-protein interaction in rat striatum. We report that the immunoreactivity of the DAT is rapidly increased by a non-toxic single dose of METH whereas the immunoreactivity of D2S receptor is increased by neurotoxic binge METH administration. Single non-toxic METH does not have much effect on D2 receptor-DAT protein-protein interaction whereas toxic METH increases the interaction between the two proteins. Our results suggest that METH can affect axonal transport of both the D2S and DAT in protein-protein interaction-dependent and –independent manner.

8. Indexing Chemicals for their Bioactivity on GPCRs by Ligand-Structural Combined Approach.
Anwar Rayan, the Drug Discovery Informatics Lab at the QRC research center – Al Qasemi Academic College & GeneArrest LTD company, Israel.
Summary: Human G-Protein Coupled Receptors cover the most prominent family of validated drug targets. More than 50% of approved drugs reveal their therapeutic effects by targeting this family. In this talk, we will describe how sequential combination of ligand-based chemoinformatics techniques with structure-based bioinformatics techniques has the potential to improve the success rate in discovering new biologically

active compounds and increase the enrichment factors in a synergistic manner. Ligand-based chemoinformatics technique: Two ligand-based chemoinformatics techniques, the Intelligent Learning Engine and Iterative Stochastic Elimination approach, were utilized to index chemicals for their molecular bioactivity. Structure-based bioinformatics technique: 3-D structure prediction of hGPCRs remains a challenge due to limited availability of resolved structure. The X-ray structures have been solved for only few receptors. The identity between hGPCRs and the potential templates is mostly less than 30%, well below the level at which sequence alignment can be done regularly and highly accurate models could be obtained. We will present our findings from analysis of a large set of comparative models as well as a large database of family-A human G-protein coupled receptors and suggest few tips for improving the quality of hGPCRs homology-based models. Acknowledgements: A.R is a management committee member of COST Action CM1207 titled "GLISTEN: GPCR-Ligand Interactions, Structures, and Transmembrane Signalling: a European Research Network".

9. Limbal Side Population cells for the treatment of limbal stem cell deficiency.

Bakiah Shaharuddin1,2, Sajjad Ahmad3,4, Simi Ali5, Annette Meeson1, 1 Institute of Genetic Medicine, Newcastle University, Newcastle Upon-Tyne, NE1 3BZ, UK. 2 Advanced Medical and Dental Institute, Universiti Sains Malaysia, 13200 Pulau Pinang, Malaysia.3 St Paul's Eye Unit, Royal Liverpool University Hospital, Prescot Street, Liverpool, L7 8XP, UK.4 Department of Eye and Vision Sciences, Institute of Ageing and Chronic Disease, University of Liverpool, 4th Floor UCD Building, Daulby Street, Liverpool, L69 3GA, UK. 5 Institute of Cellular Medicine, Newcastle University, Newcastle Upon-Tyne, NE1 7RU, UK.

Summary: Introduction: Limbal stem cell deficiency refers to a condition caused by abnormal maintenance of the limbal stem cells. Ex vivo expanded limbal epithelial stem cell transplantation is a contemporary cellular-based therapy to regenerate and reconstruct the ocular surface as a mode of treatment. The challenges in limbal stem cell biology remain in the process of identification, isolation and expansion of these adult corneal epithelial stem cells. The side population assay (SP) is an isolation method that utilises the ability of stem cells to efflux the DNA-binding dye Hoechst 33342 (or other vital dyes) combined with dual wavelength flow cytometry. Materials and Methods: Human cadaveric limbal tissue and human telomerase-immortalised corneal epithelial cells (HTCEC) were used for characterisation of cell populations of interest by PCR, flow cytometry and immuno fluorescence. Using an optimised limbal SP protocol we sorted SP and NSP cells of the HTCEC directly onto slides and stained them with antibodies to ABCG2, ΔNp63 and Sox2. Using Image J software combined with microscopy, the signal intensity for each marker was quantified. Results: Side population assay has been used to successfully identify stem/ progenitor cell populations in a variety of tissues and cell lines. We optimise this assay to identify SP cell populations in both primary human limbal epithelial cultures and in an established human corneal epithelial cell line. The limbal SP fraction showed higher expression compared to non-SP cells (NSP); ABCG2 expression (P= 0.026), ΔNp63 (P=0.007) and Sox2 (P=0.021). Discussion and Conclusions: We show that SP cells isolated from the HTCEC line using this protocol, have significantly elevated expression of ABCG2, ΔNp63 and Sox2 above that displayed by the NSP cell fraction, supporting the use of this protocol for identification and

separation of a stem cell enriched cell fraction of limbal cells. In addition, the sensitivity of the assay to different species and cell types also makes standardisation of SP protocols mandatory to ensure reliability and reproducibility of SP data. Future work involves further characterisation of by quantitative polymerase chain reaction or proliferation studies such as colony forming efficiency or spheroid formation of the limbal SP. References: 1, Goodell, M., et al., (1996). Isolation and functional properties of murine hematopoietic stem cells that are replicating in vivo. J Exp Med., 183(4), 1797-1806. 2, Budak, M.T., et al., (2005). Ocular surface epithelia contain ABCG2-dependent side population cells exhibiting features associated with stem cells. J Cell Sci, 118(Pt 8), 1715-24. 3, de Paiva, C.S., et al., (2005). ABCG2 Transporter Identifies a Population of Clonogenic Human Limbal Epithelial Cells. Stem Cells, 23(1), 63-73. Acknowledgment: Supported by grants from the Ministry of Higher Education, Malaysia and partially by Universiti Sains Malaysia, Pulau Pinang, Malaysia.

10. ß-phenylethylamine as a novel inhibitor of E. coli biofilm.

1Birgit M. Prüß, 1Meredith Irsfeld, and 2Shane J. Stafslien 1Department of Veterinary and Microbiological Sciences, North Dakota State University, Fargo ND; 2Center for Nanoscale Science and Engineering, North Dakota State University, Fargo ND, USA.

Summary: A random screen of 95 carbon and 95 nitrogen sources had previously determined that ß-phenylethylamine (PEA) performed best at reducing bacterial cell counts and biofilm amounts of E. coli O157:H7 that was grown in liquid beef broth medium at 10oC (Lynnes et al., Meat Science, 2013). In addition, PEA reduced bacterial cell counts when the bacteria were grown on small pieces of beef meat. PEA is a trace substance in chocolate that is sold in health stores to aid weight loss and mood improvement. It is generally regarded as safe (GRAS status). Our two long-term goals are to i) develop PEA into a spray that reduces bacteria on beef meat and to ii) integrate PEA into novel biomaterials that inhibit biofilm formation. Working towards the second of these goals, we used E. coli K-12 as a model bacterium and tested the effect of PEA on bacterial growth (as OD600), biofilm amounts (as OD600 of the washed and resuspended biofilm), expression of flhD (as fluorescence from flhD::gfp), bacterial cell counts (from plating serial dilutions onto LB agar plates), and stability of the biofilm (with a custom build water jet). FlhD is part of the FlhD/FlhC transcriptional activator complex that is responsible for the expression of all other flagellar genes. Since flagella mediate the first stage of attachment, reversible attachment, an inhibition of flhD would be indicative of a shut down of the initial stage of biofilm formation. The water jet has been developed by the Center for Nanoscale Science and Engineering for the measurement of attachment strength of numerous marine bacteria (Stafslien et al., Rev. Scientif. Instrum., 2007). The technique involves a spinning head that applies a controlled water pressure to the biofilm. The protocol was modified to the purpose of this experiment, which also involved a control mutation in argD that was not expected to impact E. coli biofilm. The experiment revealed that bacterial growth and cell counts were not impacted by PEA until a concentration of 20 to 40 mg/ml was reached. In contrast, flhD expression was already much reduced at 0.25 mg/ml. Biofilm amounts were much inhibited at a PEA concentration of 6 mg/ml. Our current hypothesis is that biofilm is inhibited by PEA at its very onset through inhibition of flagella expression and synthesis. The determination of biofilm stability led to an intriguing result. Until 2 mg/ml, increasing concentrations of

PEA actually increased the stability of the biofilm. We conclude from this part of the experiment that PEA does indeed reduce biofilm amounts. However, the remaining bacteria appear very tightly attached to the respective surface. In contrast, a mutant in fliA, which also can not synthesize flagella, exhibited increased biofilm removal and decreased biofilm amounts after treatment with the water jet, when compared to the isogenic parent strain. This indicates that flagella are not just important for starting the biofilm, but also contribute to its integrity. In summary, we found that PEA was indeed an inhibitor of E. coli biofilm, likely through inhibition of flhD expression and flagella synthesis. In the future, we like to use this protocol to test the effect of PEA on numerous bacterial pathogens with the ultimate goal to integrate it into novel biofilm inhibiting biomaterials.

11. Neural Stem Cell Models & Potential Anesthetic-Induced Neurotoxicity.

C Wang, F Liu, TA Patterson, MG Paule and W Slikker Jr. Division of Neurotoxicology, National Center for Toxicological Research (NCTR)/FDA, Jefferson, AR 72079, USA.*

Summary: It is known that the most frequently used general anesthetics have either N-methyl-D-Aspartate (NMDA)-type glutamate receptor blocking or GABA receptor enhancing properties. Both propofol (GABA agonist) and ketamine (NMDA antagonist) are widely used in pediatric anesthesia or analgesia. To evaluate their potential for producing developmental neurotoxicity and elucidating these underlying mechanisms, embryonic neural stem cells (NSCs) were used. NSCs were harvested from gestational day 14 rat fetuses; on day 7 in culture NSCs were exposed to 10, 50, 100, 300 and 600 μM propofol or 1, 10, 100, and 500 μM ketamine in growth medium (GM) for 24 h individually; or 50 μM propofol and 10 μM ketamine in differentiation medium (DM), respectively. In GM propofol caused a dose-dependent reduction of NSC viability (MTT-uptake); while ketamine did not have this effect except at 500 μM, an extremely high concentration. At clinically-relevant concentrations in GM, propofol (50 μM) produced a dramatic increase in ROS generation and enhanced apoptosis as evidenced by an increased number of TUNEL-positive cells and Bax (a pro-apoptotic gene) expression, indicating propofol-induced NSC apoptosis may be mediated by oxidative stress, while similar apoptotic effects were not observed when NSCs were exposed to a clinically-relevant dose of ketamine (10 μM). No significant intracellular calcium influx was detected when NSCs were stimulated with 50 μM NMDA, suggesting no functional NMDA receptors expressed on NSCs (in GM). On the other hand, most of the NSCs differentiated into neurons and glial cells in the DM (with serum). Differentiated neurons were characterized by immunocytochemical staining of PSA-NCAM (a neuron-specific marker) and an apparent calcium influx stimulated with 50 μM NMDA, suggesting the existence of functional NMDA receptors. Propofol (50 μM) and ketamine (10 μM) significantly increased ROS generation in DM. Also, propofol and ketamine exposure specifically caused neuronal damage (neuron population; PSA-NCAM positive), while glial cells, e.g., astrocytes (GFAP positive) were not significantly affected in DM. Additionally, propofol, but not ketamine, produced a significantly higher amount of glutamate release from neurons (pre-synaptic) compared with control in DM. These observations demonstrate ROS plays a key role in propofol- or ketamine-induced neuronal damage. Therefore, calcium imaging, gene and protein arrays will be critical for

further mechanistic studies. In summary, an excitatory action of glutamate neurotransmission could be closely related to anesthetic-induced toxicity during development. Supported by NCTR/FDA E-7417.

12. NO-releasing doxorubicins: new anthracycline derivatives that overcomes drug-resistance in cancer cells.

Chiara Riganti, Biochemistry, Department of Oncology, Turin School of Medicine, University of Turin, Italy.

Summary: The major limitations of doxorubicin (DOX) are the onset of drug resistance and the cardiotoxicity. In previous studies we have shown that nitric oxide (NO) donors associated with DOX overcome the resistance. NO can nitrate critical tyrosines on ATP-binding cassette (ABC) transporters, such as P-glycoprotein (Pgp/ABCB1), multidrug resistance related proteins (MRPs/ABCCs) and breast cancer resistance protein (BCRP/ABCG2). Following the nitration, the activity of ABC transporters was inhibited and DOX was less effluxed [1]. In order to improve the effects of NO in reversing drug resistance, we designed new polyvalent drugs that were at the same time anti-cancer agents and NO-delivery systems. We produced synthetic DOXs conjugated with NO-releasing groups, namely nitrooxy-DOX (NitDOX) and 3-phenylsulfonylfuroxan-DOX (FurDOX) [2]. We tested them in a panel of human drug-sensitive and drug-resistant cancer cells, created by selecting the parental cell lines in a DOX-containing medium. Nit-DOX and Fur-DOX released NO in a dose- and time-dependent manner, nitrated ABC transporters, were more accumulated than DOX and had a lower IC50 than DOX in all the drug-resistant cells analyzed. Nit-DOX was not more cytotoxic than DOX in cardiomyocytes and in non transformed epithelial cells in vitro, and was further investigated. Surprisingly NitDOX showed properties far different from a typical anthracycline: it did not inhibit the purified topoisomerase II enzyme, it was uptaken with a faster kinetics, it produced different metabolites, it showed an extranuclear distribution and a preferential accumulation in mitochondria. The mitochondrial delivery was due to the higher hydrophobicity and to the lower efflux of NitDOX, which nitrated and inhibited MRP1 and BCRP present in mitochondrial membranes. In mitochondria NitDOX inhibited the tricarboxylic acid cycle, the electron flux through Complex I and the synthesis of ATP, induced the release of cytochrome c in the cytosol and the activation of caspase-9-dependent apoptosis. All these events were dependent on the release of NO, since they were reduced by NO scavengers. Of note, the effects on mitochondrial metabolism and apoptosis were equally achieved in drug-sensitive and drug-resistant cells [3]. We propose nitrooxy-doxorubicin as the first lead compound of a new series of polyvalent anthracyclines, characterized by different mechanisms from traditional anthracyclines and able to overcome drug resistance. References [1] Riganti C, Miraglia E, Viarisio D, Costamagna C, Pescarmona G, Ghigo D, Bosia A (2005). Nitric oxide reverts the resistance to doxorubicin in human colon cancer cells by inhibiting the drug efflux. Cancer Res 65: 516-525; [2] Chegaev K, Riganti C, Lazzarato L, Rolando B, Guglielmo S, Campia I, Fruttero R, Bosia A, Gasco A (2011). Nitric oxide donor – doxorubicin conjugates accumulate into doxorubicin resistant human colon cancer cells inducing cytotoxicity. ACS Med Chem Lett 2:494-497; [3] Riganti C, Rolando B, Kopecka J, Campia I, Chegaev K, Lazzarato L, Federico A, Fruttero R, Ghigo D (2013).

Mitochondrial-targeting nitrooxy-doxorubicin: a new approach to overcome drug resistance. Mol Pharm 10:161-174.

13. Cell Directionality as an Indicator of Breast Cancer Progression.
Christina H. Stuelten, Rachel M. Lee, Michael Weiger, Lunhua Liu, Wolfgang Losert, and Carole A. Parent, Cell and Cancer Biology Branch, National Cancer Institute, USA.
Summary: During malignant progression, epithelial tumor cells invade surrounding healthy tissues and migrate to metastatic sites. Therefore, tumor cell invasion and spread represent key targets to control tumor disease. However, little is known about tumor cell migration during malignant progression. Using a series of genetically related breast cancer cell lines, MCF10A, MCF10At.1k, MCF10CA1h, MCF10CA1a, and MDA-MB-231T cells we can show that migratory speed as well as distance traveled does not distinguish invasive and metastatic cells from normal epithelia cells in established assays such as wound healing assays or Boyden chamber assays. However, more detailed analysis of migration of cell sheets by time-lapse imaging and subsequent particle image velocimetry (PIV) revealed that invasive cell lines migrated in a more random, less directional motion. Epithelial growth factor (EGF) and lysophosphatidic acid (LAP) which both have been implicated in tumorigenesis and tumor progression, exhibited distinct effects on the migratory phenotype of the investigated breast cancer cell line. Interestingly, LPA reverted the migratory pattern of invasive MCF10CA1a cells to a pattern similar to that observed in normal epithelial MCF10A cells, as it caused MCF10CA1 cells to migrate in a more orderly and directed pattern. Currently, we investigate the effects of LPA on the migratory phenotype as well as E-cadherin- and myosinIIb expression patterns in our model system.

14. Sphingosine kinase 2 as a novel therapeutic target in prostate cancer.
Helen Gosnell, Laura M. Kasman*, Lucas Vu*,Thrimoorthy Potta**, Elizabeth Garrett Mayer*, Kaushal Rege**, and Christina Voelkel-Johnson *. *Department of Microbiology and Immunology, Medical University of South Carolina, Charleston SC and **Department of Chemical Engineering, Arizona State University, Tempe, AZ, USA. Heather Venant 1, Charles D. Smith 2, Michael Lilly3, and Christina Voelkel-Johnson 1 1 Department of Microbiology and Immunology, Medical University of South Carolina, Charleston, SC, USA; 2 Department of Drug Discovery and Biomedical Sciences, Medical University of South Carolina, Charleston, SC, USA and Apogee Biotech Corporation, Hummelstown PA, USA; 3 Department of Medicine, Medical University of South Carolina, Charleston, SC, USA.*
Summary: The development of castration resistant prostate cancer (CRPC) and lack of effective therapies to treat this disease remain major clinical obstacles. Curative options are lacking and even novel therapy approaches, such as the androgen receptor inhibitor enzalutamide, prolong survival only by approximately 4-5 months. In recent years, evidence that inflammation promotes tumor growth has been mounting and levels of inflammatory cytokines correlate with the extent of the disease in prostate cancer patients. Sphingosine-1-phosphate (S1P) is an important lipid mediator that has been shown to play roles in survival, drug resistance, angiogenesis and inflammation. Consequently, S1P as well as the enzymes responsible for its production (sphingosine kinase 1 and 2) have evolved as important therapeutic targets. A small study using human

tumor cDNA arrays revealed that SphK2 but not SK1 expression was markedly elevated in prostate tumors compared to normal prostate tissue. In situ analysis of existing microarray data from patient matched normal and malignant prostate tissue indicates that SphK2 mRNA is upregulated in nearly half of the prostate cancers. Further, analysis of a prostate tissue microarray reveals that SphK2 is expressed in the prostate but that infiltrating inflammatory cells stain the strongest for this enzyme. A novel, first-in-class SphK2-selective inhibitor ABC294640 is currently under evaluation in a phase I clinical trial. In preclinical models, this drug was found to exert anti-proliferative and anti-inflammatory effects. We are currently evaluating the impact of SphK2 inhibition in prostate cancer, both alone and in combination with androgen blockade. This study may establish the foundation for novel combination therapies of advanced prostate cancer.

15. Focal stimulation of neuronal cells by optical manipulation.

Dan Cojoc, IOM-CNR, Institute of Materials- National Research Council, Italy.

Summary: Spatial regulation of secretory molecule release is a sophisticated mechanism used by the nervous system to control network development and finely tune the activity of each synapse. Great efforts have been made to develop techniques that mimic secretory molecule release with the aim of stimulating neurons as close as possible to physiological conditions. However, current techniques have poor spatial resolution or low flexibility. Here, we propose a novel approach to achieve focal stimulation of neurons by optical trapping and manipulation of micro-vectors carrying signaling molecules. We discuss two examples of vectors: microbeads functionalized with a secretory molecule, the neurotrophin brain-derived neurotrophic factor (BDNF) and liposomes encapsulating. guidance molecules Sema3A and Netrin-1. In the first example we show that single BDNF-coated microbeads can be optically manipulated from small reservoirs to specific sites on the dendrites of cultured hippocampal neurons. Localized contact of the BDNF microbead induced an increase of calcium signaling both in the soma and in the stimulated dendrite. It induced also a specific activation of the TrkB receptor pathway and influenced the development of growth cones. Remarkably, a single BDNF-coated bead localized on a dendrite was found to be enough for TrkB phosphorylation, an efficient and long-lasting activation of calcium signaling in the soma, and c-Fos signaling in the nucleus, comparable to bath stimulation conditions [1]. In the second example we discuss another type of vector, lipid vesicles, to encapsulate guidance cues. It is known that growth cones (GCs) are the major motile structures guiding neuronal navigation and guidance molecules, such as Sema3A or Netrin-1, induce GC repulsion or attraction. Nevertheless, the speed of action and efficiency of these guidance molecules is still poorly understood, requiring a local delivery and a strict control of the amount of molecules released. Therefore we developed an experimental setup based on optical manipulation techniques (i.e. optical tweezers and UV micro-dissection) to deliver controlled amounts of these molecules specifically to GCs [2]. Lipid microvesicles were used as vectors for the encapsulation of the guidance cues. By means of an IR-optical tweezers, single vesicles were selected, trapped and positioned to the site of stimulation nearby the GC. Vesicles were then broken by UV a laser pulse to release the content. Sema-3A and Netrin-1 molecules were delivered to single growth cones in hippocampal neuronal cultures, and morphological modifications of growth cones in response to the release were monitored in time lapse imaging. The amount of molecules delivered was

calculated considering the volume of the vesicle, the concentration of the signaling molecules in solution and the encapsulation efficiency. A wide range (10 to 104 molecules per vesicle) could thus be investigated. After their release the guidance molecules diffused and reached the GC membrane in a few seconds. Following their arrival GCs retracted or grew in less than 2 min. By determining the number of guidance molecules trapped inside vesicles and estimating the fraction of guidance molecules reaching the GC, we show that less than 5 Netrin-1 molecules on the GC membrane are sufficient to induce growth. In contrast, more than 200 Sema3A molecules is necessary to induce filopodia retraction. Our results show that optical manipulation techniques open new opportunities to investigate signal transduction mechanisms. References: 1. E. D'Este, G. Baj, P. Beuzer, E. Ferrari, G. Pinato, E. Tongiorgi, and D. Cojoc, "Use of optical tweezers technology for long-term, focal stimulation of specific subcellular neuronal compartments", Integr. Biol. 3, 568 (2011). 2. G. Pinato, T. Raffaelli, E. D'Este, F. Tavano, and D. Cojoc D (2011), "Optical delivery of liposome encapsulated chemical stimuli to neuronal cells", J Biomed Opt, 16:095001 (2011). 3. G. Pinato, D. Cojoc, L. Thuy Lien, A. Ansuini, J. Ban, E. D'Este, and V. Torre, "Less than 5 Netrin-1 molecules initiate attraction but 200 Sema3A molecules are necessary for repulsion," Sci. Rep. 2, 675 (2012).

16. Modeling the Evolution of Drug Resistance in Malaria.

David Hecht, Chemistry at Southwestern College in Chula Vista, California and an adjunct faculty member, San Diego State University Dept. of Chemistry, USA.

Summary: The evolution of drug resistance in malaria continues to be a widespread concern. Many of these drugs target key proteins such as dihydrofolate reductase (DHFR). However in malaria, the structural plasticity of DHFR allows it to maintain its active site and catalytic activity, while resisting drug binding. One way to better understand this process is through the appreciation of DHFR structural evolution in general, and then use in silico evolution to model both the drug docking and the likely amino acid changes in DHFR that will occur as a result. Here we study the amino acid replacements in dihydrofolate reductase (DHFR) that confer resistance to anti-folate drugs while still binding the natural DHFR substrate, 7,8-dihydrofolate, and cofactor, NADPH. Iteration of this process allows the opportunity to model the coevolutionary processes involved with drug resistance and to predict responses to pharmaceuticals in advance of their use in the field.

17. Molecular Elucidation and Engineering of the Stem Cell Fate Decisions.

David Schaffer, Chemical and Biomolecular Engineering, Bioengineering, and the Helen Wills Neuroscience Institute, Berkeley Stem Cell Center, University of California, Berkeley, CA, USA, 94720-3220.

Summary: Elucidating the mechanisms that govern stem cell self-renewal and differentiation is critical for understanding the roles these cells play in organismal development and function as well as for harnessing stem cells to repair tissues damaged by disease or injury. It has become increasingly clear that stem cells are regulated not only by biochemical signals in the niche, but also by biophysical features in the way these signals are presented, though investigating the latter is challenged by experimental complexities in investigating and mimicking the complexity of the extracellular matrix

(ECM), cell-cell interactions, and other niche components. Recent work has demonstrated that bioactive, synthetic materials can be harnessed to emulate and thereby study the effects of solid phase, biophysical cues on cell function. For example, activation of many cellular receptors involves the formation of oligomeric protein signaling complexes with ligands presented from the matrix, the surface of neighboring cells, and in some cases even from solution. We have developed multivalent ligands – polymers conjugated to signaling proteins to yield biomimetic signals with nanoscale spatial organization – which potently induce the differentiation of human pluripotent stem cells in vitro and neural stem cells in vitro and in vivo. In addition, these materials combined with optogenetics and super-resolution microscopy have yielded insights into signaling mechanisms that regulate the fate decisions of these cells. Finally, such biomimetic materials can be integrated into safe, scaleable, and robust bioprocesses for pluripotent stem cell expansion and differentiation.

18. Leveraging stem cell discoveries to enable drug discovery?
Devyn M. Smith, Pfizer's Neusentis Research Unit, USA.
Summary: Big pharma has been attempting to improve the pace and rate of new drug discovery over the last decade. Many different approaches have been used to improve R&D productivity. Stem cells provide a unique opportunity to potentially improve overall R&D productivity and many companies are testing this hypothesis. There are a few key areas where Pharma are using stem cells in their traditional R&D work. These areas include: generating early data on efficacy and safety of compounds, using stem cells to create better assays for high throughput screening of traditional libraries, and use of stem cells to enable better translation from pre-clinical to clinical data. We will discuss where iPS cells can enable pharmaceutical R&D and give specific examples to illustrate the work ongoing in Pharma.

19. Presentation Title: Signaling Mechanisms Underlying Alcohol Abuse Disorders.
Dorit Ron, Cell Biology of Addiction in Neurology, Department of Neurology, University of California, San Francisco, Gallo Research Center Investigator, USA.
Summary: Pending.

20. MicroRNAs in the tumor biology of soft tissue sarcomas.
Caroline M.M. Gits, Stefan Sleijfer, Erik A.C. Wiemer, Department of Medical Oncology, Erasmus University Medical Center – Erasmus MC Cancer Institute, Rotterdam, the Netherlands.
Summary: Sarcomas are relatively rare tumors of mesenchymal origin that comprise about 1% of all adult malignancies. They constitute a heterogeneous group of tumors consisting of more than 50 histological subtypes that can occur almost anywhere in the body such as in muscles, fat, bone, cartilage, fibrous tissue, synovial tissue and nerves. Roughly they can be classified into two large groups primary bone sarcomas and soft tissue sarcomas. Liposarcomas are one of the most common types of soft tissue sarcomas, representing approximately 10 – 15% of all mesenchymal neoplasms. They are of adipogenic origin and are currently classified into three major biological entities and five histological subtypes: differentiated/dedifferentiated, myxoid/round cell and pleomorphic liposarcomas. The subtypes display different biological characteristics and clinical

behavior. Standard treatment consists of surgery in combination with systemic chemotherapy, but nevertheless mortality rates are high. More insight into the biology of liposarcoma tumorigenesis is needed to devise novel therapeutic approaches. We demonstrate that miRNA expression profiling can be used to discriminate liposarcoma subtypes, which could aid in objective diagnostic decision making. In addition, our data indicate that miR-145 and miR-451 act as tumor suppressors in adipose tissue and show that re-expression of these miRNAs could be a promising therapeutic strategy for liposarcomas. Gastrointestinal stromal tumors (GIST) are the most common primary mesenchymal malignancies found in the gastrointestinal tract. GISTs are characterized by high expression of KIT and ETV1 which cooperate in GIST oncogenesis. We identified miRNAs that are deregulated in GIST notably miR-17-92 and miR-221/222 cluster members. Overexpression of these miRNAs in GIST cell lines lines severely inhibited cell proliferation, affected cell cycle progression, induced apoptosis and strongly downregulated protein and - to a lesser extent – mRNA levels of their predicted target genes KIT and ETV1. Luciferase reporter assays confirmed direct regulation of KIT and ETV1 by miR-222 and miR-17/20a, respectively. In conclusion our results indicate that miR-17/20a/222 play a role in GIST pathogenesis and may potentially be used as therapeutic tool.

21. The inflammatory factors and their epigenetic regulation in Multiple sclerosis.
Fanglin Zhang, Department of Neurology, Multiple Sclerosis Research Center, Vanderbilt University Medical Center, USA.
Summary: Pending.

22. Age-related dysfunction in mechano-transduction impairs differentiation of human mammary epithelial progenitors.
Fanny Pelissier, Life Science Division, Lawrence Berkeley National Laboratory, Berkeley, California, USA.
Summary: Dysfunctional progenitor cells accumulate during aging in human mammary epithelia, which is associated with increased cancer risk. We tested whether aging impaired epithelial progenitors to differentiate in response to changes in tissue mechanical properties. Culture substrata were tuned to mimic breast tissue elastic moduli, from compliant normal to stiffer malignant, to functionally probe modulus-dependent differentiation in primary multipotent progenitors from younger (<30yrs) and older (>55yrs) women. In young progenitors, compliant substrata enhanced luminal differentiation, whereas stiffer substrata favored myoepithelial differentiation, which required the YAP/TAZ transcription factors. Older progenitors showed no differential responses to physiological modulus changes. Patterns of modulus-dependent actin stress-fibers, focal-adhesions, and ERK phosphorylation were age-independent demonstrating that mechano-sensing was unaffected by age. YAP/TAZ activation in older progenitors required extra-physiological stiffness and unexpectedly caused luminal differentiation. Immortalization of old progenitors restored physiological YAP/TAZ activation, but luminal-skewed differentiation patterns persisted, congruent with durable age-related epigenetic alterations. Thus age-dependent accumulation of progenitors is explainable by inefficient transduction of pro-differentiation mechanical cues.

23. Sharpin plays an important role in the regulation of keratinocyte apoptosis and skin inflammation.

Fumiyo Ikeda, Institute of Molecular Biotechnology (IMBA) Dr. Bohr-Gasse 3, 1030, Vienna, Austria.

Summary: Sharpin is a subunit of Linear Ubiquitin chain Assembly Complex (LUBAC) E3 ligase complex, specifically generating linear (Met1-linked) ubiquitin chains. We have previously shown that Sharpin is required to fully activate the NF-kB signal induced by inflammatory cytokines. On the other hand, a Sharpin deficient mouse line, Cpdm (Chronic proliferative dermatitis mice) shows a heavy inflammatory phenotype in multiple organs including skin, gut and esophagus. Interestingly, a significant increase of apoptotic keratinocytes is observed in Cpdm. Inhibition of apoptosis by depleting TNFR1 associated death domain protein (TRADD) in epidermal keratinocytes of Cpdm mouse line rescued the inflammatory phenotype in the skin. Apoptosis in mouse embryonic fibroblasts (MEFs) derived from Cpdm was drastically increased upon TNF-a stimulation in comparison to the wild type MEFs. We found that the induction of apoptosis in Cpdm MEFs is via the Death-inducing Signaling Complex (DISC) pathway. In addition, we identified that Fas-Associated protein with Death Domain (FADD) as a novel substrate of LUBAC and FADD ubiquitination plays a role in the Sharpin-dependent anti-apoptosis signaling. In conclusion, we elucidated the regulatory mechanism of Sharpin dependent anti-apoptosis pathway via FADD ubiquitination. Further, apoptosis of keratinocytes in Cpdm is one of the major causes of the skin inflammation.

24. Proline Glutamic acid and Leucine rich Protein1 (PELP1) is a novel coregulator of β-catenin in glioblastoma.

Gangadhara R. Sareddy and Ratna K. Vadlamudi. UTHSCSA, San Antonio, TX, USA.

Summary: Glioblastoma (GBM) are the most common and deadliest intracranial neoplasms. Despite recent advances in the standard therapies, the survival of GBM patients is approximately 12-14 months. Better understanding of the molecular pathways and mechanisms that contributes to the GBM development is clinically significant and will provide novel therapeutic targets. In the present study, we examined the significance of proto-oncogene PELP1 that functions as a coregulator of many nuclear transcriptional factors. PELP1 expression is commonly deregulated in hormonal cancers, however, little is known about PELP1 and its significance in GBM. Using immunohistochemical analysis of glioma tissue microarrays that contain different grades of astrocytomas, oligodendrogliomas, ependymomas and normal brain tissues, we found that PELP1 is overexpressed in glioma compared to normal brain, with highest expression in GBM, and PELP1 expression levels were positively correlated with histological malignancy. PELP1 expression was also found to be elevated in various established and patient derived GBM cells when compared to normal astrocytes. To establish the functional significance of PELP1 in GBM, PELP1 expression was silenced using PELP1 specific siRNA and shRNA. We observed that silencing of PELP1 reduced the cell proliferation, cell migration and colony formation of U87, T98G and LN229 GBM cells. Mechanistic studies showed that PELP1 interacts with β-catenin and silencing of PELP1 resulted in decrease in β-catenin reporter gene activation. Accordingly, PELP1 knockdown dramatically reduced the expression of β-catenin target genes such as Axin2, cyclin D1,

c-Myc and MMP-2. Chromatin-immunoprecipitation assays showed that silencing of PELP1 compromised the recruitment of β-catenin to the target genes promoters. In xenograft based tumorigenecity assays we found that silencing PELP1 dramatically reduced the in vivo tumor growth of U87 GBM cells. Taken together these results provide the first evidence that PELP1 could be a potential target for therapeutic intervention in GBM.

25. Gene modified mesenchymal progenitor cells for cancer gene therapy.
Giulia Grisendi, PhD & Massimo Dominici, MD, Department of Medical and Surgical Sciences for Children & Adults, University Hospital of Modena and Reggio Emilia, Italy.
Summary: Despite significant advances in the field of gene therapy for cancer, the lack of tumor tropism of vectors and stimulation of an immune response limit the clinical potential of this approach. The use of mesenchymal stromal/ stem cells (MSC) as cellular vehicle represents an attractive option to overcome these barriers supporting targeted delivery of a gene or therapeutic protein to the tumor site. Thanks to their biological and immunological features, including easy accessibility from different source, rapid proliferation in culture and poor immunogenicity, MSC represent a powerful weapon to develop novel strategy to fight cancer. In particular the typical tropism displayed by MSC against tumor sites has aroused growing interest among researchers. Several studies on solid tumor microenvironment have indicated that MSC take active part in generation of a supportive stroma, becoming structural components of tumor architecture and releasing cytokines and chemokines at the tumor site. Based on this knowledge, we conceived to use modified adipose MSC as "trojan horse" to deliver an anticancer molecule against different tumors. We have previously demonstrated that a pro-apoptotic agent named tumor necrosis factor related apoptosis inducing ligand (TRAIL) can be effectively delivered by MSC, targeting different cancer types. More recently, we have further challenged our cell therapy approach based on MSC expressing TRAIL against mesenchymal tumors such as sarcoma. Sarcomas are a heterogeneous group of rare malignant tumors that arise from mesenchymal tissues such fat, bone, cartilage and muscle. They comprise less than 10% of all malignancies but about 15% of pediatric cancers. Several studies have demonstrated that TRAIL can induce cell death in a variety of sarcomas either alone or in concert with immunomodulation and cytotoxic therapies. Actually surgery, used in combination with chemotherapy and radiation therapy, represent the first line treatment for sarcoma, however therapies are not definitive and disseminated refractory diseases are associated with a reduced overall survival of less than 15% at 5 years. Major metastatic sites are represented by lung and, even after metastasectomy, the majority of patients (60%) do not survive more than 5 years. The poor prognosis for metastatic or tumor relapse has pointed out the needed of novel and more effective therapies. In this preclinical study, for the first time, we have explored the use of genetically modified mesenchymal progenitors expressing the anticancer molecule TRAIL in order to counteract these rare mesenchymal cancers. In vitro, MSC-TRAIL were able to induce cell death in three different sarcoma histotypes moreover, when injected into pre-established Ewing's Sarcoma xenotransplants, MSC-TRAIL counteracted tumor development causing massive cancer apoptosis and exerting potent anti-angiogenic functions. Collectively, our results suggest that MSC as cellular vehicles

for TRAIL could open a novel therapeutic opportunity for sarcomas affecting young generation and still characterized by bad prognosis.

26. The Role of Proteomics in the Elucidation of Cancer Pathways.

Iulia M. Lazar, Jingren Deng and Fumio Ikenishi, Department of Biological Sciences, Virginia Polytechnic Institute and State University, USA.*

Summary: The importance of advancing the frontiers of science to enable early cancer detection can never be over-stated. The lack of a quantitative correlation between gene and protein expression levels significantly impedes the identification of therapeutic targets and the development of novel treatment strategies for cancer. In addition, the laborious reconstruction and understanding of cellular signaling networks that lead to the progression of this disease is primarily dependent on the identification of all proteins expressed in a specific cell type, and their posttranslational modifications. At the present time, this information is incomplete. For example, reversible protein phosphorylation at Ser, Thr or Tyr residues, in response to external stimuli, represents a key signal transduction mechanism that is involved in controlling fundamental biological processes such as gene expression, cell cycle progression, cell proliferation, growth, differentiation, metabolism and apoptosis. Nevertheless, actual protein phosphorylation in a cell is not readily predictable by bioinformatics approaches, and experimental detection of this posttranslational modification is necessary. The progress in advanced technologies such mass spectrometry detection has enabled researchers in the past decade to generate a massive amount of data. The challenge, however, of making use of such data rests with finding a strategy to reduce the "dimension" of the findings and placing the data in the right biological context. In this presentation, we will describe the realm of a set of proteomic data generated through the analysis of three cell lines (MCF-7/ER+ cancer, SKBR-3/Her2+ cancer, and MCF-10 non-tumorigenic) in two different stages of the cell cycle, G1 and S. We will address the main sources of challenge, the computational techniques that are used to derive statistical significance, and the approaches that can be used to validate the results, enhance biological significance and improve the study design. Ultimately, we will discuss the pathways that were identified and matched to biological mechanisms that drive aberrant cancer cells into division.

27. Leukotriene activates Ca2+ dependent dephosphorylation of ASCT1 to down regulate Ala transport in IEC-6 cells.

Jamil Talukder, Biology, LeMoyne-Owen College, USA.

Summary: Arachidonic acid metabolite derived via Lipoxygenase pathway, leukotriene D4 (LT) inhibits Na+-dependent alanine cotransport (ASCT1, solute carrier, SLC1A4) in intestinal epithelial cell brush border membrane (BBM) by decreasing the affinity of cotransporter. However, the intracellular mechanism of LT mediated inhibition of ASCT1 is unknown. This study was designed to investigate the intracellular mechanism of ASCT1 inhibition by LT in enterocytes. [3H]-Ala uptake was measured in 10 days postconfluent rat intestinal epithelial cells (IEC-6) grown on transwell plates. IEC-6 cells were treated with different inhibitors intercepting different checkpoints of pathways for LT mediated inhibition of ASCT1 at 8 days postconfluence. LT treatment decreased ASCT1 activity and increased more than 2.5-fold intracellular cAMP. However, protein kinase A (PKA) inhibitor did not reverse the LT mediated inhibition of ASCT1. LT

increased 2-fold cytosolic Ca2+ and PKC-α antagonized LT effect on ASCT1 activity. In contrast, PKC-δ and -θ inhibitor did not reverse LT mediated inhibition of ASCT1. Further downstream of PKC-α pathway, tyrosine kinase (Akt) inhibitor also reversed LT mediated inhibition of ASCT1 activity. Kinetics, western blotting, and qRT-PCR studies demonstrated that the mechanism of reversal of LT mediated inhibition of ASCT1 by Akt inhibitor was due to the restoration of affinity of the cotransporter. Immunocytochemical and dephosphorylation studies revealed that ASCT1 was dephosphorylated by LT treatment. Therefore, we conclude that LT inhibits ASCT1 activity by dephosphorylation through Ca2+-dependent PKCα-Akt pathway in enterocytes.

28. Presentation Title: Pending.
Jianjun Sun, Biological Sciences, University of Texas at El Paso, USA.
Summary: Pending.

29. Rethinking the Traditional Western.
John Lyssand, Ph.D., Field Applications Scientist, Biotechnology, LI-COR Biosciences, USA.
Summary: Traditional Western blotting is a labor-intensive process that includes gel electrophoresis, protein transfer to a blotting membrane, incubation with primary and secondary antibodies, and chemiluminescent or fluorescent detection of target proteins. Day-to-day reproducibility is poor, because small variations in lysate preparation, gel loading, electrophoresis, transfer, and detection are unavoidable sources of technical variability. The In-Cell Western™ (ICW) assay, a quantitative immuno-fluorescent method, is an alternative to traditional Western blots that increases both reproducibility and sample throughput. Here we describe the In-Cell Western Assay. Cells are cultured and treated in microplates. After treatment, cells are fixed and permeabilized, blocked, and incubated with antibodies for detection of target proteins. Fluorophore-coupled secondary antibodies and detection with a LI-COR Odyssey® imaging system enable superior sensitivity, accurate quantitation, and easy normalization to a loading control. The traditional Western blot protocol is streamlined, eliminating cell lysis, gel electrophoresis, and membrane transfer. The In-Cell Western assay enables screening and analysis of many more samples in each experiment, eliminates error-prone protocol steps, and delivers higher reproducibility for biological and technical replicates. Tips for optimization will also be discussed.

30. The intercellular signaling systems for the virulence of the rice pathogenic bacterium Burkholderia glumae.
Jong Hyun Ham, Department of Plant Pathology and Crop Physiology, Louisiana State University Agricultural Center, Baton Rouge, LA 70803, USA.
Summary: Burkholderia glumae is the major causal agent of bacterial panicle blight, an emerging bacterial disease of rice. Phytotoxins, toxoflavin and its derivatives, are an important virulence factor of this pathogen. The quorum-sensing mediated by the LuxI and LuxR homologs, TofI and TofR, is known to be a central signaling/regulatory system for the expression of major virulence factors including toxoflavin and lipase. From our molecular genetic and genomic studies of B. glumae, novel signaling/regulatory components involved in bacterial virulence have been identified. Genetic dissection of

the tofI/tofR locus through a series of gene deletions revealed the new quorum-sensing modulator tofM located between tofI and tofR. In particular, intercellular signaling independent of tofI and tofR was discovered from the study of tofM. Transcriptome analyses through RNA-sequencing revealed genes and non-coding RNAs differentially expressed in tofI-dependent or tofI–independent ways in liquid and solid medium conditions, respectively. This transcriptome analysis also implied that DSF-type quorum-sensing and the cyclic di-GMP signaling are under the control of (or interconnected with) the TofI/TofR quorum-sensing system.

31. Heme oxygenase ameliorates cardiomyopathy by suppressing markers of heart failure and inflammation in normoglycemic obese rats".

Joseph Fomusi Ndisang, Department of Physiology, University of Saskatchewan, Canada.

Summary: Pending.

32. Friend or foe: Anti-aging cosmetics on the eye.

Juan Ding, Schepens Eye Research Institute/Massachusetts Eye and Ear, Harvard Medical School, Boston, MA, USA.

Summary: With a growing aging population, anti-aging cosmetics continue gaining popularity. However, potential concerns are raised with the main anti-aging ingredient, retinoic acid (RA), on the health of the eye. RA can have serious adverse effects on the meibomian gland, a sebaceous gland in the eye lids that secrete lipids to the tear film to prevent its evaporation. RA is known to cause keratinization and obstruction, gland atrophy, gland drop out and poor quality of meibomian gland secretions. These signs are the hallmarks of meibomian gland dysfunction (MGD), a major cause of dry eye disease (DED) that affects hundreds of millions of people world wide. The mechanism how RA induces MGD is not well understood. We hypothesize that RA alters gene and protein expression, inhibits cell proliferation, attenuates cell survival pathways and promotes cell death in human meibomian gland epithelial cells. To test our hypotheses, immortalized human meibomian gland epithelial cells were cultured with or without RA for varying doses and time. Cell proliferation, cell death, gene expression, and proteins involved in proliferation/survival and inflammation were evaluated. We found that 13-cis RA inhibited cell proliferation, induced cell death, and significantly altered the expression of 6,726 genes, including those involved in cell proliferation, cell death, differentiation, keratinization and inflammation, in human meibomian gland epithelial cells. Further, RA also reduced the phosphorylation of Akt and increased the generation of interleukin-1β and matrix metallopeptidase 9. Thus we have unraveled the mechanism of RA-induced MGD. Future studies are needed to identify molecular targets to inhibit these adverse actions of RA, with the ultimate goal of eliminating the dry eye inducing side effect of anti-aging cosmetics. [Supported by NIH grant R01EY05612 and AFER/Vistakon Dry Eye Fellowship]

33. Pax3 and Pax7 reversely interact and regulate the expression and distribution of their target genes in the chicken developing spinal cord.

Juntang Lin1,2, Congrui Wang1,2, Ciqing Yang2, Christoph Redies1 1 Institute of Anatomy I, University of Jena School of Medicine, Jena University Hospital, Teichgraben

7, D-07743 Jena, Germany; 2 Xinxiang Medical University, Jinsui Road 601, 453003 Xinxiang, China.
Summary: Pax3 and Pax7 both are transcription factors and widely expressed in the developing nervous system and somites. In the central nervous system, they both are expressed in the dorsal part of the neural tube. It is known that Pax3 and Pax7 are involved in Shh signaling pathway and inhibited by Shh over-expression. In the present study, we in vivo confirmed that of Pax3 over-expression represses the expression of Pax7, while Pax7 over-expression endogenously enhances and ectopically induces the expression of Pax3 in the developing chicken spinal cord. They both inhibit the endogenous expression of Gli1, Gli2, but induce the ectopic transcript of Gli3. To two members of cadherin family, Cadherin-7 and Cadherin-20, the over-expression of Pax3 and Pax7 repress their endogenous but induce their ectopic expression which indicate a different regulation way from Shh signaling pathway. The down-regulation of Pax3 and Pax7 with specific shRNA, not their over-expression, results in apoptosis in the developing spinal cord, suggesting Pax3 and Pax7 are involved in cell proliferation. Collectively, these results suggest that transcription factor Pax3 and Pax7 play important roles to regulate their target genes expression/distribution and cell proliferation in the developing spinal cord. Key words: Pax3; Pax7; Cadherin; Expression regulation; Spinal cord.

34. Applications of Virus Expression Vectors for Infectious Disease Research.
Kathleen L. Hefferon, University of Toronto, Canada.
Summary: As basic knowledge of the molecular biology of viruses improves, virus expression vectors increase in sophistication and their application in the field of medicine broadens. Virus expression vectors have been used as research tools for generating vaccines and have functioned as delivery vehicles for siRNAs, antiviral agents, and other drug candidates. Besides vectors based on animal viruses such as vaccinia virus, VSV, adeno-associated virus, lentivirus and herpesvirus, plant viruses have also been developed and examples of their applications are provided. The following presentation describes recent innovations with respect to the use of virus expression vectors for both therapeutics and drug development.

35. Molecular adaptations of mammalian hibernation; regulation of energy dependent cellular processes during metabolic depression.
Kenneth B. Storey and Michael Wu, Biochemistry at Carleton University in Ottawa, Canada.
Summary: For many small mammals, survival over the winter months is a serious challenge because of low environmental temperatures and limited food availability. The solution for many species, such as thirteen-lined ground squirrels (Ictidomys tridecemlineatus), is hibernation, an altered physiological state characterized by seasonal heterothermy and entry into long periods of torpor that are interspersed with short arousals back to euthermia. At the cellular level, biochemical adaptations take place to achieve metabolic re-programming during hibernation; metabolic rate is strongly reduced to achieve major energy savings, via coordinated depression of non-essential ATP-expensive functions such as protein synthesis and gene transcription. In this talk, molecular mechanisms that regulate metabolic depression will be discussed, including the

role of post-translational and transcriptional regulations in energy dependent cellular processes such as mTOR signaling and FoxO transcriptional response.

36. Profiling the Pharmacology of GPCR Complexes.

Kevin Pfleger, Molecular Endocrinology-GPCRs, Western Australian Institute for Medical Research, Australia.

Summary: G protein-coupled receptors (GPCRs) function as multi-protein complexes, signalling through and being regulated by a host of other proteins including G proteins, arrestins, ubiquitin and other GPCRs. Our work has focused upon assessing the molecular pharmacology of GPCR complexes, primarily in live cells and in real-time. We have largely used bioluminescence resonance energy transfer (BRET) to do this, measuring the non-radiative energy transfer between a luciferase donor genetically fused to one protein of interest, and a fluorophore fused to another, following addition of a suitable luciferase substrate. The very high distance dependence of this energy transfer means that the donor and acceptor, and therefore the proteins of interest, are in very close proximity, indicative of complex formation. Furthermore, the real-time nature of the measurement enables informative kinetic profiles to be established in live cells and at physiological temperature.

37. Cardiomyocyte Differentiation in Human Skeletal Muscle Stem Cells by Biophysical Factors and Post-Transcriptional Regulation.

Jason Tchao1, M.S., and Kimimasa Tobita1,2,3, M.D., Department of Bioengineering1, Developmental Biology2, McGowan Institute for Regenerative Medicine3, University of Pittsburgh, USA.

Summary: Heart failure results in significant cardiomyocyte (CM) loss, and post-natal mammalian heart has limited regenerative capacity. Cellular cardiomyoplasty has emerged as a novel therapy to restore contractile function of injured myocardium. Skeletal myoblasts can be safely isolated and showed some benefits in clinical trials, but high incidence of arrhythmias due to lack of electric coupling with host cells limits their use for cardiac repair. This limitation could be overcome by differentiating cells into CMs. Muscle derived stem cells (MDSC) possess greater phenotypic plasticity than skeletal myoblasts. Our studies showed that cardiac and skeletal muscle share major muscle transcription factor genes/proteins in native developing muscle and stem cell-derived muscle cells. Therefore, it may be possible for human MDSCs to differentiate into CM-like cells under the appropriate conditions. The results of our studies showed that differentiating muscle cells from human MDSC aggregates in 3-dimensional engineered muscle tissue (3D-EMT) beat spontaneously, displayed cyclic calcium transients, expressed cardiacspecific transcription factor and structural proteins, and responded to cardiotropic compounds. They also possessed characteristics of skeletal muscle including expression of MyoD and myogenin. Their electrical coupling also remained immature. By temporally treating 3D-EMT with 4 chemical factors (4CF: miR-206 inhibitor, IWR-1, BMP4, and LiCl) and improving aggregation conditions, 4CF-EMT showed better muscle tissue formation and more cardiac-like morphology with improved contractility, pharmacological responses, and electrical coupling. The results highlight the importance of temporal control of both biophysical and posttranscriptional factors for CM differentiation from MDSCs.

38. lncRNA 7SL represses p53 translation by competing with HuR.
Kotb Abdelmohsen, Laboratory of Cellular and Molecular Biology, NIA-IRP, NIH, Baltimore, MD, USA.
Summary: Long noncoding RNAs (lncRNAs) and RNA-binding proteins (RBPs) are potent post-transcriptional regulators of gene expression. The lncRNA 7SL is upregulated in cancer cells, but its impact on the response of cancer cells is unknown. Here, we present evidence that 7SL forms a partial hybrid with the 3'-untranslated region (UTR) of TP53 mRNA, which encodes the tumor suppressor p53. The interaction of 7SL with TP53 mRNA reduced p53 translation, as determined by analyzing p53 expression levels, nascent p53 translation, and TP53 mRNA association with polysomes. Silencing 7SL led to increased binding of HuR to TP53 mRNA, an association that led to the promotion of p53 translation and increased p53 abundance. We propose that the competition between 7SL and HuR for binding to TP53 3'UTR determines the magnitude of p53 translation, in turn affecting p53 levels, and the growth-suppressive function of p53.

39. Regulation of osteoclast differentiation by Cx37.
Lilian I. Plotkin, Department of Anatomy and Cell Biology, Indiana University School of Medicine, USA.
Summary: Connexin (Cx) proteins are essential for cell differentiation, function and survival in all tissues with Cx43 being the most studied in bone. We found that Cx37, another member of the connexin family of proteins, is expressed in osteoclasts, osteoblasts and osteocytes. Mice with global deletion of Cx37 (Cx37-/-) exhibit higher bone mineral density, increased cancellous bone volume, and improved mechanical strength compared to wild type littermates. Treatment of non-adherent Cx37-/- bone marrow cells, which contain osteoclast precursors, with the pro-osteoclastogenic cytokines Receptor activator of nuclear factor kappa-B ligand (RANKL) and macrophage colony stimulating factor (M-CSF) rendered a 5-fold lower level of osteoclast differentiation compared to Cx37+/+ cell cultures. Further, Cx37-/- osteoclasts are smaller and have fewer nuclei per cell. mRNA expression of the RANKL receptor RANK, and TRAP, cathepsin K, calcitonin receptor, MMP9, NFATc1, DCSTAMP, ATP6v0d1 and CD44, markers of osteoclast number, fusion and activity, is lower in Cx37-/- osteoclasts compared to controls. In addition, non-adherent bone marrow cells from Cx37-/- mice exhibit higher levels of markers for osteoclast precursors, suggesting altered osteoclast differentiation. Osteoclast number and surface are significantly lower in bone of Cx37-/- mice. In contrast, mineralization of differentiating bone marrow cultures ex vivo, as well as circulating levels of osteocalcin and alkaline phosphatase, expression of osteoblast markers in bone, osteoblast number and surface and bone formation rate in bones from Cx37-/- mice are unchanged. Thus, Cx37 is required for osteoclast differentiation and fusion and its absence leads to arrested osteoclast maturation and high bone mass in mice. These findings demonstrate a previously unrecognized role of Cx37 in bone homeostasis that is not compensated for by Cx43 in vivo.

40. Targeting and Tackling the Cancer Stem Cell Niche.
Lynne-Marie Postovit, Robarts Research Institute, The Schulich School of Medicine, Western University, USA.

Summary: Tumours contain populations of cells with stem cell like properties, and it is believed that these phenotypically plastic cells are responsible for cancer progression and metastatic potential. Stem cell-like populations are regulated by dynamic niches, characterized by specific growth factors and extracellular matrices, as well as biophysical features such low oxygen tensions. Moreover, a growing body of evidence suggests that cancer cells co-opt stem cell-associated regulatory networks in order to sustain plasticity. We have discovered that an embryonic-associated protein called Nodal maintains stem cell phenotypes in cancer, and that it promotes classical hallmarks of cancer such as angiogenesis, invasion and metastasis. We have also found that biophysical features of a growing tumour, in particular hypoxia, can promote tumour cell plasticity by up-regulating embryonic proteins like Nodal via a combinatorial mechanism. Finally, we have determined that exposure to normal embryonic stem cell factors can reprogram metastatic cancer cells toward a more differentiated, less tumourigenic phenotype. We are currently using quantitative SILAC-based proteomics together with developmental and cancer model systems to identify potential anti-tumourigenic proteins in stem cell-derived extracellular matrices; and to further understand how cancer cells hijack developmental signalling cascades to facilitate progression. By studying the mechanisms by which cancer cells acquire and sustain phenotypic plasticity, we may uncover novel targets for the prediction and prevention of tumour progression.

41. The pro-apoptotic protein, Bax, forms highly cooperative, voltage-gated channels.

Marco Colombini, Dept. Biology, University of Maryland, USA.

Summary: Pending.

42. Ox-LDL and Inflammatory Environment Shift Angiogenic Endothelial Progenitor Cells into Functional Antigen Presenting Cells.

Maria Cristina Vinci, Cardiovascular Tissue Engineering Laboratory, Centro Cardiologico Monzino, IRCCS, Italy.

Summary: At present, two endothelial progenies, early and late endothelial progenitor cells (EPCs), were identified according to their in vitro onset, lineage, and functional properties. Both cell types synergistically provide instructive (release of angiogenic cytokines) and structural (vessel incorporation and stabilization) functions that promote the initiation of neo-angiogenesis. Early-EPCs (eEPCs), also referred as myeloid angiogenic cells, are an important EPC subtype obtained in vitro from mononuclear cell fraction after one week of culture in angiogenic medium. The paracrine pro-angiogenic function of these cells has been well established. Several preclinical studies have indeed demonstrated their active participation in EC regeneration/vasculogenesis either as cellular placeholders of the injured endothelium, or as cytokine 'factories' for ECvascular-regenerating cells. Early EPC precursors (monocyte/macrophage mononuclear cell population) are characterized by a hidden plasticity which allows them to behave as multi/pluripotent stem cell under appropriate micro-environmental conditions. Nevertheless, angiogenic eEPCs have been extensively proposed in regenerative medicine regardless of their trans-differentiation potential and response to the host's micro-environment. In the present study we demonstrated that high levels of pro-inflammatory cytokines and oxidized-LDL, commonly present in advanced

atherosclerotic plaque milieu, shifted EPC commitment into functional inflammatory/immunomodulatory antigen presenting cells (APCs) with a distinct paracrine and transcriptional profile and potentially harmful cardiovascular effects.

43. Novel uses of circular variance for macromolecular analyses.

Mihaly Mezei, Department of Structural and Chemical Biology, Mount Sinai School of Medicine, USA.

Summary: The concept of circular variance has been shown to be useful for the characterization of macromolecular topography. The talk will discuss the use of circular variance for the characterization of molecular surface ruggedness and the possibility of using it for predicting protein-protein interaction interfaces. In addition, the idea of a putative Achilles' heel of a protein, which resulted from work with circular variance, will be discussed.

44. Prostate cancer stem cell, midkine protein and lithium chloride.

Mine Ergüven, 2 Gülperi Öktem, 3 Ali Nail Kara, 4 Ayhan Bilir 1 İstanbul Aydın University, Faculty of Engineering, İstanbul, Turkey; 2 Department of Histology And Embryology, Ege University, Faculty of Medicine, İzmir, Turkey; 3 2nd Term Student, İstanbul University, Istanbul Faculty of Medicine, İstanbul, Turkey; 4 Department of Histology and Embryology, İstanbul University, İstanbul Faculty of Medicine, İstanbul, Turkey.

Summary: The aim of this study was to investigate the effects of lithium chloride (LiCl) which has been established for more than 60 years as effective bipolar disorder treatment and is lately pronounced with its' antineoplastic effects on prostate stem cells through survival protein midkine (MK) levels. Human prostate cell line DU145 (HTB-81) was provided from American Type Culture Collection and cultured in monolayer. Cells were sorted by using FACS Diva flow cytometry (BD Biosciences) and cancer stem cell group was labeled as (+). Cells were incubated with low concentrations (1 μM, 10 μM) and high concentrations (100 μM, 500 μM) of LiCl for 72 hours. Total cell numbers, apoptotic index (flow cytometric Annexin-V-FITC/PI staining) and MK levels (ELISA) were evaluated. Istatistical analysis was proceeded with SPSS 17.0 program by using Student-t-Test. $P<0.05$ value was considered statistically significant. LiCl showed concentration and time dependent effect at both DU 145 (+) and DU 145 (-) groups ($p<0.05$). In comparison to control group and high LiCl concentrations, low LiCl concentrations increased cell numbers with MK levels and decreased apoptotic index ($p<0.05$) in all groups . It's determined that DU 145 (+) group was more resistant to the inhibitory action of LiCl, responded faster to its' stimulative action, and possessed higher MK levels ($p<0.05$.) In this study, it's shown for the first time that the effects of LiCl on prostate cancer stem cells is biphasic and MK levels were shown to change in direct proportion to that effect. Keywords Prostate cancer, Lithium chloride, Cancer stem cell, Midkine.

45. Decellularized stem cell matrix mediated cartilage regeneration and its significance for regenerative medicine.

Ming Pei, Stem Cell and Tissue Engineering Laboratory, Department of Orthopaedics, West Virginia University, Morgantown, WV 26506-9196, USA.

Summary: Cell-based therapy is a promising biological approach for the treatment of

cartilage defects. Due to the small size of autologous cartilage samples available for cell transplantation in patients, chondrocytes need to be expanded to yield sufficient cell number for cartilage repair. However, either chondrocytes or adult stem cells tend to become replicatively senescent once they are expanded on conventional plastic flasks. Many studies demonstrate that the loss of cell properties is concomitant with the decreased cell proliferation capacity. This is a significant challenge for cartilage tissue engineering and regeneration. Despite much progress having been made in cell expansion, there are still concerns over expanded cell size and quality for cell transplantation application. Recently, in vivo investigations in stem cell niches have suggested the importance of developing an in vitro stem cell microenvironment for cell expansion and tissue-specific differentiation. Our and other investigators' work indicates that a decellularized stem cell matrix (DSCM) may provide such an expansion system to yield large-quantity and high-quality cells for cartilage tissue engineering and regeneration. Further investigations of the underlying mechanism and in vivo regeneration capacity will allow this approach to be used in clinics in the near future. In this talk, tissue-specific stem cell will also be highlighted for a lineage-specific tissue regeneration, which guarantees an engineered cartilage tissue with high quality. This new strategy is also applied to other lineage tissue regeneration.

46. Metabolomics, Metaboloepigenomics, Polyomics.

Miroslava Cuperlovic-Culf, National Research Council of Canada, Moncton, Canada.

Summary: Analysis of metabolites has been part of research in life sciences for centuries. Metabolomics, defined as the high throughput study of metabolites, has a solid base in early metabolic studies as well as development of analytical and computational tools. Metabolomics holds the greatest potential in the analysis of biological systems for variety of reasons. Metabolic profiling can be performed on tissues, cells, body fluids and breath both in vivo and ex vivo. Metabolomics can be combined with other type of omics as well as biological and clinical data. Metabolism is also closely related to epigenetic changes of cells; hence metabolic profiling can be used for the investigation of epigenetics of cells while metabolites can influence epigenics of cells. Within our group we have been involved in many of these different types of analysis. In this talk I will provide an overview of some of our results touching on the variety of metabolomics applications including tumour subtyping, analysis of various drug effects of cells, investigation of histone deacetylase relationship with metabolism in human tumours as well as other organisms. Although biological results and applications will be the primary focus of this talk, number of different data analysis methodologies will also be outlined.

47. Diagnostic yield of primary circulating tumor cells in women with suspicion of breast cancer: Study BEST (Breast Early Screening Test).

Nigel P Murray, Roxana Miranda, Amparo Ruiz, Elsa Droguett. Hospital de Carabineros de Chile, Santiago, Chile.

Summary: Objective: To determine the diagnostic yield of primary circulating tumor cells in women with suspicion of breast cancer, detected as a result of an abnormal mammography. Methods and Patients: Consecutive women presenting for breast biopsy as a result of a mammogram BiRADs 3 o more, had an 8ml blood sample taken for primary circulating tumor cell (CTC) detection. Mononuclear cells were obtained using

differential gel centrifugation and CTCs identified using standard immunocytochemistry using a cocktail of anti-pancytokeratin and anti-mammoglobin. A test was determined to be positive if 1 CTC was detected. Positive biopsy and CTC samples underwent immunophenotype for estrogen and progesterone receptors, HER-2 and metalloproteinase 2 expression. Results: 144 women with a mean age of 54.7 ± 15.6 years participated, 78/144 (53.0%) had breast cancer on biopsy, 65/140 (46.3%) benign pathologies y 1(0.7%) Non-Hogkins Lymphoma. Increasing BiRADs score was associated with increased cancer detection (p=0.004, RR 1.00, 4.24, 8.50). CTCs cytokeratin positive and mammoglobin positive had a sensitivity of 89.55% and 81.1% and specificity of 84.4% and 90.9% respectively. For cytokeratin and mammoglobin positive CTCs the PPVs were 87.2% and 90.9% and NPVs 87.1% and 81.1% respectively. Neither marker was positive for the 6 intraductal carcinomas, for infiltrative cancer, cytokeratin detected 98% of cancers and mammoglobin 87%, poorly differentiated cancers were mammoglobin CTC negative. Both markers were negative in 6 of 12 (50%) of cancer in situ. Expression of estrogen and progresterone receptors in CTCs was concordant with the primary tumor, whereas HER-2 and MMP-2 expressions were significantly higher in primary CTCs. There was a significant trend ($p<0.0001$ Chi squared for trends) in CTC detection frequency from intraductal, in situ and invasive (OR 1.00, 8.00, 472.00). Conclusions: The use of primary CTC detection in women with suspicion of breast cancer has potential uses, especially with invasive cancer, however failed to detect intra-ductal cancer and in 50% of in situ cancer. Further larger scale studies are warranted, to try to reduce the number of unnecessary biopsies, especially in women with BIRADs 4 mamagrams. The different phenotypic expression of CTCs for HER-2 and MMP-2 may have implications for targeted therapy. Key words: breast cancer detection, circulating tumor cells, mammogram, HER-2.

48. Functions of p63 and its miR-205 target in cell migration and metastasis.
Paola Tucci, Department of Pharmacy, Health and Nutritional Sciences, University of Calabria, Italy.
Summary: The precise role of p63 in tumour progression and metastasis has been hotly debated and the molecular mechanisms that underlie the role of p63 in tumour are not clearly described. Although some studies show p63 overexpression in human cancer, some demonstrate a loss of p63 associated with tumour progression and metastasis. Much of this controversy is due to the existence of multiple isoforms. The full-length TA isoform of p63 bears structural and functional similarity to p53, whereas the ΔN isoforms of p63, which lack the transactivation (TA) domain, act primarily in dominant-negative fashion against p53, TAp63 and TAp73. The clinical problem of human cancer is metastasis. There is now evidence that, perhaps as a reflection of its role in epithelial development and in stemness, p63 as an "epithelial organizer" is also important in epithelial to mesenchimal transition (EMT), an essential prerequisite for invasion and migration of tumour cells. Transcription factors exert their effects not only by regulating transcription of protein coding sequences, but also by activating or repressing expression of small non-coding RNA sequences such as micro-RNAs (miRs). In this study we show that p63 (both TAp63 and ΔNp63 isoforms) regulates expression of miR-205 in prostate cancer cells, and miR-205 is essential for the inhibitory effects of p63 on markers of EMT, such as ZEB1 and vimentin. Correspondingly, the inhibitory effect of p63 on

EMT markers and cell migration is reverted by anti-miR-205. p53 mutants inhibit expression of both p63 and miR-205, and the cell migration, in a cell line expressing endogenous mutated p53, can be abrogated by pre-miR-205 or silencing of mutated p53. In accordance with this in vitro data, ΔNp63 or miR-205 significantly inhibits the incidence of lung metastasis in vivo in a mouse tail vein model. Similarly, one or both components of the p63/miR-205 axis were absent in metastases or colonized lymph nodes in a set of 218 human prostate cancer samples. This was confirmed in an independent clinical data set of 281 patients. Loss of this axis was associated with higher Gleason scores, an increased likelihood of metastatic and infiltration events and worse prognosis. These data suggest that p63/miR-205 may be a useful clinical predictor of metastatic behaviour in prostate cancer.

49. Circulating complementary innate IgM originating from ancestral antigen completeness in reduction of O-glycosylations.

Peter Arend, ret. Philipps University of Marburg/Lahn, Germany.

Summary: The murine and human immune systems have fundamental properties in common. E.g. the histo (blood) group anti-A-specific complementary IgM in the mouse and related human innate isoagglutinin represent developmen-tal, 2-mercaptoethanol-sensitive, complement-binding glycoproteins, which do not arise from any measurable environmentally-induced or auto- immune response. So the murine glycoprotein appearing in parallel with auto-reactive O-glycan-bearing ovarian glycolipids certainly originates from a cell surface- or cell adhesion molecule, which in the course of germ cell development becomes devoid of O-GalNAc-transferase activity and is released into the circulation. In human sera a blood group AB-reactive α2-macroglobulin occurs together with O-GalNAc-transferase activity exclusively in those of blood group A- and AB subjects, while in group O(H) an identically encoded protein, but devoid of the transferase activity, suggests an opposite function and appears in conjunction with a complementary anti-A reactive IgM-like glycoprotein. Since O-glycosylations rule the carbohydrate metabolism in growth and reproduction processes, we have proposed that the ancestral histo-(blood)-group A-molecule arises in the course of O-GalNAc-glycosylations of glycolipids and protein envelops at progenitor cell surfaces. Germ cell development postulates embryonic stem cell fidelity, which is characterised by persistent production of α-linked O-GalNAc-glycans, encoded by the A-allele of a "complete" histo (blood) group AB (O) structure that in early ontogeny is hypothesised to be synthesised independently from the final phenotype. The structure either passes "completely" through the germline, in mature tissues becoming the "complete" phenotype AB, or disappears in exhaustive glycotransferase depletion from differentiating cell surfaces and leaves behind the "incomplete" blood group O-phenotype, which has released a transferase- and O-glycan-depleted, complementary glycoprotein (IgM) into the circulation. The process implies, that in humans the different blood phenotypes evolve from a "complete" AB (O) molecular complex in a dis-tinct enzymatic and/or complement cascade suggesting O-glycanase activities. While the murine and human oocyte zona pellucida express identical O-glycans, the human phenotype O might be explainable by the kinetics of the murine ovarian O-GalNAc-glycan synthesis and the complementary anti-A released into the circulation. So the maturing murine ovary may provide insight into encoding of the physiologically superior α-linked O-GalNAc ancestral epitope that becomes essential in

reproduction as well as in tissue renewal events. And human stem cell generation based on oocyte genome transitions may capitalise on an obviously pronounced fertility of by O-glycosylation- protected reproduction in blood group A females. Abbreviations: IgM: Immunoglobulin M; O-GalNAc: O-N-acetyl-D-galactosamine.

50. Application of human cardiomyocytes derived from pluripotent stem cells for toxicity testing and disease modeling.

Peter Sartipy, Stem Cell Discovery and Senior Principal Scientist, Cellectis AB, Arvid Wallgrens Backe 20, 413 46 Göteborg, Sweden.

Summary: Human pluripotent stem cells can be differentiated with high efficiency to cardiomyocytes in 2D and 3D cultures. Extensive characterization of the differentiated cardiomyocytes has shown that the cells share many similarities with bona fide human cardiomyocytes, while some functional aspects remain fetal-like. Even though much research remains to generate fully mature cardiomyocytes, the current state-of-the-art processes of cost-effective derivation of cardiomyocytes from hPSCs have been standardized and implemented in industrial settings. The cells are now being used for in vitro applications in drug discovery. The utility of these cells in long term toxicity testing and repeated dose toxicity testing will be demonstrated as well as bench-marking studies comparing in vitro testing with animal experimentation. In addition, induced pluripotent stem cells created from healthy donors and individuals suffering from specific diseases now allow detailed investigations of drug responses and potential adverse effects in physiologically relevant model systems.

51. Presentation Title: Pending.

Rahul Saxons, Department of Biochemistry and Molecular & Cellular Biology Georgetown University Medical Center, Washington, USA.

Summary: Pending.

52. FKBP51 orchestrates the evil axis EMT/ cancer stemness/drug resistance, in malignant melanoma: a matter of protein/protein interaction .

Romano Maria Fiammetta, Department of Biochemistry and Medical Biotechnology, Federico II University of Naples, Naples, Italy.

Summary: Recent breakthroughs suggest that induction of the EMT transdifferentiation program in cancer cells enables them not only to disseminate from primary tumours and form metastases, but also to acquire resistance to therapy and self-renewal capability which is crucial to their subsequent expansion at sites of dissemination. In recent years, research studies from our laboratory highlighted functions for the FK506 binding protein 51 (FKBP51) in the control of apoptosis, invasiveness and aggressiveness of melanoma. Herein, we show that FKBP51 acts as a cochaperone of IKK components and the general transcriptional coactivator p300 and, the interactions between a deregulated FKBP51 and these proteins enable melanoma to resist apoptosis and promote CSC and EMT genetic programs. Our findings point to FKBP51 as a common denominator to EMT, cancer stemness and drug resistance, in melanoma.

53. Is it possible to fight influenza by targeting intracellular redox state?

Rossella Sgarbanti, Università Telematica San Raffaele, IRCCS San Raffaele Roma,

Italy.
Summary: Influenza viruses induce a redox imbalance in the host cells, characterized by depletion of the main intracellular antioxidant glutathione (GSH) and increase in Reactive Oxygen Species (ROS). This oxidative stress may play a role in activating intracellular redox-sensitive pathways that are exploited by the virus for its own replication. The activation of the redox-regulated machinery may also play a role in the dysregulated pro-inflammatory responses and severe lung injury caused by highly pathogenic influenza viruses. We have recently demonstrated that it is possible to inhibit influenza virus replication by treating infected cells or mice with a derivative of GSH, GSH-C4. In particular, GSH-C4 is able to impair hemagglutinin (HA) maturation in the endoplasmic reticulum and, as a consequence, to block the progression of virus replicative cycle. This effect is related to the correction of virus-induced GSH depletion that, in turn, affects the redox state of PDI, a cellular oxidoreductase involved in disulfide bond formation of glycoproteins. It has also been demonstrated that pro-GSH molecules, including GSH-C4, are able to increase the intra-macrophage thiol content in vitro and in vivo as well as to shift the immune response towards Th1 which plays a pivotal role in antiviral immunity. Our aim was to investigate whether: i) the ability to induce oxidative stress in the host cell depends on the type of viral strain (human or avian viruses); ii) eradication of oxidative stress inflicted by influenza virus, by using different redox modulator compounds, would affect infectivity and/or to prevent excessive cytokine production. We found that human influenza virus induced a continuous and progressive increase of intracellular ROS levels from three to five hours after infection. Avian virus induced multiple waves of ROS hyperproduction and the ROS levels were significantly higher than that observed in cells infected with human virus. Among different redox modulating compounds tested, differently from GSH-C4, N-acetyl cysteine (a GSH precursor) and Trolox (a derivative of Vitamin E with ROS scavenging activity) exhibited short-term anti-influenza activity in infected lung epithelial cells, without interfering with viral protein expression or HA folding. In addition, these compounds produced different effects on the inflammatory cytokine production, suggesting that different redox-regulated pathways (GSH-mediated or ROS-mediated) may be specifically involved in the regulation of virus life-cycle and/or inflammatory responses. Overall, these results indicate that GSH-C4 is effective in both inhibiting influenza virus replication and blocking the cytokine storm responsible for the lethality of some viral strains. Our data also demonstrate that not all the so-called “antioxidant drugs” are able to control viral infection and inflammatory responses. Thus, the efficacy of a specific compound depends on its real ability to affect redox-regulated pathways in different cellular contexts.

54. Sexually dimorphic microRNA expression: a new thought on sex bias of autoimmune diseases.

Rujuan Dai, Department of Biomedical Sciences and Pathology, Virginia-Maryland Regional College of Veterinary Medicine, Virginia Tech, Blacksburg, VA24060, USA.

Summary: A striking feature of autoimmune diseases is that a majority of these disorders occur predominantly in females: about 80% of autoimmune patients are women. The basis of sex bias in autoimmune diseases is complex and remains elusive. It potentially involves multiple factors such as sex chromosomes, sex hormones, sex-

specific gene expression regulation and environmental exposures. Systemic Lupus Erythematosus (SLE) is a prototype, female predominant autoimmune disease. microRNAs (miRNAs) are small, non-coding RNAs that are critically involved in the pathogenesis of a broad range of human diseases including autoimmune lupus. We have recently reported a common set of lupus-associated miRNAs including miR-182-96-183 cluster, miR-155, miR-31, miR-127, and miR-379 in three spontaneous murine lupus models including NZB/WF1, a classical murine lupus model with significant female bias. We further hypothesized that miRNAs are differentially expressed between males and females in the context of autoimmune diseases, leading to sex differences in disease susceptibility and severity. To test this hypothesis, we analyzed aforementioned lupus-associated miRNAs expression in splenocytes from male and female NZB/WF1. We found that the sex differences in the expression of lupus-associated miRNAs in splenocytes were markedly evident after the onset of lupus. Prior to the onset of lupus, only miR-127 and miR-379 displayed slight, but significant increase in female NZB/WF1 mice when compared to age-matched male counterparts. Considering that female hormone estrogen plays an important role in the sex differences in immune function and autoimmunity, we investigated the effect of estrogen on miRNA expression in the context of lupus. Our data indicated that estrogen treatment of orchidectomized male NZB/WF1 mice promoted the expression of lupus-associated miRNAs including miR-182-96-183 cluster, miR-379, and miR-148a, but did not affect miR-155 in splenocytes. Together, our study demonstrated that female NZB/WF1 mice displayed increased expression levels of lupus-associated miRNAs after the onset of lupus when compared to age-matched males. Importantly, these miRNAs were disease associated and were upregulated by estrogen treatment. We believe that the finding of sexually differential expression and estrogen regulation of miRNA in the context of lupus shall provide us new perspective to understand the mechanism of sex bias of autoimmune lupus.

55. Expressioneering Technology accelerates Functional Expression and Crystallization of GPCRs for Drug Discovery.

Saurabh Sen, R&D, Lucigen Corp, USA.

Summary: Structural biology of membrane proteins and GPCRs has seen major advances over the past few years, but overcoming the challenges of functional GPCR expression and structural stabilization are still time-consuming and expensive. We are developing new tools to streamline these processes, and further enhance the pace of drug discovery. We present the application of several new technologies to the challenges of functional membrane protein expression. A rapid recombination-based cloning technology accelerates optimal GPCR expression through fusion to a variety of transmembrane guides and novel visualization tags. We have been successful in rapidly generating and expressing hundreds of brain GPCR fusion constructs in E. coli and mammalian cells with this system. We will also present our use of a novel fluorescent protein, LucY (for Lucigen Yellow) in a loop insertion strategy to express stabilized GPCRs for crystallization trials. This strategy allows fluorescent visualization of membrane proteins during expression, solubilization, purification, and crystallization. We have found that insertion of LucY into ICL3 of GPCRs allows retention of ligand-binding activity and may promote GPCR crystallization. We have obtained fluorescent putative crystals of turkey β1-adrenergic receptor expressed in bacterial cells using a rhamnose

promoter system with LucY inserted in the ICL3. We are also applying this strategy to human brain GPCRs.

56. Vesicular trafficking protein, Rab25 is a conditional oncogene in breast cancer.
Shreya Mitra, Department of Systems Biology, University of Texas MD Anderson Cancer Center, USA.
Summary: Pending.

57. MicroRNAs in the malignant transformation of colon adenoma to Adenocarcinoma.
Subbaya Subramanian, Department of Surgery, The University of Minnesota, USA.
Summary: Progression from benign adenoma to colon cancer is a complex multi-step process mediated by genetic alterations in driver genes. Although miRNAs are implicated in this multihit model of progression, their precise role during the transformation of colon adenomas to adenocarcinoma is unknown. This talk will discuss the role of miRNAs in the transformation of colon adenoma to adenocarcinoma by cooperatively regulating the tumor suppressor driver gene, FBXW7. Our studies show that a step-wise expression of miRNAs in benign adenoma synergistically regulates the driver genes such as FBXW7, thus contributing to the progression of colon adenoma to adenocarcinoma.

58. Monte Carlo simulation elucidates the type 1/ type 2 choice in apoptosis under death ligand induction.
Subhadip Raychaudhuri, Indraprastha Institute of Information Technology, India.
Summary: The problem of understanding type 1/type 2 choice in apoptosis is crucial for exploring the systems level regulatory mechanisms of cell death activation and is of much current interest. To address this important biological problem we have carried out in silico studies of apoptosis signaling under death ligand induction. A hybrid Monte Carlo simulation has been developed that can link a free energy based model of membrane proximal events with the type 1/type 2 pathways of signaling. Our results indicate that the type 1/type 2 choice is regulated at a system level and cell-type specific expression levels of signaling molecules shape the phase diagram. Effects of some of the key molecules, such as those involved in opening and closing of the type1/type 2 loop, are analyzed in the context of experimental observations. In addition, death ligand concentration is shown to have a key role in deciding between the type 1 and type 2 pathways as increased level of death ligands resulted in increased type 1 activation, irrespective of cell types. We also explored the type 1/type 2 choice in cancer cells having markedly altered proteome (compared with healthy cells) and its implications for selective killing of cancer cells. Our results indicate that inherent differences in the membrane proximal signaling module, between cancer and healthy cells, can allow such selective activation of apoptosis in tumor cells.

59. Surrogate reporter-based enrichment of cells containing RNA-guided Cas9 nuclease-induced mutations.
Suresh Ramakrishna, Stem Cell Research, College of Medicine, Hanyang University, Seoul-133-791, South Korea.
Summary: RNA-guided endonucleases (RGENs), which are based on the clustered,

regularly interspaced, short palindromic repeat (CRISPR)-CRISPR-associated (Cas) system, have recently emerged as a simple and efficient tool for genome editing. However, the activities of prepared RGENs are sometimes low, hampering the generation of cells containing RGEN-induced mutations. Here we report efficient methods to enrich cells containing RGEN-induced mutations by using surrogate reporters. HEK293T cells are cotransfected with the reporter plasmid, a plasmid encoding Cas9, and a plasmid encoding crRNA and tracrRNA, and subjected to flow cytometric sorting, magnetic separation, or hygromycin selection. The selected cell populations are highly enriched with cells containing RGEN-induced mutations, by a factor of up to 11-fold as compared with the unselected population. The fold enrichment tends to be high when RGEN activity is low. We envision that these reporters will facilitate the use of RGEN in a wide range of biomedical research.

60. Presentation Title: Pending.

Tammy A. Butterick-Peterson, Minnesota Obesity Neuroscience Lab Group, University of Minnesota, USA.

Summary: Pending.

61. Deficient Aldehyde Dehydrogenase 1A1 Expression In Primary Cells Isolated From Gorlin Syndrome Patients: Implications For Radiation Carcinogenesis and Developmental Defects.

Thomas Weber, FSD/Cell Biology and Biochemistry, Pacific Northwest National Laboratory, USA.

Summary: Many cancer prone human phenotypes have been identified. Sensitive phenotypes often display robust regulation of molecular features that modify biological response, which can facilitate identification of the pathways/networks that contribute to pathophysiological outcomes. We have interrogated primary dermal fibroblasts isolated from Gorlin Syndrome patients (GDFs), who display a pronounced inducible tumorigenic response to radiation, in comparison to normal human dermal fibroblasts (NHDFs) using newly developed thiol-reactive probes to define changes in protein thiol profiles in live cell studies. Redox probes revealed deficient expression of aldehyde dehydrogenase 1A1 (ALDH1A1), a key enzyme regulating retinoic acid synthesis, and ALDH1A1 protein deficiency in GDFs was confirmed by Western blot. A number of additional protein thiol differences in GDFs were identified, including radiation responsive annexin family members. The molecular features identified in our study are of likely importance to cancer susceptibility in Gorlin Syndrome patients and radiation health effects broadly.

62. Alcohol: A Glimpse at Direct, and Indirect Organ Damage; With Application to Future Research.

Tiana V. Curry-McCoy, Medical Laboratory Imaging Radiologic Sciences-Clinical Laboratory Science, College of Allied Health Sciences, Georgia Regents University (MCG&ASU), USA.

Summary: Alcoholism is best known to have damaging effects on the liver and brain. It is commonly known that alcohol can be detected in urine and blood. The transfer of alcohol from the “first pass” mechanism of mouth, esophagus, stomach, liver through to blood which distributes alcohol on its “second pass” to other bodily organs such as the

lungs and sex organs. Here we will discuss cellular damage from alcohol and its secondary metabolites to the liver and the lung. In our liver studies we hypothesized that the lack of cellular Cu/Zn-SOD, an enzyme that prevents cellular damage from superoxide, would induce increased generation of oxidants, thereby causing damage to hepatic proteins, and the hepatic proteolytic system. We used SOD1 null and wild type mice to determine how ethanol-induced oxidation and nitration altered hepatic proteins and how hepatic proteolytic systems are effected by ethanol-induced oxidative stress in vivo. Next, in alveolar cells we performed in vitro experiments exposing the rat AM cell line (NR8383) to 0.2% ethanol for four weeks. We also exposed these cells to granulocyte-macrophage colony-stimulating factor (GM-CSF) for 24 hours. Next, we performed in vivo studies using AM and epithelial cells from control and alcohol-fed rats. Gene expression and DNA binding in these cells were examined independently or after overnight treatment with GM-CSF. Intracellular zinc levels were measured by flow cytometric analysis of cells that were stained with FluoZin-3. It is our belief that understanding of alcohol damage to the total body will help research and treatment of this disease.

63. Signal transduction in innate immunity - what can we learn from the Caspase Activation Domains (CARDs) of the NLR family members NOD1 and NOD2.
Tom Monie, Department of Biochemistry, University of Cambridge, Cambridge, UK.
Summary: Pending.

64. The involvement of Phosphoinositide signal transduction pathway in angiogenesis.
Vincenza Rita, Surname Lo Vasco, Department of Sense Organs, Sapienza University of Rome, Italy.
Summary: Besides the control of calcium levels, the Phosphoinositide-specific phospholipases C (PI-PLCs), main players in the Phosphoinositide signalling pathway, contribute to a number of cell activities. The signalling system of Phosphoinositides (PIs) is involved in a variety of cell and tissue functions, including membrane trafficking, ion channel activity, cell cycle, apoptosis, differentiation, cell and tissue polarity. Recently, a role in cell migration was hypothesized for PI and related molecules, such as the phosphoinositide-specific phospholipases C (PI-PLCs), main players in PI signalling. The expression of PI-PLCs is tissue specific, and evidences suggest that it varies under different conditions, such as tumour progression or cell activation. In order to obtain a complete panel, we first analyzed the expression of all PI-PLC isoforms in human endothelial cells (EC). We investigated the human umbilical vein endothelial cells (HUVEC), a widely used experimental model. Then, we analyzed the mRNA concentration of PI-PLCs in LPS treated HUVEC by using the multiliquid bioanalyzer methodology after 3, 6, 24 48 and 72 hours from LPS administration. Marked differences in the expression of most PI-PLC codifying genes were evident, suggesting that the expression of the PLC genes varies under inflammatory stimulation. The Fibroblast Growth Factor (FGF) activates the PI-PLC □1 isoform. In a further study, PI-PLCs expression in FGF treated HUVEC was performed by using RT-PCR, observed after 24 hours from stimulation. The expression of selected genes after stimulation was perturbed, suggesting that FGF affects gene transcription in PI signalling as a possible mechanism

of regulation of its activity upon the AkT-PLC pathway. The most efficient effects of FGF were recorded in the 3-6hrs interval. The growing interest for the complex cascade of events occurring in angiogenesis will provide useful insights for therapeutic strategies. However, although HUVEC represent a widely used experimental model for human macrovascular EC, limitations remain in that they cannot fully represent the metabolic properties and interactions of the EC distributed in the entire organism.

65. Bioprinted Neocartilage Formation in Poly(ethylene) Glycol and Gelatin Methacrylate Copolymer Using Human Mesenchymal Stem Cells.

Xiaofeng Cui, Institute of Advanced Study, Technical University of Munich; Director of Research, Stemorgan Therapeutics, New York, USA.

Summary: Current cartilage tissue engineering strategies still can yet fabricate new tissue that is indistinguishable from native cartilage with respect to zonal organization, extracellular matrix composition, and mechanical properties. Integration of implants with surrounding native tissues is crucial for long term stability and enhanced functionality. Direct cartilage repair with engineered tissue closely mimicking native cartilage to the site of the lesion without any additional damage to the existing healthy tissue is therefore very attractive. The ideal implanted tissue is expected to integrate with existing native cartilage and to repair lesions of different sizes and thicknesses. The multifaceted mature of this challenge requires a technique adaptable to variable physical dimensions and properties for tissue repair; we believe that bioprinting, based on inkjet printing technology, provides the necessary capabilities. A copolymer of poly(ethylene glycol) dimethacrylate and gelatin methacrylate was used to suspend human mesenchymal stem cells to form the bioink. The cartilage construct was printed in a layer-by-layer fashion. The copolymer demonstrated a great integration with the native tissue as well as excellent compressive modulus, which was close to the range of reported properties of native human articular cartilage. Printed human stem cells maintained their originally deposited positions due to simultaneous photopolymerization. This is ideal in precise cell distribution for zonal cartilage engineering. Gene expression and biochemistry analysis of printed neocartilage showed increased cartilage gene expression and extracellular matrix production in chondrogenic differentiation medium during the culture. Therefore, this copolymer is an ideal bioink to support mesenchymal stem cells for cartilage tissue engineering.

66. Reciprocal regulation of microRNA and long non-coding RNAs in cancer cells.

Yin-Yuan Mo, Cancer Institute, University of Mississippi Medical Center, Jackson, MS, USA.

Summary: In addition to protein-coding genes, the human genome makes a large amount of non-coding RNAs including microRNAs and long non-coding RNAs (lncRNAs). Both microRNAs and lncRNAs have been shown to play a critical role in regulation of cellular processes such as cell growth and apoptosis as well as cancer progression and metastasis. It is well known that microRNAs can target a large number of protein-coding genes. However, little is known whether microRNAs can also target lncRNAs. Furthermore, it is largely unknown whether microRNAs can be regulated by lncRNAs. In the present talk, I will discuss our recent work in this front and provide three examples of microRNA-lncRNA interactions, through which they may impact tumorigenesis. For example, miR-

21 is a well-known oncogenic microRNA that can target a larger number of protein-coding genes. Of interest, we showed that miR-21 is also capable of repressing the growth arrest specific 5 (GAS5) lncRNA which was previously shown to be involved in growth arrest. This negative regulation between miR-21 and GAS5 was also detected in breast tumor specimens. Moreover, GAS5 can also repress miR-21 expression. RNA precipitation assays with biotin-labeled GAS5-RNA probe was able to pull down the RNA-induced silencing complex (RISC) and subsequently identified miR-21 in this GAS5-RISC complex, implying that miR-21 and GAS5 may regulate each other in a way similar to the microRNA-mediated silencing of target protein-coding mRNAs. Finally, we demonstrated a similar regulation mechanism for RoR and miR-145, loc285194 and miR-211. Together, these results suggest that microRNAs can target not only tumor suppressive protein-coding genes, but also lncRNAs; as the same time, microRNAs are also under control of lncRNAs.

67. Development of sexually dimorphic nuclei and the influence of estrogen-like compound exposure.

Zhen He1, 2, Sherry Ann Ferguson1, Li Cui 2, Lazar John Greenfield2, Merle Gale Paule1 1 Division of Neurotoxicology, National Center for Toxicological Research, Food and Drug Administration, Jefferson, AR 72079, USA; 2 Department of Neurology, University of Arkansas for Medical Sciences, Little Rock, AR 72005, USA.

Summary: One of the well-defined sexually dimorphic structures in the brain is the sexually dimorphic nucleus of the preoptic area (SDN-POA) in the hypothalamus. This presentation covers the following topics: Background information concerning the SDN-POA. How the SDN-POA is studied. The effects of estrogens and estrogen-like compounds on the SDN-POA. Potential developmental mechanisms underlying the expression of the sexual dimorphism of the SDN-POA. The role of neural stem cell activity in the development of the SDN-POA. Current progress in our studies exploring the mechanisms by which sex hormones and estrogen-like compounds affect the development of the SDN-POA. The sexually dimorphic nucleus is an easily modifiable structure that can serve as a model system for the study of how sex differences in brain structure and function arise and are maintained. Processes underlying this phenomenon are highly clinically relevant for understanding the origins of sex biases in psychiatric syndromes and for identifying novel clinical targets. There is increasing evidence that perinatal exposure to estrogen or estrogen-like compounds may be associated with a host of health problems, including obesity and certain mental disorders such as depression. Bisphenol A (BPA), a compound found to be estrogen-like in some model systems, has been shown to alter the SDN-POA. Thus, exploring the mechanisms by which BPA affects sexual dimorphic structures of the brain might lead to the development of new protective strategies and/or therapeutic approaches.