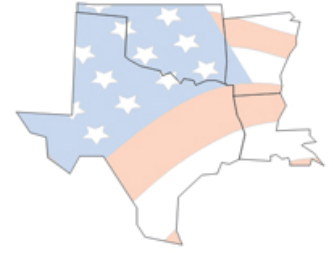




COM.IT.ES
Comitato degli Italiani all'Estero
Committee for Italians Abroad



in cooperation with

BCM
Baylor College of Medicine



under the auspices of the Consulate General of Italy in Houston

Presents the 2nd Conference of Italian Researchers:
The Contribution of the Italian Researchers in the World
The Past - The Present - The Future

Chairman - Vincenzo Arcobelli, President Comites
Moderator - Andrea Duchini, M.D., Gastroenterology, BCM

Sunday, October 8, 2006
4:30 p.m.

Baylor College of Medicine
Alkek Building, Room N-315
One Baylor Plaza
Houston, Texas 77030

The Contribution of the Italian Researcher in the World The Past-The Present -The Future

4:45-5:00 p.m.

Opening Remarks and Introduction
Moderator Andrea Duchini, M.D., Division of Gastroenterology, BCM
Vincenzo Arcobelli - President (Comites) Committee for Italians Abroad
Cristiano Maggipinto - Consul General of Italy in Houston

5:00-5:15 p.m.

Mauro Ferrari, Professor, Brown Institute of Molecular Medicine
Chairman, Department of Biomedical Engineering , The University of Texas Health
Science Center, Houston, TX.

Nanomedicine

Audience Questions

5:20-5:35 p.m.

Marco Marcelli M.D., Associate Professor, Department of Medicine, Baylor College
of Medicine Chief of Endocrinology
Michael E. DeBakey VA Medical Center
Houston TX 77030

***A New Approach to Study and Treat the Spectrum of Diseases Associated with
Abnormal Activation of the Androgen Receptor***

Audience Questions

5:40-5:55 p.m.

Paolo Nespoli, ESA Astronaut
NASA/JSC-CB 2101 NASA Parkway Houston, TX 77058
The Italian Contribution to the International Space Station
Audience questions

6:00-6:15 p.m.

Nicola Perone, M.D., Clinical Professor
Dept. Of Obstetrics, Gynecology & Reproductive Sciences
The University Of Texas Medical School At Houston
***Bringing Operative Vaginal Delivery Into The New Millennium: The
Electronically-Controlled Forceps Delivery System***
Audience Questions

6:20-6:35 p.m.

Giulio Tagliatela, Ph.D., Associate Professor
Department of Neuroscience & Cell Biology, The University of Texas
Medical Branch, Galveston, TX 77555
An Emerging New Therapy For Alzheimer's Disease
Audience Questions

6:40-6:55 p.m.

Matteo Vatta, Assistant Professor
Associate Director-Pediatric Cardiac Genetic Research
Baylor College of Medicine, Houston, TX, Texas Children's Hospital
Cytoskeletal Basis of Ion Channel Function in Cardiac Muscle
Audience Questions

7:00-7:30 p.m. Refreshments

Indirizzo di saluto del Console Generale d'Italia a Houston

Giunta alla sua seconda edizione, la Conferenza dei Ricercatori Italiani costituisce un importante momento di riflessione che serve a dar risalto ai risultati conseguiti da medici, scienziati e studiosi italiani residenti a Houston, in Texas e, piu` in generale, negli altri tre Stati inclusi nella circoscrizione del Consolato Generale d'Italia a Houston (Arkansas, Louisiana, Oklahoma).

Non vi e` settore della ricerca in cui i nostri connazionali non dimostrino di eccellere, riscuotendo l'apprezzamento dei loro colleghi americani, cosi` come il riconoscimento da parte di quelli di altri Paesi che, con i risultati delle loro ricerche vengono, in un mondo globale, rapidamente in contatto. Si tratta spesso di risultati altamente innovativi, che consentono l'introduzione di nuovi metodi diagnostici o terapeutici, che affrontano difficili problemi connessi con l'esplorazione dello spazio o che, in qualche caso, contribuiscono al progresso di discipline del tutto nuove, addirittura avveniristiche, quali le nanotecnologie.

La Conferenza dei Ricercatori, la cui organizzazione e` dovuta all'instancabile lavoro del Comitato di Houston ed in particolare del suo Presidente Vincenzo Arcobelli e del Dr. Andrea Duchini, cui va il merito di aver fatto da coordinatore dell'iniziativa, costituisce quindi una occasione di divulgazione non solo a favore degli addetti ai lavori ma anche del grande pubblico, che viene cosi` tenuto al corrente di importanti sviluppi in vari settori di ricerca.

I ricercatori italiani all'estero sono un patrimonio notevole per il nostro Paese: da un lato essi testimoniano dell'avanzamento della ricerca nel nostro Paese e sono cosi` i migliori Ambasciatori di un'Italia all'avanguardia nella scienza e nella tecnica; dall'altro, con i risultati delle loro ricerche, contribuiscono all'accrescimento globale del livello di conoscenza, con effetti che si riverberano positivamente sul Paese che li accoglie, sull'Italia e sul resto del mondo.

Desidero infine ringraziare il Baylor College of Medicine la cui collaborazione ha reso possibile tale iniziativa e gli ospedali e le istituzioni di ricerca di questo grande Paese che ha accolto e continua ad accogliere con entusiasmo i ricercatori e gli scienziati italiani, dando spesso, anche ai nostri giovani, non comuni opportunita` di crescita professionale.

Auguro buon lavoro a tutti i partecipanti.

Console Generale Dr. Cristiano Maggipinto

Messaggio del Presidente del Comites

A nome di tutto il Comites della circoscrizione consolare di Houston, desidero salutare e dare il benvenuto a tutti i partecipanti a questa manifestazione ,che coincide con la ricorrenza delle festività del Columbus Day

La Conferenza sarà incentrata sul ruolo ed il contributo degli Italiani e Italo-Americani nel campo della scienza e tecnologia con presentazioni da parte di ricercatori, ora residenti in Texas ed una sessione "posters" dedicata ai ricercatori degli istituti accademici e di ricerca. L'Agenda è acclusa e contiene la scaletta degli interventi riguardanti recenti sviluppi nel campo della medicina, tecnologia e scienze..

Questa è la seconda conferenza che viene organizzata da questo comitato, l'anno scorso a Dallas mentre quest'anno a Houston, un programma specificamente indirizzato ai ricercatori Italiani e Italoamericani residenti nello stato del Texas, e agli stati vicini ed appartenenti alla Circoscrizione Consolare di Houston.

Le nostre comunità all'estero rappresentano una parte importante dell'Italia che vive al di fuori dei nostri confini. La loro presenza nel mondo garantisce una proiezione integrante della Nazione, un valore aggiunto che ci consente di accrescere la nostra ricchezza e il prestigio che l'Italia raccoglie nella comunità internazionale.

I nostri connazionali sono un ponte prezioso con culture e società diverse, mantenendo intatti i valori e i tratti distintivi dell'italianità: gli affetti familiari, l'amore per la terra, la dignità nel lavoro, una profonda umanità; la tenacia; l'ingegnosità.

Desidero ringraziare tutti i collaboratori , in particolar modo Andrea Duchini per coordinare l'evento, il Baylor College of Medicine per l'ospitalità, il Console Generale d'Italia a Houston Cristiano Maggipinto e il suo staff per la loro disponibilità , Andrea Barattini e Bice Ristorante per il servizio catering, ma soprattutto tutti i ricercatori

che hanno contribuito con le loro presentazioni e posters, e che contribuiscono quotidianamente e meritatamente in ogni campo a cui sono specializzati e si dedicano con passione nel progresso scientifico, sociale, civile e culturale a livello mondiale.

Una dedica particolare va alle donne e agli uomini, personale militare e civile , che hanno sacrificato la propria vita durante missioni di ricerca e sperimentazione.

Un sentito Grazie dal cuore a tutti.

Vincenzo Arcobelli
Presidente del Comites
Circoscrizione Consolare di Houston

Participants

Nicola Abate, M.D.

Associate Professor of Internal Medicine
The Center for Human Nutrition Division of
Endocrinology and Metabolism
The University of Texas Southwestern Medical
Center at Dallas, Texas

Alessandrini, Matteo

RA at Texas Center for Superconductivity-TCSUH
Department of Mechanical Engineering
University of Houston
Houston, TX 77204-4006
Office: 713-743-4081
Cell: 832-264-8888
Email: amatteo@uh.edu

Bottiglieri Teodoro, Ph.D.

*Baylor University Medical Center
Institute of Metabolic Disease
Dallas, Texas*

Brancaleon, Lorenzo, PhD

Department of Physics and Astronomy
The University of Texas at San Antonio
6900 N Loop 1604 W
San Antonio, TX
Phone: 210-458-5694 Fax: 210-458-4919
Email: lorenzo.brancaleon@utsa.edu

Crosetto, Dario, Inventor (Physics)

3D-Computing, Inc.
900 Hideaway Pl
DeSoto, TX 75115
Email: Crosetto@3d/computing.com
Website: www.crosettofoundation.org

Di Pucchio, Tiziana, PhD

Istituto Superiore di Sanita', Rome, Italy
Baylor Institute for Immunology Research
Dallas, TX

Duchini, Andrea, MD

Division of Gastroenterology
Baylor College of Medicine
Houston TX 77030
Aduchini@bcm.tmc.edu
713-798-0950

Faccin, Stefano, MS

Nokia Research Center,
Mobile Network Laboratory
Dallas, TX

Ferrari, Mauro, Ph.D.

Brown Institute of Molecular Medicine
Chairman, Department of Biomedical Engineering
The University of Texas Health Science Center
Houston, TX
Professor of Experimental Therapeutics,
The University of Texas M.D. Anderson Cancer Center,
Houston, TX
Professor of Bioengineering, Rice University, Houston, TX
President, Alliance for NanoHealth
Houston, TX

Forni, Sabrina, PhD

Clinical Chemistry Abbott Diagnostics,
Irving TX 75038

Iacobellis, Gianluca, MD, PhD

Center for Human Nutrition,
The University of Texas Southwestern Medical Center at
Dallas, Texas, USA
Endocrinology, Department of Clinical Sciences,
La Sapienza University, Rome, Italy

Innocenti, Barbara, Ph.D.

Dept. Neurobiology and Anatomy
The University of Texas Health Science Center at Houston
6431 Fannin Str, MSB 7.001
Houston, TX 77030
Phone: 713-500-5571 Fax: 713-500-0621
email: barbara.innocenti@uth.tmc.edu

Longo, Monica, MD, PhD,

*Dept. of Obstetrics & Gynecology,
Div. Maternal Fetal Medicine
The University of Texas Medical Branch at
Galveston, Texas*

Marcelli, Marco, M.D, PhD

Department of Medicine, Baylor College of Medicine
Chief of Endocrinology, Michael E. DeBakey Veterans
Affairs Medical Center
Houston TX 77030

Marchetti, Dario, PhD

Director, Tumor Biology Laboratories
Department of Comparative Biomedical
Sciences - SVM, Room 2522

Skip Bertman Drive
Louisiana State University at Baton Rouge
Baton Rouge, LA 70803, U.S.A.
Phone Nos.: 225-578-9897 or 578-9743
Fax No.: 225-578-9895
E-mail: dmarchetti@vetmed.lsu.edu

Massarelli, Erminia, MD, PhD

Postdoctoral Fellow
Department of Thoracic/Head and Neck
Medical Oncology
MD Anderson Cancer Center
Tel: 713-745-0483
Pager: 713-404-7007
Email: EMassare@mdanderson.org

Nespoli, Paolo,

ESA Astronaut
NASA/JSC-CB 2101 NASA Parkway
Houston, TX 77058
Paolo.nespoli-1@nasa.gov
281-244-2626

Papi, Paolo

PDT Sr. Project Manager, Optimization Products, ITIL
Certified
IBM Software Group, Tivoli Software
512-838-1728, t/l 678-1728
ppapi@us.ibm.com
11501 Burnet Road
Austin, Texas 78758

Perazzona, Bastianella, Ph.D

Department of Molecular Pathology (Unit 951)
The University of Texas M. D. Anderson Cancer Center
PO BOX 301429
Houston, TX 77230-1429
Office: 713-834-6037 Lab: 713-834-6027/1800
Fax: 713-834-6082
Email: BPerazzo@mdanderson.org

Perone, Nicola, MD

Dept. of Obstetrics, Gynecology & Reproductive
Sciences
The University of Texas Medical School at Houston
President of the Houston Gynecological and Obstetrical
Society, Houston, TX 77030

Pinto, Angelo, PhD

PDF solutions Inc.
San Jose, 95110 CA, USA

Piccotti, Lucia, MD

Department of Biochemistry and Molecular Biology, The

University of Texas-Houston Medical School, 77225,
USA.

Laboratory of Biochemistry, Department of Internal
Medicine, University of Perugia, 06122, Perugia, Italy

Righetti, Raffaella, PhD

Department of Diagnostic and Interventional Imaging,
Ultrasonics Laboratory
The University of Texas Medical School
Houston, Texas, 77030, USA

Tagialatela, Giulio, PhD

Dept. of Neuroscience & Cell Biology
The University of Texas Medical Branch at Galveston
Galveston, TX 77555-1043
Phone: 1-409-772-1679 Fax: 1-409-772-1861

Toracchio, Sonia, PhD^{1,2}

¹Dept of Pathology & Medicine, Baylor College of
Medicine, Houston, 77030, Texas, United States.
²Department of Oncology and Neuroscience, Section
of Molecular Pathology, University "G. d'Annunzio",
and Center of Excellence on Aging, "G. d'Annunzio"
Foundation, Chieti, Italy

Vannucci, Marina, PhD

Department of Statistics
439 Blocker Building
Texas A&M University
3143 TAMU
College Station TX 77843-3143
Phone: +1-979-845-3164 Fax: +1-979-845-3144
URL: <http://stat.tamu.edu/~mvannucci/>

Vatta, Matteo, Ph.D

Pediatrics (Cardiology)-Baylor College of Medicine
Texas Children's Hospital
6621 Fannin Street-Houston, Texas, 77030
Tel: 832-824-4153 Fax: 832-825-4153
Email: mvatta@bcm.edu

Anna Zacchi, Ph.D.

Department of Computer Science, Texas A&M University
College Station, Texas.

Zorzi, Daria, MD

Department of Surgical Oncology
UT M.D. Anderson Cancer Center
1400 Holcombe Blvd Houston, TX 77030
Office: (713) 794-3071
Fax: (713) 745-1921
dzorzi@mdanderson.org

Abstracts 2006

Design and Testing of Superconducting Magnets made with MgB_2 for Space Propulsion.

Activity: Matteo Alessandrini is a PhD student in the Materials Engineering Program at University of Houston and Research Assistant in Dr Salama's group at the Texas Center for Superconductivity. Matteo is primarily involved in the development of superconducting magnets for space propulsion applications. His financial support is granted by Ad Astra Rocket Company, which is currently developing the VASIMR engine at the NASA Johnson Space Center, in Houston.

Abstract: Electric space propulsion systems are the best candidate to reduce mission time and costs, thanks to the higher efficiency and higher exhaust speed (at least one order of magnitude higher than chemical rockets). In the last ten years, electric space propulsion has been demonstrated as a key technology for robotic exploration of the solar system. The use of superconducting magnets in electric thrusters was reported for the first time in a paper more than 30 years ago by NASA. The VASIMR engine (Fig. 1), under development at NASA-JSC, is an electromagnetic thruster with the need of large bore solenoids and relatively high magnetic field, thus it is the best candidate for the use of superconducting magnets. The use of magnesium diboride (MgB_2) for the superconducting magnets of the VASIMR engine is mainly suggested by three factors: (1) magnesium diboride is intrinsically the most lightweight superconducting material, (2) the copper solenoid magnets, currently used in the VASIMR engine, have a central warm bore of about 15 cm and an axial magnetic flux density below 1 tesla, (3) the flow of high density hot plasma through the magnet bores suggest the use of a superconducting material with high critical temperature.

A superconducting magnet (Fig. 2) was wound with about 400 m of a 14 filaments copper-stabilized MgB_2 tape produced by Columbus Superconductors, and tested at ASG-Superconductors (ex-Ansaldo Superconduttori). The data are studied together with researchers from the Italian Institute of Nuclear Physics in Italy. First results were presented at an invited talk to the Applied Superconductivity Conference 2006, in Seattle.

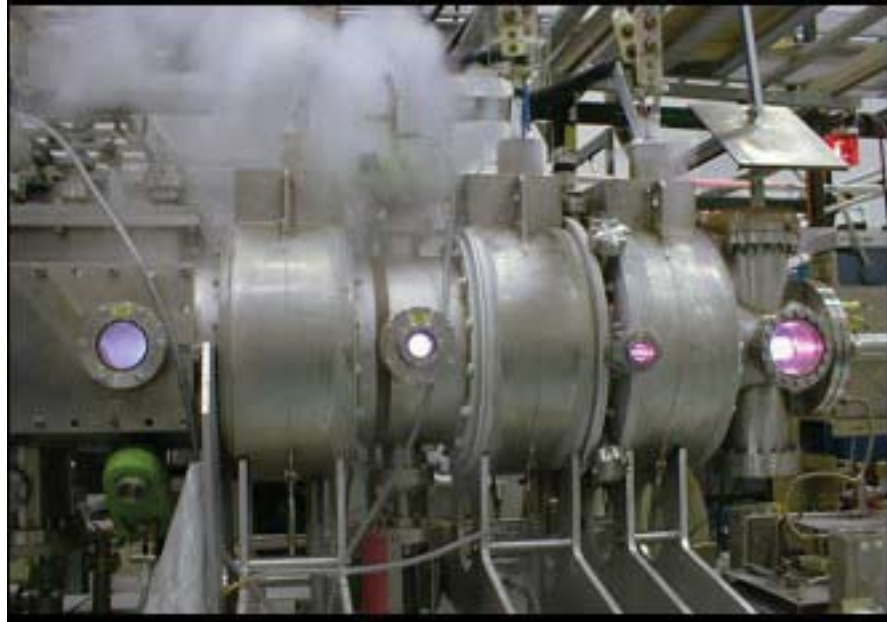


Fig. 1 VASIMR engine under test at NASA-JSC, Houston



Fig. 2 Superconducting magnet made with MgB₂ wire.

Innovative technology for early cancer detection

Dario Crosetto, Inventor (Physics), 3D-Computing, Inc. 900 Hideaway PI
DeSoto, TX 75115

3-D Complete Body Screening (3D-CBS) technology combines CT (CAT scan) and Positron Emission Technology. It is 400 times more efficient than current PET (Positron Emission Tomography) and visualizes cancer by looking at its biological activity process even before morphological changes take place. Because it exposes patients 30 times less radiation than conventional PET, 3D-CBS allows safe screening of asymptomatic people at high risk as well as those who have previously had cancer substantially reducing cancer deaths through early detection.

See website: www.crosettofoundation.org

References

Book: Crosetto, D.: "Come Vincere il Cancro". Ed. Clavilux. 2005. Available at www.clavilux.it, or free electronic version at www.3d-computing.com

Article: Crosetto, D.: "Rethinking Positron Emission Technology for Early Cancer Detection" Book: Astroparticle, Particle and Space Physics, Detectors and Medical Physics Applications. Editor: World Scientific, 2006, pp. 692-696.

Cellular vaccine: Therapeutic challenge for cancer treatment

Tiziana Di Pucchio, PhD
Istituto Superiore di Sanita', Rome, Italy
Baylor Institute for Immunology Research, Dallas, TX

Conventional therapies, such as chemotherapy and radiotherapy, can achieve positive clinical tumor responses, in terms of first tumor remission. However, these treatments not only lack tumor specificity but induce multi-drug resistance along with high systemic toxic effects. Emerging preclinical and clinical data suggest that immune cells can recognize and kill tumor cells. In addition, advances in molecular identification of tumor-associated markers have generated great interest in vaccination strategies. These results are encouraging the use of immune cells as specific immunotherapy based on the immune cell ability to recognize and destroy tumor cells.

Recently, several protocols have been developed for the *in vitro* generation of dendritic cells, which are immune cell key players in the induction of immune response. Active specific immunization aims to enhance tumor-specific activity and memory tumor-specific immune response without systemic toxic effects.

Keywords; Cancer; Dendritic cells; Cellular vaccines

Vaccinations In Adult Solid Organ Transplant Recipients; Current Recommendations and Protocols

Andrea Duchini, MD, ^John A Goss, MD, `Saul Karpen, MD, *Paul J Pockros, MD

Division of Gastroenterology, ^Surgery and Organ Transplantation and `Pediatrics, Baylor College of Medicine, Houston TX 77030. *Division of Gastroenterology, Scripps Clinic, La Jolla, CA

Recipients of solid organ transplantation are at risk of severe infections due to their life-long immunosuppression. Despite emerging evidence that vaccinations are safe and effective among immunosuppressed patients, most vaccines are still underutilized in these patients. The efficacy, safety and protocols of several vaccines in this patient population are poorly understood. Timing of vaccination appears to be critical because response to vaccinations is decreased in patients with end-stage organ disease and in the first 6 months after transplantation. For these reasons the primary immunizations should be given before transplantation, as early as possible during the course of disease. Vaccination strategy should include vaccination of household contacts and health care workers of transplant centers unless contraindicated. No conclusive data are available on the use of immunoadjuvants or screening for protective titers. Most vaccines appear to be safe in solid organ transplantation recipients, but live vaccines should be avoided until further studies are available. The risk of rejection appears minimal. Recommended vaccines include pneumovax, hepatitis A, B, influenza and tetanus/diphtheria. We outline specific protocols and recommendations in this particular patient population. Specific contraindications exist for other vaccines such as yellow fever, OPV, BCG and vaccinia.

We conclude that solid organ recipients will benefit from consistent immunization practices. Further studies are recommended to improve established protocols in this patient population.

Nanomedicine

Mauro Ferrari, Ph.D., Brown Institute of Molecular Medicine, Dept. of Biomedical Engineering,
The University of Texas health Science Center, Houston, TX

What innovations, if any, will nanotechnology generate in the fight against disease? Answers in oncology, cardiovascular disease and infectious pathologies will be explored, with special emphasis on early detection, molecular imaging, and directed, personalized therapeutics.

Glutamate Release in Vertebrate Cone Photoreceptors

Barbara Innocenti, Ph.D.

Dept. Neurobiology and Anatomy
The University of Texas Health Science Center at Houston

In the dark, vertebrate photoreceptors tonically release the neurotransmitter glutamate via exocytosis. This raises the question of whether photoreceptors possess a highly efficient mechanism for replenishing the supply of releasable synaptic vesicles and/or have a virtually limitless releasable pool. To distinguish between these possibilities, we examined the properties and kinetics of neurotransmitter release in isolated cone photoreceptors.

Electrophysiological recordings were performed in the large, physiologically accessible cones of tiger salamander retina. Exocytosis was evoked by a depolarizing voltage step from -70 mV to 0 mV and detected as an increase in membrane capacitance (C_m). The corresponding calcium current and change in intracellular calcium concentration were simultaneously recorded.

Two distinct components of exocytosis were identified using a pulse-duration protocol. For membrane depolarizations up to 2 s in length, the evoked ΔC_m increased with pulse duration until it reached a plateau at ~ 68 fF. This component of release could be described by a single exponential function with a time constant of ~ 450 ms and manifested a voltage dependence that resembled that of calcium entry. With sustained depolarizations (>3 s), the evoked ΔC_m jump increased so that at 5 sec the mean increase in ΔC_m was 157 ± 39.5 fF.

Similar to other ribbon synapses, cone photoreceptors exhibit two kinetic components of release. The refilling rate of the first component is relatively fast and presumably contributes to maintained release. It's presently unknown whether a similarly efficient refilling mechanism characterizes the second component of vesicular release. Further characterization of exocytosis in cone photoreceptors will enhance our understanding of the mechanisms that underlie the ability of sensory-transducing synapses to maintain continuous neurotransmitter release.

Blood pressure in NOS3 Knockout mice during pregnancy and in their offspring: effect of the intrauterine environment

M Longo MD, PhD, F Lu MD, EH Tamayo, GDV Hankins MD, GD Anderson MD, GR. Saade MD.

*Dept. of Obstetrics & Gynecology, Div., Maternal Fetal Medicine,
The University of Texas Medical Branch at Galveston*

Objective: Using a transgenic mouse model we demonstrate that the intrauterine environment contributes to fetal vascular programming in later life. Our aim was to measure blood pressure in pregnant NOS3 knockout mice and in their offspring.

Material/Methods: NOS3 knockout (-/-KO) and wild type mice (WT) were bred to obtain heterozygous offspring born to KO mothers (+/-Mat) versus WT mothers (+/-Pat). Blood pressure (BP) catheters were inserted into the aortic arch in 10-12 wks. old female/male offspring and in -/-KO and WT mothers at day 10 of gestation. BP was recorded for 4 days in the offspring and until gestational day 18 in the mothers. Mean BP was calculated, Student's t-test and one way ANOVA used for statistical analysis.

Results: Mean BP (mmHg) was significantly higher from day 12 of gestation until day 18. At day 18 was: -/-KO; 127.4±1.1 vs. WT; 95.1±3.1. The average pup and placental weights were significantly lower in -/-KO versus WT mothers. The mean BP (mmHg) was significantly higher from the start of recording in -/-KO and +/-Mat offspring versus WT and +/-Pat offspring (-/-KO, 150.9±10.4; +/-Mat, 133.6.9±14.5 versus WT, 113.6±4; +/-Pat, 118.2.±7.8), and remain higher until the end of recording.

Conclusion: NOS3 deficiency in pregnancy leads to abnormal fetal growth and hypertension in the offspring later in life. This hypertension is most likely the result of the altered fetal vascular programming that we have previously demonstrated. These findings highlight the role of the intrauterine environment in the developmental origin of adult disease.

A new approach to study and treat the spectrum of diseases associated with abnormal activation of the androgen receptor

Marco Marcelli, Shihua Sun, Adam Szafram, Michael Mancini

Presented by:

Marco Marcelli M.D., Associate Professor, Department of Medicine, Baylor College of Medicine Chief of Endocrinology, Michael E. DeBakey VA Medical Center
Houston TX 77030

Three main diseases are associated with androgen receptor (AR) mutations; Androgen Independent Prostate Cancer (CaP), Kennedy's disease, and the Syndromes of Androgen Insensitivity (AIS). Little can be done to treat successfully these diseases. We have created a new single cell-based model to visualize on the microscope the various phases of AR action in the cell. This new model is currently being developed to generate information on how AR activity changes from physiologic to pathologic conditions, and to screen for new drugs capable to affect its action in an agonistic or antagonist way.

**FGF2 BINDING, SIGNALING AND ANGIOGENESIS ARE MODULATED BY
HEPARANASE IN METASTATIC MELANOMA CELLS**

**Jane Reiland, Doty Kempf, Madhuchhanda Roy, Yvonne Denkins,
and Dario Marchetti**

Department of Comparative Biomedical Sciences-SVM, Louisiana State University-
Baton Rouge, Baton Rouge, Louisiana 70803.

Heparanase (HPSE) and fibroblast growth factor-2 (FGF2) are critical regulators of melanoma angiogenesis and metastasis. Elevated HPSE expression contributes to melanoma progression; however, further augmentation of HPSE presence can inhibit tumorigenicity. HPSE enzymatically cleaves heparan sulfate glycosaminoglycan chains (HS) from proteoglycans. HS acts as both low-affinity FGF2 receptors and co-receptors in the formation of high-affinity FGF2 receptors. We have investigated HPSE's ability to modulate FGF2 activity through HS remodeling. Extensive HPSE degradation of human metastatic melanoma cells (70W) inhibited FGF2 binding. Unexpectedly, treatment of 70W cells with low HPSE concentrations enhanced FGF2 binding. In addition, HPSE-unexposed cells did not phosphorylate extracellular signal-related kinase (ERK) or focal adhesion kinase (FAK) in response to FGF2. Conversely, in cells treated with HPSE, FGF2 stimulated ERK and FAK phosphorylation. Secondly, presence of soluble HPSE-degraded HS enhanced FGF2 binding and ERK phosphorylation at low HS concentrations. Higher concentrations of soluble HS inhibited FGF2 binding but FGF2 signaling through ERK remained enhanced. Soluble HS were unable to support FGF2-stimulated FAK phosphorylation irrespective of HPSE treatment. Finally, cell exposure to HPSE or to HPSE-degraded HS modulated FGF2-induced angiogenesis in melanoma. In conclusion, these effects suggest relevant mechanisms for HPSE modulation melanoma growth factor responsiveness and tumorigenicity.

HEPARANASE EXPRESSION AND TrkC/p75^{NTR} RATIOS IN HUMAN MEDULLOBLASTOMA

**Neeta D. Sinnappah-Kang⁴, Robert E. Mrak², Daniel B. Paulsen³
and Dario Marchetti¹**

¹Department of Comparative Biomedical Sciences and ³Department of Pathobiological Sciences, School of Veterinary Medicine, Louisiana State University – Baton Rouge, Baton Rouge LA 70803; ²Department of Pathology, University of Arkansas for Medical Sciences, Little Rock, AR 72223; and ⁴Division of Pediatrics, U.T. M.D. Anderson Cancer Center, Houston, TX 77030.

Medulloblastoma (MB), the most devastating and common brain tumor in children, is highly invasive and extremely difficult to treat. Identifying the properties of MB tumors that cause them to invade and metastasize is therefore imperative for the development of novel treatments. We performed investigations to elucidate prognostic implications of heparanase (HPSE-1) and TrkC/p75^{NTR} expression in MB using formalin-fixed, paraffin-embedded (FFPE) MB clinical specimens from children aged 1 to 19 years. Expressions of p75^{NTR} and HPSE-1 correlated with each other (Pearson's correlation $R = 0.899$; $p < 0.0001$; $R^2 = 81\%$; $n = 13$). In addition, TrkC:p75^{NTR} ratios correlated with MB meningeal spread ($R = 0.608$; $p = 0.0212$; $R^2 = 37\%$; $n = 14$). Secondly, using antibodies specific to TrkC and HPSE-1, we carried out immunohistochemistry (IHC) on 22 human MB tissue samples. IHC reaction scores revealed a significant expression of HPSE-1 in 76% of MB tissues from children aged 3 years and older ($p = 0.0490$; $n = 17$) while TrkC immunoreactivity was detected in 71% of these patient samples. Of note, TrkC was significantly present in 100% of MB female patients ($p = 0.0313$; $n = 6$). These studies support the role of p75^{NTR} and HPSE-1 as two novel molecular determinants involved in the biology and clinical progression of MB.

HPSE ESPRESSION AND FUNCTIONALITY IN DIFFERENTIATING NEURAL CELLS

Massimo Moretti^{1*}, Neeta Devi Sinnappah-Kang^{3*}, Matteo Toller¹, Francesco
Curcio¹, and Dario Marchetti²

¹Dipartimento di Patologia e Medicina Sperimentale e Clinica (DPMSC), and Centro Interdipartimentale di Medicina Rigenerativa (CIME), University of Udine, 33100 Udine, Italy. ²Department of Comparative Biomedical Science, School of Veterinary Medicine,

Louisiana State University – Baton Rouge, Baton Rouge, Louisiana 70803, USA.

³Division of Pediatrics, U.T. M.D. Anderson Cancer Center, Houston, TX 77030, USA.

*These Authors contributed equally well.

The study of cellular differentiation encompasses many vital entities of biology and medicine. Heparan sulfate proteoglycans (HSPG) are essential and ubiquitous macromolecules associated with the cell surface and extracellular matrix (ECM) of a wide range of cells and tissues. Heparan sulfate chains (HS) of HSPG bind and sequester a multitude of extracellular ligands including growth factors, cytokines, chemokines, enzymes, and lipoproteins. Enzymatic degradation of HS is therefore involved in processes such as cell proliferation, migration, and differentiation.

Heparanase (HPSE) is a HS-degradative enzyme being associated with inflammation, lipid metabolism, and a critical molecular determinant in cancer metastasis. The enzyme acts as an endo- β -D-glucuronidase which degrades HS at specific intrachain sites, resulting in HS fragments of discrete molecular weight size which retain biological function. HPSE relevance as the only example of cloned/purified mammalian HS degradative enzyme lead us to investigate its functionality in human olfactory epithelium (HOE) cells as a paradigm for HPSE roles in

neural cell differentiation. We provide first-time evidence of 1) HPSE presence in HOE cells, and 2) a highly significant increase of HPSE mRNA and enzyme activity in differentiating versus proliferating HOE cells.

Our data suggest that an augmented HPSE activity may represent a physiological mechanism involved in neural cellular differentiation.

HEPARANASE MECHANISMS OF MELANOMA METASTASIS TO THE BRAIN: DEVELOPMENT AND USE OF A BRAIN SLICE MODEL

**Brian P. Murry¹, Bryan E. Blust¹, Amandip Singh¹, Timothy P. Foster², and
Dario Marchetti¹**

¹Department of Comparative Biomedical Sciences, and ²Department of Pathobiological Sciences, School of Veterinary Medicine, Louisiana State University at Baton Rouge, Baton Rouge, LA, 70803

Heparanase (HPSE) is an endo-beta-D-glucuronidase that cleaves heparan sulfate (HS) chains of proteoglycans (HSPG), and its expression has been associated with increased cell growth, invasion, and angiogenesis of tumors as well as with embryogenesis and tissue development. Since metastatic cancer cells express HPSE, we have developed an orthotopic brain slice model to study HPSE involvement in brain-metastatic melanoma. This model allows for the characterization of tumor cell invasion at both quantitative and qualitative levels. Brain-metastatic melanoma cells (B16B15b) showed augmenting levels of HPSE protein expression in a time-dependent manner. Secondly, B16B15b cells pre-treated with HPSE showed a significant increase in the number of cells that invaded into the brain tissue. Finally, HPSE exposure augmented invasion depth in brain sections by brain-metastatic melanoma cells. We concluded that applying this brain slice model can be beneficial to investigate HPSE - related *in vivo* modalities in brain-metastatic melanoma and brain invasion in general. These results also further emphasize the potential relevance of using this model to design therapies for controlling this type of cancer by blocking HPSE functionality.

Prognostic role of EGFR pathway in non-small cell lung cancer (NSCLC)

Erminia Massarelli, MD, PhD

Department of Thoracic/Head and Neck Medical Oncology, The University of Texas
M. D. Anderson Cancer Center, Houston, Texas 77030

NSCLC is the most frequent cause of cancer death in the Western world. Only patients with surgically resectable tumors have a significant chance of cure. Agents targeting epidermal growth factor receptor (EGFR) signaling have demonstrated efficacy in the treatment of advanced NSCLC. To explore the potential use of EGFR inhibitors in the early stages of disease, we have investigated the prognostic role of EGFR pathway in a large cohort of surgically resected early stage NSCLCs by tissue microarray technique.

Keywords: Lung cancer, EGFR pathway, prognostic factors

The Italian Contribution to the International Space Station

Paolo Nespoli, ESA Astronaut
NASA/JSC-CB 2101 NASA Parkway
Houston, TX 77058

The United States, Russia, the European Space Agency (representing 10 European countries), Japan and Canada have started in the late eighties an ambitious project to put in space an International Space Station (ISS): a permanently manned pressurized structure located in low Earth orbit, used as a technological platform, a scientific research laboratory and as a springboard for the exploration of our solar system.

Italy has contributed to this project both with direct cooperation with NASA and through the European Space Agency. These efforts have qualified the Italian industry as a world leader in the design and production of space qualified pressurized modules. Three of these modules, called Multi-purposes Logistic Modules, are routinely used by the Space Shuttle to carry experiments and equipment and to and from the ISS. Three other modules, more complex both from a structural and functionality point of view, will be launched during the next few years.

An Italian astronaut will be part of the crew of the Space Shuttle mission STS-120, currently planned for August 2007. One of the main goals of the mission is the delivery in space and installation on the ISS of the pressurized module Node 2, designed and built in Italy. This module has six docking ports and will allow the further expansion of the station.

Improvement of Information Technology (IT) services through Service Management, based on the Information Technology Infrastructure Library (ITIL) framework

Paolo Papi, Sr Project Manager, Master in Electronic Engineering and Computer Science, ITIL Certified,
IBM Tivoli, 11501 Burnet Rd, Austin, TX, 78758

Abstract

The three key objectives of Service Management are:

- To align Information Technology (IT) services with the current and future needs of the business and its customers
- To improve the quality of the IT services delivered
- To reduce the long-term cost of service provision

IT has been widely utilized for decades but more recently the Internet has demonstrated that for many modern e-business based organizations "IT is the business, and the business is IT".

It is essential therefore to recognize the absolute dependency of most businesses upon the Information Technology infrastructure and quantity, quality and the availability of the information that such an infrastructure provides and supports.

The challenges facing the IT managers of today are to coordinate and work in partnership with the business to create new business opportunities. This has to be achieved while reducing the total cost of ownership. The main method of realizing this goal is the reduction of the overall management and support costs, while developing new business models to maintain or improve the quality of service delivered to the business. In order to do this the correct business and IT processes need to be developed and implemented. The management of IT is all about the efficient and effective use of the three P's: people, processes and products (tools and technology).

The Information Technology Infrastructure Library (ITIL) philosophy adopts a process driven approach which is scalable to fit both large and small IT organizations. It considers Service Management to consist of a number of closely related and highly integrated processes. To realize the key objective of Service Management these processes must use the people and the products effectively, efficiently and economically in the delivery of high quality, innovative IT services aligned to business purposes.

BCR as inhibitor of BCR-ABL in Chronic Myelogenous Leukemia (CML)

Bastianella Perazzona

Department of Molecular Pathology, The University of Texas M. D. Anderson Cancer,
Houston, Texas 77030

CML is a disease of the hematopoietic system with an initial chronic phase with excessive production of myeloid cells and an acute phase that resembles acute leukemia. The causative agent of CML is the BCR-ABL protein, product of the Philadelphia chromosome. We are currently investigating the role of the BCR protein as a suppressor of BCR-ABL induced oncogenicity both in vitro and in an animal model and evaluating the potential applications of this protein in the therapy for CML.

Bringing Operative Vaginal Delivery into the New Millennium: I. The Electronically-controlled Forceps Delivery System

NICOLA PERONE, M.D., F.A.C.O.G., F.A.C.S

Clinical Professor

Dept. of Obstetrics, Gynecology & Reproductive Sciences

The University of Texas Medical School at Houston

Abstract

The obstetrical forceps is unquestionably a very useful instrument in the hands of properly trained obstetricians. As the medical-legal consequences of obstetric action have solidified, it has become clear, however, that for this instrument to keep its place in the armamentarium of the obstetrician, it must be modernized. An electronically-controlled forceps delivery system is described, which allows to measure in real-time the traction applied during a delivery, to alert the doctor when preset safety limits are exceeded, and to generate a graphic representation of the force applied.

An Emerging New Therapy for Alzheimer's Disease

Giulio Tagliatela, Ph.D.

Department of Neuroscience & Cell Biology,
The University of Texas Medical Branch at Galveston, TX 77539

Alzheimer's Disease (AD) is a terminal age-associated dementia involving memory deficits and loss of brain neurons caused by the presence of the toxic amyloid beta ($A\beta$) protein. We have discovered that in transgenic mice that accumulate human $A\beta$ and show AD symptoms Calcineurin, a protein important for neuronal viability and memory, is abnormal and that treatment of these mice with an inhibitor of calcineurin completely reverses memory deficits. These results indicate Calcineurin inhibitors as possible pharmacological tools in AD.

Translocation (11;18) and Gastric High-grade Lymphoma Risk

Sonia Toracchio^{1,2}, PhD, Daphne de Jong³, MD, Andrew Wotherspoon⁴, MD, Massimo Rugge⁵, MD, Hiroyoshi Ota⁶, MD, PhD, David Y Graham¹, MD and Hala El-Zimaity¹, MD.

¹ Dept of Pathology & Medicine, Baylor College of Medicine, Houston, Texas, United States; ² Department of Oncology and Neuroscience, Section of Molecular Pathology, University "G. d'Annunzio", and Center of Excellence on Aging, "G. d'Annunzio" Foundation, Chieti, Italy; ³ Dept of Pathology, The Netherlands Cancer Institute, Amsterdam, Netherlands; ⁴ Department of Histopathology, Royal Marsden Hospital, London, United Kingdom; ⁵ Dept. of Oncological & Surgical Sciences, University of Padova, Padova, Italy; and ⁶ Dept. of Biomedical Laboratory Sciences, School of Medicine Shinshu University, Matsumoto, Nagano, Japan

Purpose: Translocation t(11;18)(q21;q21) is the most frequent chromosomal aberration in extranodal marginal zone lymphoma of the MALT type. It has been associated with an aggressive course but has not been described in high-grade gastric MALT lymphoma. Some authors propose that tumors with this translocation rarely or never progress to high-grade lymphomas. However, these conclusions are based on examining few specimens. This study examines the frequency of chromosomal translocation t(11;18)(q21;q21) in lymphomas from patients with low-grade and high-grade marginal zone lymphoma of the MALT type.

Keywords: t(11;18) translocation, gastric MALT lymphoma, high-grade risk.

Acknowledgments: Dr. Sonia Toracchio was supported by a fellowship from Fondazione Italiana per la Ricerca sul Cancro (FIRC), Milan, Italy.

MARINA VANNUCCI

Professor of Statistics, Texas A&M University

Visiting Scholar at Rice University

MVANNUCCI@STAT.TAMU.EDU

RESEARCH INTERESTS

I got a B.S. in Mathematics in 1992 and a Ph.D. in Statistics in 1996, both from the University of Florence, Italy. I am currently a Professor of Statistics at Texas A&M University. I am also Visiting Scholar at Rice University for this Fall 2006. I was a Research Fellow at the Institute of Mathematics and Statistics, University of Kent at Canterbury, UK, from 1996 to 1998. I moved to Texas A&M University in 1998 where I was Assistant Professor during 1998-2003 and Associate Professor during 2003-2005.

At Texas A&M I am also the co-Director of the Biostatistics and Bioinformatics Facility Core of the Center for Environmental and Rural Health and a Program Coordinator and co-P.I. of a Training Program in Bioinformatics. My responsibilities include teaching statistics courses, supervising graduate students and postdoctoral trainees, developing an independent research program in statistics and bioinformatics and collaborating with life science researchers.

My research focuses on the theory and practice of Bayesian methods for Genomics and on the development of wavelet-based statistical models for application to biomedical data. My work is often motivated by real problems that need to be addressed with suitable statistical methods. I provide here brief descriptions of some of my major projects.

Bayesian Methods for Genomics:

I coordinate the BMG (Bayesian Methods for Genomics) research group, a group of faculty, postdoctoral trainees and students working on statistical Bayesian approaches for the analysis and modeling of high-throughput data and of biological systems. This work is funded by the National Human Genome Research Institute through and R01 mechanism.

Microarray data represent a challenge to statistical analyses because of their high-dimensionality. Our work has focussed on the development of Bayesian methods for variable (gene) selection for sample classification and clustering and for survival models. Our methodologies have been applied to immunologic studies on arthritis and to DNA microarray data from an endometrial cancer study. Recent developments of the Bayesian techniques we have proposed for gene selection include extensions to the analysis of censored survival data. When applied to microarray data the proposed approaches identify relevant genes and provide a prediction of the survivor function. We have applied these methods to breast cancer data and to B-cell lymphoma microarray studies.

We also have an interest in methods that integrate data of different forms, for example we have worked on models that combine DNA microarray data with genome sequence information for the identification of DNA regulatory motifs. We have applied our procedures to well-studied pathways of *Saccharomyces cerevisiae* and *Schizosaccharomyces pombe*.

Our research extends to the emerging important field of proteomic data and to protein structure prediction.

Wavelet-based Methods for Biomedical Data:

I have been interested in the development of wavelet-based methods since my Ph.D. thesis work. Wavelets are a mathematical tool for data analysis and have found application in several fields, such as engineering, biology and recently bioinformatics. My work on functional data was the first contribution to the use of wavelet methods for dimension reduction when multiple curves are under study. Contributions include curve regression models, nonparametric modeling of hierarchical functions, classification and clustering settings with functional data. In 2001 I received an NSF CAREER award for my research on these topics.

The scientific problems to which I have applied my methodologies include in particular those involving chemometrics datasets for Near-Infrared spectra measured at as many as a thousand frequencies and novel applications to experimental data arising from carcinogen-induced colon cancer in rodent models. Currently I am engaged in collaborations with investigators at the New York Psychiatric Institute at Columbia University. As part of this effort I have become interested in the development of wavelet-based statistical modeling suitable for the analysis of data such as tidal volume traces, heart rates, response time data and fMRI image data.

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Cytoskeletal Basis of Ion Channel Function in Cardiac Muscle

Matteo Vatta, PhD

Assistant Professor

Associate Director-Pediatric Cardiac Genetic Research

Baylor College of Medicine, Houston, TX

Texas Children's Hospital

The heart contracts upon self-generated electrical stimuli and relies on the structural apparatus of each cardiac cell to endure the repetitive morphological changes during each cycle. Structural defects affect the mechanical stability of each cell and lead to altered electrical activity causing rhythm disorders. Arrhythmias secondary to myocardial structural alterations have been increasingly studied, although the precise molecular mechanisms are still elusive. Our investigation tries to elucidate the molecular and functional relationships between the cellular structural apparatus and ion channels.

Key words: heart failure, cardiomyopathy, arrhythmia, ion channels, scaffolding protein

1. Proposal of a new staging for the intra-hepatic cholangiocarcinoma

Daria Zorzi, MD

Department of Surgical Oncology, Liver Service, The University of Texas M. D.

Anderson Cancer Center, Houston, Texas, 77030

The intra-hepatic cholangiocarcinoma (IHCC) should be considered a different pathologic entity from hepatocellular carcinoma. In the 6th edition of the American Joint Committee on Cancer the IHCC is included in the liver staging. In order to propose a new separate staging for IHCC we started a multi-institutional project to review the outcome of resection in a large cohort.

Keywords: Intra-hepatic cholangiocarcinoma, staging, resection, outcome

2. Hepatotoxicity and Efficacy of Oxaliplatin-based Chemotherapy with or without Bevacizumab for colorectal liver metastases

Daria Zorzi, MD

Department of Surgical Oncology, Liver Service, University of Texas M.D.

Anderson Cancer Center, Houston, Texas, 77030

Drug specific chemotherapy-associated hepatic injury is increasingly recognized as a result of chemotherapy associated toxicity in patients treated for colorectal liver metastases.

Recently, targeted biologic therapy with the vascular endothelial growth factor (VEGF) antibody, bevacizumab, has been used in association with irinotecan and oxaliplatin for the treatment of metastatic colorectal cancer. Although preliminary data indicate an increase in response rate and survival, the rationale for its use in patients with hepatic colorectal metastases has not been investigated.

The objective of this study was to determine whether bevacizumab should be recommended in patients receiving preoperative oxaliplatin-based chemotherapy for colorectal liver metastases.

Keywords: bevacizumab, liver metastases, colorectal cancer, preoperative chemotherapy

VISUAL KNOWLEDGE BUILDER

Anna Zacchi, Ph.D.

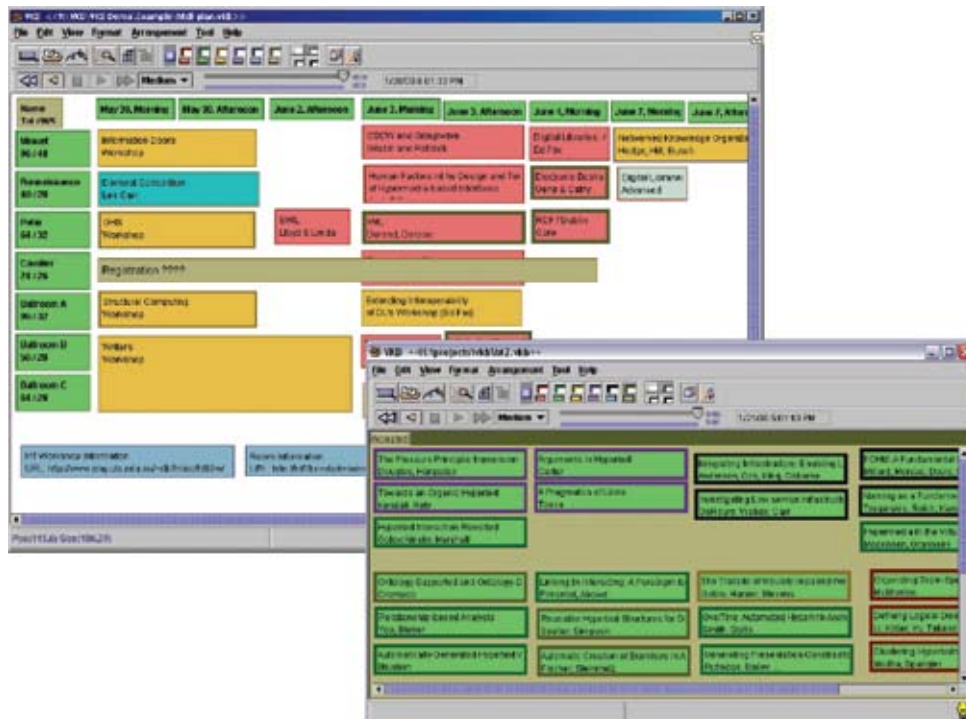
Department of Computer Science
Texas A&M University, College Station, Texas

Visual information workspaces for analysis allow users to collect, organize, and interpret information during knowledge-intensive tasks. Users non-verbally express formative interpretations through visual attributes and spatial layout. Over time, these visual codings evolve into visual languages categorizing and expressing relationships among information objects. To better support this process of emergence, the Visual Knowledge Builder (**VKB**) extends prior work on visual information workspaces. Similar to prior systems, users manipulate visual symbols representing information objects in a hierarchy of two-dimensional workspaces called collections. The Visual Knowledge Builder includes an embedded history mechanism for returning to prior states of the information space and replaying the unfolding interpretation. The Visual Knowledge Builder has been used for both short-term and long-term tasks, identifying potential enhancements and refining our understanding of the effects of visual workspaces on analytic practice.

VKB is an ongoing project at Texas A&M University. It started in 2000 under the direction of prof. Frank M. Shipman III. Several authors participated in its development. Among the authors are Dr. Haowei Hsieh, J. Michael Moore, Anna Zacchi, Yoon Jung Hur, Soonil Bae, Konstantinos Meintanis, Dohyoung Kim, and Dr. Luis Francisco-Revilla.

VKB is available for free download from :
<http://www.csd.tamu.edu/VKB/>

I plan to do a demo of the software.



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For this reason also, since the day we heard of it, we have not ceased to pray for you and to ask that you may be filled with the knowledge of His will in all spiritual wisdom and understanding, so that you will walk in a manner worthy of the Lord to please Him in all respects, bearing fruit in every good work and increasing in the knowledge of God, strengthened with all power, according to His glorious might, for the attaining of all steadfastness and patience; giving thanks to the Father, who has qualified us to share in the inheritance of the saints in Light.

Who **Where** **Why**
What **When** **How**

what is spiritual wisdom/understanding
 what does it mean to be filled with the knowledge of His will?
 What do you must be Colossians pray in being filled?
 His will for what? (2:12) Is it integrate experience?
 Are they just freed or must they be active in some sense?

For this reason also
 since the day we heard of it
 we have not ceased to
 to pray for you and
 to ask that you be filled
 with the knowledge of His will in all
 spiritual wisdom
 understanding
 So that
 you will walk
 in a manner worthy of the Lord
 to please Him in all respects
 strengthened
 with all power
 according to His glorious might
 we in some way have access to the strength that

Paul includes himself in the 'us' who are qualified to share in the inheritance
 giving thanks
 to the Father
 who has qualified us
 to share in the inheritance of the saints
 in Light
 How can we walk in a manner worthy of the Lord?
 bearing fruit results from
 ing that
 big deal. Its about being worthy of the Lord - not, I don't think, earning anything but acting in a manner that's in keeping with what God has given us
 note the purpose for which P prays and why he wants them to grow in knowledge
 P's prayers are in light of their belief and possibly also the hope that comes from the active nature of the gospel
 What are the saints?

Abstracts 2005

Recent Advances on Diabetes Prevention

Nicola Abate, M.D., Associate Professor of Internal Medicine
The Center for Human Nutrition Division of Endocrinology and Metabolism
The University of Texas Southwestern Medical Center at Dallas, Texas

Obesity affects 97 million adults in the USA and is considered an epidemic disease throughout the world. Accumulation of fat determines increased risk for diabetes and premature cardiovascular disease or death. During the past 10 years, Dr. Abate's clinical research has established mechanisms of interactions between genetic and fat accumulation in determining whether a person will develop diabetes and heart disease. These studies have the long term goals of finding new modalities for prevention and treatment of persons at risk.

Design and manufacturing of innovative advanced superconducting coils in magnesium diboride (MgB_2) for the VASIMR experiment at NASA-JSC

Matteo Alessandrin

Materials Engineering program, University of Houston

Peculiar features of magnesium diboride (i.e., lightweight and high critical temperature) make it a very attractive material for space applications. The Advanced Space Propulsion Laboratory (ASPL) at NASA-Houston is currently supporting the development of innovative superconducting magnets, which will be main components of the VARIable Specific Impulse Magnetoplasma Rocket (VASIMR), a plasma engine for future human space travel to Mars and beyond. Current MRI (Magnetic Resonance Imaging) machines use niobium alloy wires which require liquid helium to cool them down to temperatures low enough for them to be superconducting, instead MgB_2 could be cooled with the much more affordable liquid neon which, besides to be used in neon advertising signs, is already useful to the space program as a coolant for ultra-sensitive infrared imaging and detection equipment and for creating deep-space environmental temperatures during satellite testing. Thus, even if the operation temperature is below the boiling point of liquid nitrogen, recent advances in cooling technology have made such low temperatures acceptable and commercial cryocoolers already exist for experimental and commercial applications. As far as space applications are concerned, at the 20°K temperature range it is reasonable to foresee the use of liquid hydrogen. This element is presently used in the energy sector only in industrial applications, but it sounds very promising that one of the few cases where hydrogen is used as a commercial product is the space sector where it has already been serving as liquid propulsion fuel for many decades.

Role of photoactive molecules in the damage of proteins

Lorenzo Brancaleon

Department of Physics and Astronomy, The University of Texas at San Antonio

Photoactive molecules such as Protoporphyrin IX (PPIX) and meso-tetra-sulphonato-phenyl porphyrin (TSPP) have been employed for basic research and clinical phototherapy of abnormal tissues. The field of cancer phototherapy has recently lost a little of its previous prominence; nonetheless, we think that many molecular mechanisms responsible for the cellular damage produced by phototherapy need to be investigated in order to improve future applications of phototherapy and revive this once very promising field. In addition, the interaction of photoactive molecules could be useful in the study of protein folding as they may provide an alternative way to induce conformational changes under more “physiological” conditions.

Recent results show that photoactive molecules damage certain proteins and that this damage may be related to a selective induction of apoptosis over necrosis. Thus, for the last five years a major line of research in my group has been dedicated to the investigation of the interaction of clinically useful photoactive molecules with proteins. We first selected the investigation of PPIX with large plasma proteins such as Albumins and Immunoglobulins. More recently we started to investigate the interaction of photoactive molecules with smaller globular proteins such as α -lactoglobulin and tubulin. The interaction with lactoglobulin is not directly relevant to phototherapy but represents a useful biophysical model and may be used for a more specific targeting of abnormal cells. Tubulin instead has been shown to be directly targeted by porphyrin-like photoactive molecules.

Using a combination of spectroscopic and time-resolved optical methods we characterized the binding parameter and estimated the location of the binding sites which in the case of lactoglobulin is modulated by the pH of the solution. We have also been investigating how the irradiation of PPIX and TSPP changes the conformation of the proteins. Both PPIX and TSPP appear to cause conformational effects on lactoglobulin and tubulin as shown by changes in the intrinsic fluorescence properties of the proteins. Future investigations and better understanding of these mechanisms may lead to improvement of the application of phototherapy and the possibility of employing photoactive molecules to unfold proteins.

Advances in ad-hoc communications

Stefano Faccin

Nokia Research Center, Mobile Network Laboratory, Dallas

Wireless ad-hoc networks enable information exchange among mobile entities without a fixed infrastructure, and are very attractive for applications where preexisting infrastructures are either infeasible or too expensive. (e.g., “home” scenarios, military and public safety applications). This new form of communications poses new challenges to traditional networking architectures and protocols designed for infrastructure-based wireless networks such as current cellular networks. This presentation summarizes some recent achievements in the area.

Routine Whole Blood μ -sampling and LC-MS/MS Determination of Small Molecules in Discovery Drug Metabolism

Elizabeth A. Mahan, Sabrina Forni*, Rick King, Debra McLoughlin, Debbie Defeo-Jones, Anne Taylor, and Carmen Fernandez-Metzler**

Department of Drug Metabolism, Merck Research Laboratories, West Point, PA 19486

*Clinical Chemistry Abbott Diagnostics, Irving TX 75038

**Department of Cancer Research, Merck Research Laboratories,
West Point, PA 19486

Sampling technique for mouse tail bleeding as an innovative example of preclinical discovery approach to bioanalytical assays. A method for routine whole blood μ -sampling and LC-MS/MS determination of small molecules in drug discovery was recently developed. With using this technique, sacrificing mice is avoided.

The major obstacles associated with the use of such small volumes: sample collection and handling requires smaller vessels and separate addition of anticoagulant; following analysis, there is no option to re-inject the ALQ samples since the entire volume is used for analysis. This investigation will look at the introduction of whole blood assay as a routine approach in the discovery laboratory and strategies to overcome the challenges associated with the handling of very small sample volumes.

The LOQ of the assay for compound A was 2 ng/mL, with accuracy better than 80% of nominal concentration. Replicate quality control samples showed very good reproducibility, with precision better than 20% CV, and accuracy greater than 80%. The upper limit of quantitation for the standard assay was 25,000 ng/mL.

The advantages of μ -sampling and whole blood assays as well as the possible repercussions on in vivo experiments planning and PK data handling will be discussed.

Obese, but unexpectedly healthy

Gianluca Iacobellis

¹ Center for Human Nutrition, The University of Texas Southwestern Medical Center at Dallas, Texas, USA

² Cardiovascular Obesity Research & Management, Michael G deGroote School of Medicine, McMaster University, Hamilton General Hospital, ON, Canada.

³ Endocrinology, Department of Clinical Sciences, La Sapienza University, Rome, Italy

Obesity is widely accepted as an important risk factor for the development of cardiovascular and metabolic diseases. Nevertheless my recent studies show, for the first time, that a substantial part of an Italian obese population is metabolically “healthy” and clinically uncomplicated. In addition, the prevalence of adverse risk factors in the 700 Italian obese subjects we studied is unexpectedly low and partially independent of obesity degree. The evidence arising from our data clearly shows that approximately the 30% (*see pie graphic*) of this Italian obese sample has no glucose intolerance, impaired fasting glucose, diabetes, hypertension, atherogenic dyslipidemia, such as increased small LDL cholesterol particles and pathological cardiac changes, as well as left ventricular hypertrophy, although a long duration of disease (at least 10 years) and wide range of BMI (from 30 to 81 kg/m²). Uncomplicated obesity is associated with a lower cardiovascular risk and represents a well-defined clinical entity, as previously suggested, but not clearly reported.

71% = morbid



29% = healthy

Kinetics of exocytosis at the cone photoreceptor synapse

B. Innocenti and R. Heidelberger

Dept. Neurobiology and Anatomy, The University of Texas Health Science Center at Houston,
Houston, TX

Our laboratory is interested in investigating the mechanisms that control neurotransmitter release at chemical synapses, the specialized contact sites between neurons where transfer of information occurs. Vertebrate photoreceptors respond to light stimuli with graded changes in membrane potential that are faithfully translated into graded variations in the release of neurotransmitter. In order to understand the regulatory mechanism(s) underlying this tightly controlled synaptic transmission, we are characterizing the properties and kinetics of neurotransmitter release in cone photoreceptors.

To achieve our goals, we employ a combination of different electrophysiological and fluorescence techniques on the big and thus easily accessible cones isolated from tiger salamander retina.

Two kinetic components of exocytosis were identified in cone photoreceptors.

The first component has amplitude of ~50 fF and quickly recovers from depletion ($t \approx 1$ second). The second component was suggested for depolarizations > 1 second and showed evidence of depletion at ≈ 10 seconds stimulus duration.

Both components exhibited a similar relationship to intracellular Ca^{2+} . However, meanwhile the first component of release clearly relies on Ca entry from the extracellular space; the Ca^{2+} signal underlying the second component might involve the presence of additional Ca^{2+} sources.

Characterization of the properties and kinetics of release in cones will enhance our understanding of how tonically active synapses work. In addition, disclosure of properties unique to secretion in cone photoreceptors will allow us to better understand information processing in the vertebrate retina.

Heparanase cleavage of HeparanSulfate Modulates FGF2 Binding and Signal

Transduction in Metastatic Melanoma Cells

Jane Reiland, Doty Kempf and Dario Marchetti¹

¹Department of Comparative Biomedical Sciences-SVM, Louisiana State University, Baton Rouge, Louisiana 70803

Heparanase (HPSE-1), a unique mammalian endo- β -D-glucuronidase, and fibroblast growth factor-2 (FGF2), are critical regulators of melanoma angiogenesis and metastasis. Elevated HPSE-1 expression is linked to melanoma progression; however, further augmentation of HPSE-1 presence can inhibit tumorigenicity. HPSE-1 enzymatically cleaves heparan sulfate glycosaminoglycan chains (HS) from proteoglycans. HS acts as both low-affinity FGF2 receptors and co-receptors in the formation of high-affinity FGF2 receptors. It is established that removing HS from cells inhibits FGF2 binding and signaling. Furthermore, soluble HS can inhibit or potentiate FGF2 binding and signaling depending upon the cellular environment and HS composition. We have investigated the ability of HPSE-1 to modulate FGF2 activity through HS remodeling. HPSE-1 digestion of human metastatic melanoma 70W cells enhanced FGF2 binding at low HPSE-1 concentrations whereas higher HPSE-1 concentrations inhibited it. Secondly, despite FGF2 binding, 70W cells did not phosphorylate extracellular signal-related kinase (ERK) or focal adhesion kinase (FAK) in response to FGF2. However, FGF2 stimulated phosphorylation of ERK and FAK was enhanced at low HPSE-1 levels and inhibited in the presence of higher HPSE-1 levels. Thirdly, the addition of soluble HS digested with HPSE-1 enhanced FGF2 binding and ERK phosphorylation at low HS concentrations. Higher concentrations of soluble HS inhibited FGF2 binding; however, FGF2 signaling through ERK was enhanced. Finally, soluble HS were unable to stimulate FAK phosphorylation irrespective of HPSE-1 treatment. We have demonstrated a HPSE-1 concentration-dependent alteration of FGF2 binding and signaling. These HPSE-1 effects suggest a relevant mechanism for HPSE-1 modulation of melanoma tumorigenicity.

HPSE-1 Expression and Functionality in Differentiating Neural Cells

Massimo Moretti^{1*}, Neeta Devi Sinnappah-Kang^{2*}, Matteo Toller¹, Francesco Curcio¹, and Dario Marchetti^{2⁶}

¹Dipartimento di Patologia e Medicina Sperimentale e Clinica (DPMSC), and Centro Interdipartimentale di Medicina Rigenerativa (CIME), University of Udine, 33100 Udine, Italy.

²Department of Comparative Biomedical Science, School of Veterinary Medicine, Louisiana State University – Baton Rouge, Baton Rouge, Louisiana 70803, USA.

* These Authors contributed equally well.

The study of cellular differentiation encompasses many vital entities of biology and medicine. Heparan sulfate proteoglycans (HSPG) are essential and ubiquitous macromolecules associated with the cell surface and extracellular matrix (ECM) of a wide range of cells and tissues. Heparan sulfate chains (HS) of HSPG bind and sequester a multitude of extracellular ligands including growth factors, cytokines, chemokines, enzymes, and lipoproteins. Enzymatic degradation of HS is therefore involved in processes such as cell proliferation, migration, and differentiation.

Heparanase (HPSE-1) is a HS-degradative enzyme being associated with inflammation, lipid metabolism, and a critical molecular determinant in cancer metastasis. The enzyme acts as an endo- β -D-glucuronidase which degrades HS at specific intrachain sites, resulting in HS fragments of discrete molecular weight size which retain biological function. HPSE-1 relevance as the only example of cloned/purified mammalian HS degradative enzyme lead us to investigate its functionality in human olfactory epithelium (HOE) cells as a paradigm for HPSE-1 roles in neural cell differentiation. We provide first-time evidence of 1) HPSE-1 presence in HOE cells, and 2) a highly significant increase of HPSE-1 mRNA and enzyme activity in differentiating versus proliferating HOE cells.

Our data suggest that an augmented HPSE-1 activity may represent a physiological mechanism involved in neural cellular differentiation.

Heparanase Mechanisms of Melanoma Metastasis to the Brain: Development and use of a Brain Slice Model”

Brian P. Murry¹, Bryan E. Blust¹, Timothy P. Foster², and Dario Marchetti^{1*}

¹Department of Comparative Biomedical Sciences, and ²Department of Pathobiological Sciences, School of Veterinary Medicine, Louisiana State University-Baton Rouge, Baton Rouge, LA, 70803

Heparanase (HPSE-1) is an endo- β -D-glucuronidase that cleaves heparan sulfate (HS) chains of proteoglycans (HSPG), and its expression has been associated with increased cell growth, invasion, and angiogenesis of tumors as well as with embryogenesis and tissue development. Since metastatic cancer cells express high HPSE-1 levels, we have developed an orthotopic brain slice model to study HPSE-1 involvement in brain-metastatic melanoma onset. This model allows for the characterization of tumor cell invasion at both quantitative and qualitative levels. Brain-metastatic melanoma cells pre-treated with HPSE-1 showed a significant increase in the number of cells that invaded into brain tissue. Secondly, HPSE-1 exposure augmented invasion depth in brain sections by brain- metastatic melanoma cells. Finally, melanoma cells showed increasing HPSE-1 protein expression in a time-dependent manner. We concluded that applying this brain slice model can be beneficial to investigate HPSE-1-related *in vivo* modalities in brain-metastatic melanoma and brain metastasis in general. These results also further emphasize the potential relevance of using this model to design therapies for controlling this type of cancer by blocking HPSE-1 functionality.

NAO as a Selective Probe to Study the Content and the Organization of Cardiolipin in Mitochondria

Piccotti L. , Mileykowskaya E.* , Haines T.‡ , Corazzi L.# , Dowhan W.**

*Department of Biochemistry and Molecular Biology, University of Texas-Houston Medical School, 77225, USA; ‡Department of Chemistry, City College of the City University of New York, New York 10031, USA, \; #Laboratory of Biochemistry, Department of Internal Medicine, University of Perugia, 06122, Perugia, Italy

Cardiolipin (CL) is a ubiquitous anionic phospholipid mostly localized to membranes involved in oxygen dependent energy transducing processes such as bacterial membranes, inner membrane of chloroplasts, and the inner mitochondrial membrane of eukaryotes. CL plays a crucial role in the structural and functional organization of the components of the mitochondrial respiratory engine. As a consequence, the modulation of many physiological processes, such as mitochondrial respiration efficiency and mitochondrial response to apoptotic stimuli is related to the presence of CL and to its ultrastructural organization into the membrane. The non-cytotoxic fluorescent probe 10-N-nonyl-3,6-bis(dimethylamino)acridine (10-N-nonyl acridine orange, NAO) displays high affinity for anionic phospholipids. The shift from green to red in the emission spectra exclusively observed for the NAO-CL interaction, makes NAO a selective probe to investigate, both *in vivo* and *in vitro*, the CL content and distribution in mitochondrial membranes. In this work, the use of NAO to specifically measure the amount of CL in artificial and natural membranes and to analyze its reorganization in patches was optimized. Furthermore, evidence is furnished for the reorganization of CL-rich micro domains in mitochondrial membrane of yeast *S. cerevisiae* following the variation of bioenergetic parameters, such as the respiratory rate.

A High Performance 0.18 μ m BiCMOS technology employing high carbon content in the base layer of the SiGe HBT to achieve low variability of hFE

S. Sawada¹, T. Ohnishi¹, T. Saitoh², K. Yuki¹, K. Hasegawa¹, K. Shimizu¹, P. A Clifton³, A. Gallerano³, and A. Pinto³

(1) Semiconductor Company, Matsushita Electric Industrial Co., Ltd., Kyoto, Japan
tel.: +81-75-662-8989; fax: +81-75-662-8995; e-mail: sawada.shigeiki@jp.panasonic.com

(2) Advanced Technology Research Laboratories, Matsushita Electric Industrial Co., Ltd., Osaka, Japan

(3) PDF solutions Inc., San Jose, 95110 CA, USA

We present a 0.18 μ m BiCMOS technology in which hFE variability of Silicon-Germanium Heterojunction Bipolar Transistors (SiGe HBTs) is greatly minimized by means of increased Neutral Base Recombination adding high carbon content in the base layer. In this work, we propose, for the first time, to use a high concentration of carbon in the base of SiGe HBTs as a practical way to increase the base current in a predictable and controlled way. Consequently, variability of hFE is greatly decreased and a significant improvement of device matching can be achieved. Furthermore, to guarantee a sufficiently high value of hFE we propose a Silicon-Germanium cap architecture to increase the collector current. HBTs fabricated using this technology exhibit a peak f_T of 90GHz and a peak f_{MAX} of 140GHz with an $f_T \times BV_{ceo}$ of 255GHzV. Together with state of the art 0.18 μ m CMOS platform and high quality passives this technology is a viable candidate for the design of high frequency analog circuits.

Poroelastography: a new ultrasound elastographic Technique to image the spatial and tTemporal Poroelastic Behavior of Biological Tissues

Raffaella Righetti

The University of Texas Medical School, Department of Diagnostic and Interventional Imaging,
Ultrasonics Laboratory, Houston, Texas, USA

Elastography is a well-established imaging modality that utilizes an applied quasi-static compression to estimate and image the elastic properties of ultrasonically scanned tissues. Due to pathological conditions or simply due to their inherent structure, some hydrated soft tissues are characterized by a high water content that is free to move in the interstitial spaces. These tissues can be modeled as poroelastic materials, and their time-dependent mechanical behavior is primarily described by their elastic and permeability properties.

We have recently introduced a new imaging technique, named as “poroelastography” that uses standard elastographic methods to estimate and create quality images of the time-dependent mechanical behavior of poroelastic materials in unconfined uniaxial compression. Poroelastography requires the application of a displacement function, consequent collection of ultrasonic data from the material under compression and the generation of Poisson’s ratio (lateral-to-axial strain ratio) elastograms at various time intervals. The resulting series of time-sequenced Poisson’s ratio elastograms has been defined as a “poroelastogram”. This sequence provides an estimation of the change in volume of a poroelastic material, which is related to the dynamics of the fluid flow and to the elastic and permeability properties of the materials. From the poroelastograms, new types of elastograms, called Poisson’s ratio time constant elastograms and permeability elastograms, may be computed to obtain information about the underlying permeability distribution of the materials that ostensibly causes the time-dependent changes observed in the poroelastograms.

Figure 1 shows an example of a poroelastogram obtained from an *in vitro* porcine muscle with PSE (Pale, Soft and Exudative), a meat quality condition that is characterized by a pale color, soft texture, and low water holding capacity. Observe that the novel Poisson's ratio elastogram, Poisson's ratio time constant elastograms and poroelastogram appear to convey information on the mechanical behavior of the tissue that is not obtainable from the corresponding other images, both spatially and temporally. Consistently distinct spatial poroelastic features are present in the poroelastogram, which appear to follow the general direction of the anisotropic muscle fiber orientation. Furthermore, certain tissue areas (for example the area within the black circle) appear to experience significant time-dependent changes while other areas do not change as much with time. These time-dependent changes are presumably related to the local tissue water content and permeability. Thus, the spatial distribution of the poroelastogram and their temporal evolution under load may contain structural as well as temporal tissue information. This information may provide a better understanding of the complex mechanical behavior of poroelastic tissues and might be useful for assessing the degree of pathological involvement and monitoring their treatment.

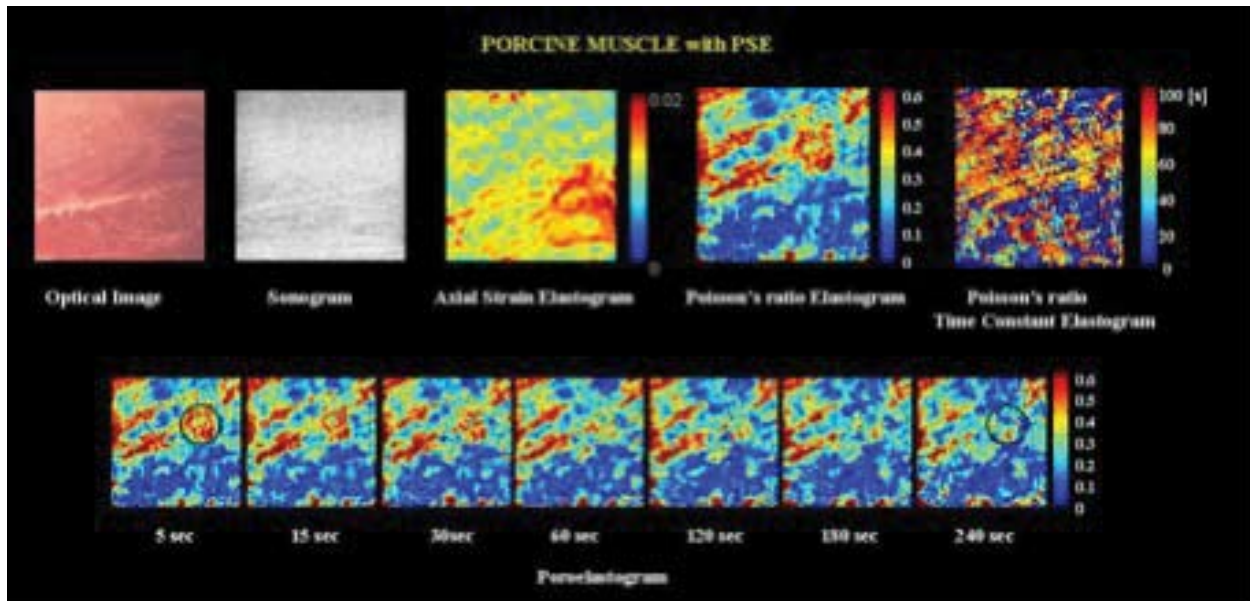


Figure 1.

**Poster Presentations
7:00 - 7:30 p.m.**

**Refreshments
7:30 - 8:00 p.m.**



Texas Medical Center, Houston, Texas

