

# **Conference Handbook**

# TM's 2nd World Cancer Online Conference

January 8-11, 2013



# **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 standardsetting 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.



Merck Millipore is the Life Science division of Merck KGaA of Germany and offers a broad range of innovative, performance products, services and business relationships that enable our customers' success in research, development and production of biotech and pharmaceutical drug therapies. Through dedicated collaboration on new scientific and engineering insights, and as one of the top three R&D investors in the Life Science Tools industry, Merck Millipore serves as a strategic partner to customers and helps

advance the promise of life science. Headquartered in Billerica, Massachusetts, the division has around 10,000 employees and operations in 67 countries.



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 <u>www.medicalnewstoday.com</u>.



Advaxis Inc is leading the evolution of living bacteria-based immunotherapies with the development of highly attenuated strains of Listeria monocytogenes (Lm) that are bioengineered to synthesize and secrete specific antigens fused to the adjuvant protein listeriolysin O (LLO). The efficacy demonstrated by Lm-LLO immunotherapies is due, in part, to a localized effect in the tumor microenvironment of increases in antigen-specific effector cells and tumor specific decreases in the numbers and function of suppressor cells that protect the tumor from immune attack, as well as modulation of

systemic immunity and immune memory. Lm-LLO active immunotherapy invokes the molecular pattern recognition receptors that underlie the in-born protective immune response that enable us to co-exist with ubiquitous environmental Lm. ADXS-HPV, is the first Lm-LLO immunotherapy to reach the clinic and is being evaluated in 4 Phase 2 clinical trials for HPV-associated dysplasia and malignancies.



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 (<u>www.businesswithindia.in</u>) 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 (<u>www.51atgc.com</u>) 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 myrialaminar 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 highstage 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: 8:00AM – 18:00 PM, January 8, 2013

Session 1: Breast cancer - part I 8:00 AM - 10:30 AM

Session 2: Breast cancer - part II 10:30 AM – 12:30 PM

Session 3: Breast cancer – part III 12:30 PM – 15:00 PM

Session 4: Cancer immunology 15:00 PM – 18:00 PM

#### Track 2: 8:00 AM - 18:00 PM, January 9, 2013

Session 5: Cancer stem cells 8:00 AM - 10:00 AM

Session 6: Signaling pathways in cancer – part I 10:00 AM – 12:30 PM

Session 7: Signaling pathways in cancer – part II 12:30 PM – 15:00 PM

Session 8: Prognostic-diagnostic biomarkers in cancer 15:00 PM – 18:00 PM

#### Track 3: 8:00 AM - 18:00 PM, January 10, 2013

Session 9: Clinical case presentations 8:00 AM - 10:30 AM

**Session 10: Cancer surgery** 10:30 AM – 14:00 PM

Session 11: Radiotherapy & chemotherapy 14:00 PM – 16:00 PM

Session 12: Cancer genomics & genetics 16:00 PM – 18:30 PM

Track 4: 8:00 AM – 18:00 PM, January 11, 2013

Session 13: Cancer epidemiology – part I 8:00 AM – 10:30 AM

Session 14: Cancer epidemiology – part II 10:30 AM – 13:30 PM

Session 15: Cancer epidemiology – part III 13:30 PM – 15:00 PM

Session 16: Cancer epidemiology – part IV 15:00 PM – 17:00 PM

### Track 1: 8:00 AM- 18:00 PM, January 8, 2013

**7:30 – 8:00 AM** Speakers and attendees can login the online conference.

Session 1: Session 1: Breast cancer - part I 8:00 AM – 10:30 AM Session Chair: Dr. Domenico Gerbasi

#### 8:00 - 8:30 AM

**Presentation Title:** Targeting Breast Tumor Imaging With 99mTc Radiolabeled PR81 and Its F(ab')2 Fragment in Nuclear Medicine. **Mojtaba Salouti**, Associate professor, Biology Research Center, Zanjan Branch, Islamic

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

#### 8:30 – 9:00 AM

Azad University, Iran.

**Presentation Title:** Extra-mammary Inferior Approach in Breast Conserving Surgery for Cancer.

**Domenico Gerbasi**, General Surgeon, Director of Breast Unit, Department of Surgery, A.O. "Bolognini" Seriate, ITALY.

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

#### 9:00 – 9:30 AM

**Presentation Title:** Acupuncture for the treatment of hot flashes in breast cancer patients, a randomized, controlled trial.

**Jill Brook Hervik**, Physical therapist/acupuncturist, Pain Clinic, Vestfold Hospital, Norway.

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

#### 9:30 – 10:00 AM

**Presentation Title:** Combined approach of Fine Needle Aspiration Cytology and Ultrasonography in the Diagnosis of Breast Lump.

**Md. Zillur Rahman**, Head & Associate Professor, Department of Pathology, Chittagong Medical College, Chittagong, Bangladesh.

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

#### 10:00 – 10:30 AM

**Presentation Title:** Normal to cancer microbiome transformation: Giving clue for cancer detection.

**Abdul Arif Khan,** Assistant Professor in College of Pharmacy, King Saud University, KSA.

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: Breast cancer - part II 10:30 AM – 12:30 PM Session Chair: Dr. Warren Ladiges

# 10:30 - 11:00 PM

**Presentation Title:** Nutrition for the breast cancer patient: therapeutic optimization based on population-specific factors. **Alvaro L. Ronco**, Professor, Depto. De Epidemiologia, Facultad de Medicina,

Alvaro L. Ronco, Professor, Depto. De Epidemiologia, Facultad de Medicina IUCLAEH, Uruguay.

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

# 11:00 – 11:30 PM

**Presentation Title**: Breast cancer and internal ionising radiation exposure. **Christopher Busby**, Professor, Dept of Physical Chemistry, Wellcome Research Laboratory, Langley Park, Beckenham.

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

#### 11:30 - 12:00 PM

**Presentation Title**: Physical and psychological effects of exercise training with Greek traditional dancing in breast cancer survivors.

Antonia Kaltsatou, Physical Education Graduate, MSc, PhD, Research Fellow at Sports Medicine Laboratory, Department of Physical Education and Sports Science, Aristotle University of Thessaloniki, Greece.

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

#### 12:00 – 12:30 PM

**Presentation Title:** Breast cancer progression in old mice is delayed with exercise training.

**Warren Ladiges**, DVM, MS, DACLAM, Professor and Director, Functional Genomics Program, Department of Comparative Medicine, School of Medicine, University of Washington, USA.

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

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Session 3: Breast cancer – part III 12:30 PM – 15:00 PM Session Chair: Dr. Kevin M. Kelly

### 12:30 - 13:00 PM

**Presentation Title:** Her2 expression in breast cancer tissues: not just a morphological issue.

**Anna Sapino**, Full Professor of Pathological Anatomy and Histology, Medical School, University of Torino. Head of the III Service of Surgical Pathology, Azienda Ospedaliera Città della Salute e della Scienza, Torino, Italy. Head of the Centro Unificato per lo Screening dei Tumori della Cervice Uterina della Città di Torino.

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

13:00 – 13:30 PM
Presentation Title: Breast Cancer Screening & Diagnosis in 2013.
Kevin M. Kelly, MD, Chief Medical Officer, Board Chairman, SonoCiné, USA

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

# 13:30 - 14:00 PM

**Presentation Title:** Breast conservation in breast cancer patients with cardiac pacing devices.

**Mark Trombetta**, System Director of Clinical Program Development, Breast and Brachytherapy Program Leader, Associate Residency Program Director, Allegheny General Hospital Dept. of Radiation Oncology, Associate Professor of Radiation Oncology, Drexel University College of Medicine, Temple University School of Medicine, USA.

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

#### 14:00 – 14:30 PM

**Presentation Title:** Practical aspects of digital mammography. **Gary J. Whitman**, M.D., Professor of Radiology with Tenure and Radiologist, Department of Diagnostic Radiology, Division of Diagnostic Imaging, The University of Texas MD Anderson Cancer Center, USA.

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

# 14:30 - 15:00 PM

**Presentation Title:** Potential Effects of Angelica Sinensis on Breast Cancer Treatment and Prevention.

**Hong-Hong (Helen) Zhu**, MD, PhD, faculty member in the Department of Public Health, College of Human and Health Sciences, Western Kentucky University, Bowling

Green KY, USA.

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

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Session 4: Cancer immunology 15:00 PM – 18:00 PM Session Chair: Dr. Guru Sonpavde

# 15:00 – 15:30 PM

**Presentation Title:** Image-guided personalized anti-EMMPRIN therapy. **Hyunki Kim**, Ph.D., M.B.A. Associate Professor, Departments of Radiology and Biomedical Engineering, Comprehensive Cancer Center, University of Alabama at Birmingham, USA.

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

#### 15:30 – 16:00 PM

**Presentation Title**: The relationship of coagulation with cancer. **Ernesto de Meis**, hematologist, M.D. Ph.D., Professor of the Federal University of Rio de Janeiro and Gama Filho University; Coordinator of the committee of thrombosis and hemostasis -National Cancer Institute in Rio de Janeiro, Brazil.

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

#### 16:00 – 16:30 PM

**Presentation Title**: Advances in the management of castration-resistant prostate cancer. **Guru Sonpavde**, MD, Associate Professor of Medicine, Director, Urologic Oncology UAB Cancer center, Birmingham, AL, USA.

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

#### 16:30 - 17:00 PM

**Presentation Title**: Cancer Testis (CT) Antigens: an immunotherapic perspective in Advanced Squamous Cell Carcinoma of the Larynx.

**David Livingstone A Figueiredo**, MD, PhD., Head and Neck Surgeon, Professor, MD, PhD, Researcher- National Institute of Science and Technology in Stem Cell and Cell Therapy/Pharmacy Department UNICENTRO/ Department of Otolaryngology, Ophtalmology and Head and Neck Surgery, Ribeirao Preto-Sao Paulo University, Brazil, Titular member of Brazilian Head and Neck Surgery Society.

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

17:00 – 17:30 PM

**Presentation Title:** Modeling of tumor growth and immune system interactions: Role of growth model.

**Wayne Eby**, Assistant Professor, Department of Mathematical Sciences, Cameron University, Lawton, OK, USA.

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

17:30 – 18:00 PMPresentation Title: The multifaceted nature of aptamers.Sarah Shidgar, Research Fellow at School of Medicine, Deakin University, Australia.

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

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#### Track 2: 8:00 AM- 18:00 PM, January 9, 2013

**7:30 – 8:00 AM** Speakers and attendees can login the online conference.

Session 5: Cancer stem cells 8:00 AM – 10:00 AM Session Chair: Dr. David Schiffer

8:00 – 8:30 AM
Presentation Title: Role of cyclin D1 and molecular pathogenesis of Oral squamous cell carcinoma.
Rohit Moharil, Researcher, Department of Oral & Maxillofacial Pathology, VSPM's Dental College & Research Center, Hingna Road, Nagpur, Maharashtra, India.

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

8:30 – 9:00 AM
Presentation Title: Role of the PI3K/AKT/Mtor pathway in the regulation of glioma cancer stem cells.
LIAS EL HABR, PhD, INSERM U894 Glial Plasticity Team, Psychiatry & Neurosciences Center, St Anne Hospital, Paris, France.

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

#### 9:00 – 9:30 AM

**Presentation Title:** Regional heterogeneity of glioblastoma and its MRI, PET and in vitro correlates.

**David Schiffer**, Professor Emeritus of Neurology, University of Turin, Neuro-Bio-Oncology Center of Policlinico di Monza Foundation (Vercelli), Italy.

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

# 9:30 – 10:00 AM

**Presentation Title**: SSEA-5 and L1CAM are pluripotent markers expressed in both human retinoblastoma cells and induced pluripotent stem cells. **Gail M. Seigel**, Principal Investigator at the State University of New York at Buffalo in the Center for Hearing and Deafness and a member of the SUNY Eye Institute, USA.

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

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# Session 6: Signaling pathways in cancer – part I 10:00 AM – 12:30 PM Session Chair: Dr. Wai-Yuan Tan

# 10:00 - 10:30 AM

**Presentation Title:** Environmental Estrogen Mixtures Signaling Via Nongenomic Mechanisms.

**Cheryl S. Watson**, PhD, Professor, Biochemistry & Molecular Biology Dept., University of Texas Medical Branch, Galveston, USA.

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

# 10:30 - 11:00 PM

**Presentation Title:** Targeting of PDGFR $\beta$  with an RNA-aptamer inhibitor inhibits glioma cell survival, growth, invasion and enhances antitumor activity of an anti-EGFR aptamer.

**Laura Cerchia,** Associate Professor, Istituto per l'Endocrinologia e l'Oncologia Sperimentale del CNR "G. Salvatore", Italy.

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

#### 11:00 - 11:30 PM

**Presentation Title:** Basal/ Squamous cell carcinomas induce differential expression of Bcl-2 and Bax molecules in tumor infiltrating lymphocytes of xeroderma pigmentosum patients.

Kalthoum Abid, MD, Immuno-Histology Lab, Medicine University of Tunis, Tunisia.

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

#### 11:30 – 12:00 PM

**Presentation Title:** Affibody molecules for HER2 imaging and targeted drug delivery. **Rafal Zielinski**, PhD, Department of Experimental Therapeutics, The University of Texas M.D. Anderson Cancer Center, USA.

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

#### 12:00 – 12:30 PM

**Presentation Title:** New Biologically Supported Models of Carcinogenesis Involving Hereditary and Non-Hereditary Cancer Cases.

**Wai-Yuan Tan**, Professor, Department of Mathematical Sciences, The University of Memphis, USA; **Hong Zhou**, Assistant Professor, Arkansas State University, USA.

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

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Session 7: Signaling pathways in cancer – part II 12:30 PM – 15:00 PM Session Chair: Dr. Farid Menaa

12:30 – 13:00 PMPresentation Title: Quantitative Protein Analysis in Cancer Research.Amy Geschwender, Principal Scientist at LI-COR® Biosciences, USA.

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

13:00 – 13:30 PM
Presentation Title: Melanoma Stem Cells and *B-RAF* Mutations are Mutually Exclusive Markers of Melanoma Severity.
Farid Menaa, Director R&D, Fluorotronics, Inc. San Diego, CA, USA.

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

13:30 – 14:00 PM
Presentation Title: Identification of Amplified Oncogenes with Potential to Modulate Metabolism in Brain Tumors.
Marie E. Beckner, Assistant Professor, Dept. of Neurology, Louisiana St Univ Hlth Sci

Cen-Shreveport, USA.

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

**14:00 – 14:30 PM Presentation Title**: "MET" the challenge in non-small cell lung cancer: EGFR crosstalk and the rationale for combinational targeted therapy. **Yu-Wen Zhang**, MD, PhD, Senior Research Scientist, Van Andel Research Institute, Grand Rapids, Michigan, USA.

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

#### 14:30 - 15:00 PM

**Presentation Title:** Oral carcinogenesis: a pathway-based approach. **Rui Amaral Mendes**, DMD, PhD, Professor of Oral Medicine, Oral Oncology and Clinical Pathology, Head of the DMD Program and Clinical Director, The Catholic University of Portugal, Visiting Clinical Associate Professor, University of Michigan, Fellow of the International Association of Oral and Maxillofacial Surgeons, Fellow of the International Academy of Oral Oncology.

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

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Session 8: Prognostic-diagnostic biomarkers in cancer 15:00 PM – 18:00 PM Session Chair: Dr. Martin C. Mihm

15:00 – 15:30 PM Presentation Title: Updates in diagnosis and management of bone tumors in children. Youssef AL-Tonbary, Professor, Mansoura University Children Hospital, Egypt.

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

15:30 – 16:00 PM
Presentation Title: Ten Years Experience of the Glasgow Prognostic Score Relating to Cancer Outcomes.
Clem Imrie, Emeritus Professor, Lister Dept of Surgery, Royal Infirmary, Glasgow, UK.

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

16:00 – 16:30 PM
Presentation Title: Prognostic/Diagnostic Biomarkers in Melanoma.
Martin C. Mihm, Director, Professor, Melanoma Program, Department of Dermatology, Brigham and Women's Hospital, Harvard University, USA.

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

**16:30 – 17:00 PM Presentation Title:** Genetic prognostic research in cancer: What are the promises and current challenges?

**Sevtap Savas,** PhD, Assistant Professor, Discipline of Genetics and Discipline of Oncology, Faculty of Medicine, Memorial University of Newfoundland, St. John's, NL, Canada.

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

# 17:00 – 17:30 PM Presentation Title: MicroRNA Biomarkers for Carcinogen Exposure. Tao Chen, Ph.D., D.A.B.T. National Center for Toxicological Research, U.S. Food and Drug Administration, Jefferson, Arkansas, USA.

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

# 17:30 - 18:00 PM

**Presentation Title:** The Benefit of Centralized Healthcare System - It's Role in Reestablishing a Community Hospital Pathology Service Using Telepathology and Supportive Service Corridors.

**Irwin W. Kuzmarov**, Director of Professional and Hospital Services, Santa Cabrini Hospital, Assistant Professor of Surgery (Urology) McGill University, Past President of the Quebec Urologic Association.

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

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# Track 3: 8:00 AM- 18:00 PM, January 10, 2013

**7:30 – 8:00 AM** Speakers and attendees can login the online conference.

Session 9: Clinical case presentations 8:00 AM – 10:30 AM Session Chair: Dr. Prasad K Shetty

8:00 – 8:30 AM Presentation Title: Pending Suman Mallik, Department of Radiation Oncology, Centre for Cancer, Kokilaben Dhirubhai Ambani Hospital and Research Institute, India.

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

8:30 – 9:00 AM Presentation Title: Primary Hepatic Neuroendocrine Tumor: An Unusual Cystic Presentation. **Prasad K Shetty**, Professor, Consultant Surgical Pathologist, Bhagwan Mahaveer Jain Hospital, Bangalore, India.

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

# 9:00 – 9:30 AM

**Presentation Title:** The real cause of a severely anaemia syndrome original case report. **Manuela Stoicescu**, Internal Medicine Department, PhD, assistant professor, University of Oradea, Faculty of Medicine and Pharmacy, Medical Disciplines Department, Romania.

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

# 9:30 - 10:00 AM

**Presentation Title:** An ounce of prevention is worth a pound of cure"-The case for and against GnRH-agonist for fertility preservation.

**Zeev Blumenfeld**, M.D., Reproductive Endocrinology, OB/GYN, Rambam Health Care campus, Technion-Faculty of Medicine, Haifa, Israel.

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

# 10:00 – 10:30 AM

**Presentation Title:** Quality of life of patients with lymphoedema post cancer therapy. **TANJA PLANINŠEK RUČIGAJ**, Head of University Dermatovenerological clinic, Clinical centre in Ljubljana; president of Slovenian association for dermatovenerologist, president of Slovenian Wound Management association and vice president of Balkan venous forum. Slovenia.

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

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Session 10: Cancer surgery 10:30 AM – 14:00 PM Session Chair: Dr. Raja Kummoona

10:30 – 11:00 PM
Presentation Title: Surgery for locally advanced and metastatic renal cell cnacer.
M Hammad Ather, Associate Prof and Director Urology residency, Aga Khan University.

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

11:00 – 11:30 PM

**Presentation Title:** Quality of life and rectal cancer surgery. **Antonio Amato**, Professor, Head of Unit of Coloproctology, Dept. of Surgery, Hospital of Sanremo, Italy.

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

11:30 – 12:00 PM
Presentation Title: Surgical management of ovarian cancer.
Ignacio Zapardiel, MD, PhD, Assistant Professor, European Network Young Gyn
Oncologists - Executive board member, Consultant. Gynecologic Oncology Unit, La Paz
University Hospital. Madrid. Spain.

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

# 12:00 – 12:30 PM

**Presentation Title:** Lateral cervical flap for immediate reconstruction of the oral cavity after radical cancer surgery.

**Raja Kummoona**, Emeritus Professor of Maxillofacial Surgery, Iraqi Board for Medical Specializations, Baghdad, Iraq.

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

# 12:30 - 13:00 PM

**Presentation Title:** Ovarian cryoopreservation- from SILS to microorgan transplanataion.

Ariel Revel, Professor, Department of Obstetrics and Gynecology, Hadassah Medical Center and Hebrew University-Hadassah Medical School, Jerusalem 91120, Israel.

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

# 13:00 - 13:30 PM

**Presentation Title:** Ovarian tissue cry preservation in oncological patients: state of the art.

**Raffaella Fabbri**, Assistant Professor, Human Reproductive Medicine Unit, Obstetrics and Gynaecology, S. Orsola Hospital, University of Bologna, Italy.

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

#### 13:30 – 14:00 PM

**Presentation Title:** Integrated surgical procedures for locally advanced cancers. **Alessandro Testori**, MD, Director, Melanoma and muscle-cutaneous sarcomas Division, Istituto Europeo di Oncologia, 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 11: Radiotherapy & chemotherapy 14:00 PM – 16:00 PM Session Chair: Dr. Rebecca K.S. Wong

#### 14:00 - 14:30 PM

**Presentation Title:** Prediction and Tracking of Moving Tumors can Result in Significant Reduction in Dose to Critical Organs and Tissue.

**Ivan Buzurovic**, Research Scientist and the leader of Medical Robotics Research Group of the Department of Radiation Oncology, Thomas Jefferson University, Philadelphia, USA.

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

14:30 – 15:00 PM
Presentation Title: Virtual consultation and spinal cord compression.
Rebecca K.S. Wong, MBChB MSc FRCP, Professor, Radiation Oncology, Princess Margaret Hospital, USA.

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

**15:00 – 15:30 PM Presentation Title:** New Emerging Therapies in Colorectal Cancer. **Minsig Choi**, M.D., Associate Professor, Karmanos Cancer Center, USA.

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

#### 15:30 – 16:00 PM

**Presentation Title**: Clinical Trials in Adolescent and Young Adult Oncology: Current Challenges and the Road ahead.

**Vivek Subbiah**, Associate Professor, Division of Cancer Medicine, UT MD Anderson Cancer Center, USA.

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

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Session 12: Cancer genomics & genetics 16:00 PM – 18:30 PM Session Chair: Dr. Henry H.Q. Heng

16:00 – 16:30 PM

**Presentation Title:** Colorectal Cancer Inherited Susceptibility in the Brazilian population: the first replication study in Latin America **Israel Gomy**, AC Camargo Cancer Hospital in Sao Paulo; Cancer geneticist at Sao Paulo State Cancer Institute.

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

### 16:30 - 17:00 PM

**Presentation Title**: Genome chaos and rapid cancer evolution.

**Henry H.Q. Heng**, Associate Professor, Center for Molecular Medicine and Genetics, and Department of Pathology, and Karmanos Cancer Institute, Wayne State University School of Medicine, Detroit, USA.

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

# 17:00 – 17:30 PM

**Presentation Title:** Genetic variations in mitochondrial DNA and hypoxia pathway genes and clinical outcomes in colorectal cancer.

**Asan M. S. Haja Mohideen**, Discipline of Genetics, Faculty of Medicine, Memorial University of Newfoundland, St. John's, NL, Canada.

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

# 17:30 – 18:00 PM

**Presentation Title:** Tumor growth in vivo can induce oxidatively-induced clustered DNA lesions.

Alex Georgakilas, PhD, Associate Professor, Department of Biology East Carolina University Greenville, NC 27858, USA.

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

#### 18:00 - 18:30 PM

**Presentation Title:** Application of Non-Invasive Serum/Plasma miRNA Markers for Early Detection in Pancreatic Cancer.

**Robert-A. Ollar**, Assistant Professor of Neurology, New York Medical College, Director, Molecular Biology Research Program, Biliary and Pancreatic Surgery Division, Comprehensive Digestive Diseases Center of New York, at Beth Israel Medical Center of 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.

#### Track 4: 8:00 AM- 18:00 PM, January 11, 2013

#### 7:30 - 8:00 AM

Speakers and attendees can login the online conference.

Session 13: Cancer epidemiology – part I 8:00 AM – 10:30 AM Session Chair: Dr. Anjana Chauhan

#### 8:00 - 8:30 AM

**Presentation Title:** Pregnancy with Yolk-Sac Tumor of Ovary – A Case Report. **Anjana Chauhan**, Associate Professor, Gujarat Cancer and Research Institute, Regional Tertiary Cancer Center, B. J. Medical College Campus, Aswara, Ahmedabad, Gujarat, India.

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

#### 8:30 – 9:00 AM

Presentation Title: Myofibroblast presence in histologically normal mucosa adjacent to oral squamous cell carcinoma: evidence for field cancerisation.
Punnya Angadi, Reader, Department of Oral Pathology and Microbiology, KLEVK Institute of Dental Sciences and Hospital, Belgaum, Karnataka, India.

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

#### 9:00 – 9:30 AM

**Presentation Title:** Sentinel lymph node biopsy in selected cas of ductal carcinoma in situ.

Marcinova Marta., III. Clinic of Surgery - l. Private Hospital, Košice - Šaca, Slovakia.

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

#### 9:30 – 10:00 AM

**Presentation Title**: Exploring patients' needs in a Surgical Oncology unit - The contribution of the social worker.

**Maria Trigoni**, Head of Department of Social Work, University Hospital of Crete, Greece.

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

10:00 – 10:30 AM Presentation Title: Endometrial cancer screening – is it necessary? Gina Opolskiene, MD, PhD, Vilnius University Hospital Santariskiu Klinikos as a consulting obstetrician – gynecologist.

**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: Cancer epidemiology – part II 10:30 AM – 13:30 PM Session Chair: Dr. Xaveer Van Ostade

# 10:30 - 11:00 PM

**Presentation Title**: Increasing incidence of malignant melanoma in the elderly aged  $\geq 65$  years.

**Anjum Memon**, MBBS, D.Phil, FFPH, Senior Lecturer and Consultant in Public Health Medicine, Division of Primary Care and Public Health, Brighton and Sussex Medical School, United Kingdom.

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

# 11:00 – 11:30 PM

**Presentation Title**: Polymorphic variants into angiogenesis pathways and non-small-cell lung cancer: overcoming a challenge.

**Ramon Andrade Mello**, Assistant Professor, Department of Medicine, São João Hospital, Faculty of Medicine, University of Porto, Portugal.

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

#### 11:30 - 12:00 PM

**Presentation Title:** Neural network intelligent diagnosis system to classify normal, precancerous and cancerous cervical cells based on pathological cell images. **Babak Sokouti**, Department of biomedical engineering, Tabriz Branch, Islamic Azad University, Tabriz, Iran.

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

#### 12:00 – 12:30 PM

**Presentation Title**: Initiating a Regional Comparative Breast Cancer Research Program in the Eastern Mediterranean Region.

**Nada Alwan** (MD), Professor & Director, National Cancer Research Center; Executive Director, Iraqi National Cancer Research Program; Principal Investigator, Regional Comparative Breast Cancer Research Project, Iraq.

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

#### 12:30 - 13:00 PM

**Presentation Title**: Insulin-like growth factor-1 and childhood cancer risk. **Mohamed ahmed badr**, Professor of Pediatrics hematology and oncology, Zagazig University, Egypt.

#### 13:00 - 13:30 PM

**Presentation Title:** Proteomic Analysis of the Cervicovaginal Fluid Leads to Identification of Biomarkers for Cervix Cancer.

**Xaveer Van Ostade**, Professor, Laboratory of Proteinscience, Proteomics and Epigenetic Signaling (PPES), Department of Biomedical Sciences, University of Antwerp Antwerp, Belgium.

**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: Cancer epidemiology – part III 13:30 PM – 15:00 PM Session Chair: Dr. Luz Ma. Ruíz Godoy Rivera

# 13:30 - 14:00 PM

**Presentation Title:** Metronomics: bringing target tretments to low income countries. **Nicolas ANDRE**, MD, PhD, Inserm, UMR911, Aix Marseille University, Pediatric Oncology and Hematology Unit Children Hospital of La Timone, AP-HM, Metronomics Global Health Initiative, Marseille, France.

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

# 14:00 – 14:30 PM

**Presentation Title:** Tumors Bank of the National Cancer Institute of Mexico. **Luz Ma. Ruíz Godoy Rivera**, National Cancer Institute of Mexico (INCan), Mexico City, Mexico.

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

# 14:30 - 15:00 PM

**Presentation Title**: Addressing fear of cancer recurrence: A pilot test of a 6-week cognitive existential group intervention with breast and ovarian cancer patients. **Christine Maheu**, RN, PhD, Associate Professor, Ingram School of Nursing, McGill University, Butterfield/Drew Fellow in Breast Cancer Survivorship & Research Associate, Cancer Survivorship Program, PMH, ELLICSR: Health, Wellness & Cancer Survivorship Centre, Toronto General Hospital, Canada.

**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: Cancer epidemiology – part IV 15:00 PM – 17:00 PM Session Chair: Dr. Shawn Ritchie

15:00 – 15:30 PMPresentation Title: What is the brain-cancer connection?Lei Cao, Ph.D., Assistant Professor, Nuclear Engineering, Department of Mechanical and Aerospace Engineering, The Ohio State University, USA.

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

15:30 – 16:00 PM

**Presentation Title:** The pancreatic cancer serum metabolome: Implications for screening and early detection.

Shawn Ritchie, PhD. Director, Discovery Research, Phenomenome Discoveries Inc., Canada.

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

#### 16:00 – 16:30 PM

**Presentation Title:** An Ecological Study of Associations between Cancer Rates and Quality of Air and Streams.

**Raid W Amin**, Professor of Statistics, Director of the UWF Statistical Consulting Services, USA.

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

16:30 – 17:00 PM
Presentation Title: Cancer Survivorship: Myth or Reality.
Pam McGrath, B.Soc.Wk., MA., Ph D, Associate Professor, Senior Research Fellow at Griffith University, Australia.

**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.

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#### 1. Normal to cancer microbiome transformation: Giving clue for cancer detection.

Abdul Arif Khan, College of Pharmacy, King Saud University, KSA.

**Summary:** Normal to cancer cell transformation involves several changes in body environment. Some of these changes are utilized as cancer indicators. Microbiome is also an integral part of body environment and several studies are deciphering its potential role in human health. Normal microbiome includes several microbial communities coexisting with an individual. These microbial communities are peculiar for particular sites of an individual. Thus same sites of two individual can have almost similar microbiome while the different sites of same individual may be different in microbial communities. During normal to cancer cell transformation, change in normal microbiome composition is also an early event. Thus these changes can also be capitalized for detection of cancer and prediction of cancer risk in some cases. Although our current knowledge about human microbiome and underlying changes during normal to cancer microbiome transformation is limited, but global efforts to understand microbiome increase our knowledge and gather optimism about this facet of cancer diagnostics. Perhaps rigorous future studies can give us microbial cancer indicators from complex cancer microbiome. Present work will focus on changes of microbial communities with cancer development, reasons behind these changes, challenges before appraisal of this idea in cancer diagnostics and benefits of using these changes as cancer indicators.

# 2. Integrated surgical procedures for locally advanced cancers.

Alessandro Testori, Melanoma and muscle-cutaneous sarcomas Division, Istituto Europeo di Oncologia, Italy. Summary: Pending

#### 3. Tumor growth in vivo can induce oxidatively-induced clustered DNA lesions.

Alex Georgakilas, Department of Biology East Carolina University Greenville, NC 27858, USA.

**Summary:** Cancer cells can transmit signals and their environment that cause DNA damage healthy neighboring cells, mainly through their membranes and produce active free radicals (ROS). We have hypothesized that some tissues and organs may be more vulnerable than others in the in vivo tumor growth-induced damage to DNA. Indices of DNA damage in such tissues could be used as a common detector to instability of the genome and oncogenic transformation. To test this hypothesis, we compared the tumor-bearing mice with age-and sex-witnesses with the aggregated damage DNA (OCDLs) that accumulate in various tissues and a short distance away from the tumor. This study shows that the tumors through the oxidative stress and inflammation pathways can directly cause DNA damage to organs induced remote from the tumor tissue (long-range bystander effects), and thus emphasizes the application range of OCDLs and oxidative lesions in general as potential cancer biomarkers.

# **4.** Nutrition for the breast cancer patient: therapeutic optimization based on population-specific factors.

Alvaro L. Ronco, Depto. De Epidemiologia, Facultad de Medicina, IUCLAEH, Uruguay. **Summary:** In the last years scientific studies are showing the advantages of an adequate diet for those women who were diagnosed with a breast cancer have appeared regarding

the disease-free survival and the overall survival. In addition, there were some communications that reported an improvement when some nutritional guidelines were followed focusing on the management of overweight and obesity. We have recently proposed a risk profile, based on several items which were drawn from selected data obtained in local case-control studies: intake of red meat, white meat, dairy foods, oils and fats, high glycemic load foods, vegetables and fruits; alcohol consumption; physical activity; psychosocial stressors; metabolic disturbances; other medical factors; fat-tomuscle ratio; serum vitamin D level; urine  $2/16-\alpha$ -OH estrogen ratio; serum triglycerides/HDL ratio and fasting insulinemia. The assignment of a low, medium and high risk value was done depending on the variable nature and its association to the risk of BC. Unlike some laboratory results, the cut-off points used for classification might represent population-specific features. The proposal is next to make a nutritional equalization, that is, change the exposure to the putative risk and protective factors to the lowest possible risk level in a tailored way. The change in the profile attempts to modify the ratios of  $2/16-\alpha$ -OH estrogen metabolites and  $\Omega$ - $6/\Omega$ -3 fatty acids, the body composition, as well as other relevant nutritional features in order to improve the patient's hormonal, metabolic and immunity status. Although generalization is limited by the local value of certain variables, methodology seems to be feasible elsewhere from a practical viewpoint. Each country or region could construct its own reference values, since some items (diet, anthropometry) may be population-specific. Because no studies indicate that a prudent diet is pejorative for health, we are trying to change an inadequate nutritional pattern into an adequate one, probably through its actions on epigenetic mechanisms, in order to make feasible a subsequent change of the prognosis.

#### 5. Quantitative Protein Analysis in Cancer Research.

#### Amy Geschwender, LI-COR® Biosciences, USA.

**Summary:** This webinar will examine near-infrared fluorescent methods for protein analysis and quantification. We will discuss how quantitative analysis of protein levels contributes to a deeper understanding of cell biology and cancer. Examples from the literature will illustrate how infrared fluorescent Western blots, In-Cell Western immunofluorescent assays, and microwestern arrays are used in the context of cancer research.

#### 6. Pregnancy with Yolk-Sac Tumor of Ovary - A Case Report.

Anjana Chauhan, Gujarat Cancer and Research Institute, Regional Tertiary Cancer Center, B. J. Medical College Campus, Aswara, Ahmedabad, Gujarat, India. **Summary:** Goal: A successful outcome of a patient presenting with 22weeks pregnancy & yolk-sac tumor of ovary, managed by fertility preserving surgery & BEPchemotherapy. Methods: A 24yr, pregnant woman with 5months of pregnancy was referred with ovarian mass & FNAC report of Yolk sac tumor was reported in 2008. Routine investigation: normal,  $\alpha$ -FP: 296ng/ml, CA 125:793U/L, LDH: 1092 Utrasonography showed 22 weeks of live intrauterine pregnancy & 12X12 cm solidcystic-complex ovarian mass above the uterus. After informed consent regarding risk to pregnancy she was planned for Staging Laparotomy. Intraoperative there was tumour of about 15X20cm solid to cystic on left side, which was mobile and there was mild hemorrhagic ascites. Multiple cytologies +Removal of Left Ovarian Mass+Infracolic omentectomy+Left side Pelvic Lymph node sampling was done .Intraoperative uterus was enlarged to 22 weeks size and other ovary was normal. Obstetrician consulted regarding fetal well being. Final Histopathology was Yolk-Sac Tumor measuring 24cm in greatest diameter, with growth on the capsule. FIGO- Surgico-pathological stage was Ic Postoperative adjuvant treatment three cycles of BEP (Bleomycin, Etoposide, Cisplatinum) was given with intra uterine pregnancy and continuation of pregnancy. Chemotherapy was given with consent and explanation of all the consequences. Results: She underwent Caesarean-section after completion of chemotherapy. Full-term-IUGR Female-baby of wt: 1.5kg was delivered. During Caesarean opposite ovary & abdominal structures: normal. The child showed normal laboratory, pediatric, and neurologic parameters. Both mother & baby were fine. Patient is under observation since then. She is disease free since last three years and baby is normal. Conclusion: A rare case of pregnant woman with Yolk-Sac tumor treated successfully with surgery & chemotherapy and delivered a normal-baby at-term. Management of ovarian mass with pregnancy depends upon the type of tumor, stage, duration of pregnancy & patient's desire.

#### 7. Increasing incidence of malignant melanoma in the elderly aged $\geq 65$ years.

# J R Weaver and Anjum Memon, Division of Primary Care and Public Health, Brighton and Sussex Medical School, Falmer, Sussex, UK.

Summary: Background: Malignant melanoma is the 6th most common cancer in the UK. Over the past three decades, incidence rates of melanoma have increased more than for any other common cancer. The highest incidence rates are observed in the elderly aged  $\geq$ 65 years (accounting for about 40% of all cases). Method: We analysed the populationbased incidence data from the Scottish Cancer Registry to study the descriptive epidemiology of malignant melanoma (ICD-9: 172; ICD-10: C43) among the elderly in Scotland for the period 1971-2006, with respect to distribution by age, gender, type and site of tumour and trends in incidence over time. Results: During the 36-year period, a total of 6484 cases of melanoma among the elderly aged >65 years were registered in Scotland (40.8% males, 59.2% females). The number of cases increased from 293 in 1971-75 (59 cases/year) to 2006 in 2001-06 (334 cases/year). The average annual incidence rate (per 100 000) increased from 7.1 in 1971-75 to 48.6 in 2001-06 in males (7-fold); and from 9.7 to 35.0 in females (4-fold), respectively. The majority of cases (97.6%) were diagnosed by histology of the primary tumour. The most common morphological subtype was superficial spreading melanoma (24.6%); and in 2001-06, the most common anatomical site was 'head and neck' (41%) in males and 'lower limb' (37%) in females. During the study period, the largest increase in incidence rate according to anatomical site was observed for 'upper limb' (12-fold) and 'trunk' (11fold) in men and 'upper limb' (5-fold) and 'lower limb' (5-fold) in females. Conclusion: During the past three decades, there has been a remarkable increase in the incidence of malignant melanoma among the elderly in Scotland. The largest increase was observed in the melanoma involving the 'upper limb' and 'trunk' in males. More effective public education is required for primary prevention. The findings are also relevant for the organisation of oncology services and resource allocation.

#### 8. Her2 expression in breast cancer tissues: not just a morphological issue.

Anna Sapino, Pathological Anatomy and Histology, Medical School, University of

# Torino; the III Service of Surgical Pathology, Azienda Ospedaliera Città della Salute e della Scienza, Torino, Italy.

**Summary:** HER2 is an oncogene amplified and overexpressed in approximately 15% of breast cancers. HER2 positive breast cancers represent a unique molecular category and the target of specific therapy. Pathologists are requested to test by immunocytochemistry and or by in situ hybridization (FISH/SISH) the status of HER2 in invasive breast cancer tissues, to address oncologists for therapy. However the response to treatment may not correspond to the expression levels reported by the pathologist. This is not always related to the poor quality of the test, but it may be related to protein or chromosomal alterations of HER2 positive cells. In this section we will (i) discuss briefly the biases related to HER2 analysis on tissues and (ii) try to give a biological meaning to some of the inconsistent results of the tests performed by pathologists.

# **9.** Physical and psychological effects of exercise training with Greek traditional dancing in breast cancer survivors.

# Antonia Kaltsatou, Department of Physical Education and Sports Science, Aristotle University of Thessaloniki, Greece.

Summary: Physical exercise in women with breast cancer has been identified as a potential intervention to improve quality of life and reduce the side effects of breast cancer treatment, such as fatigue and decreased aerobic capacity. However, in order to ensure regular participation and obtain all benefits of exercise the exercise program should be enjoyable and agreeable for the participants. It has been thought that dancebased exercise approach could make the process more interesting and be a beneficial form of physical activity. The purpose of the present study was to evaluate the influence of a mixed exercise program, including Greek traditional dances and upper body training, in physical function, strength and psychological condition of breast cancer survivors. Twenty-seven women (N=27), who had been diagnosed and surgically treated for breast cancer, volunteered to participate in this study. The experimental group consisted of 14 women with mean age 56.6 (4.2) years. They at- tended supervised Greek traditional dance courses and upper body training (1 h, 3 sessions/week) for 24 weeks. The control group consisted of 13 sedentary women with mean age 57.1 (4.1) years. Blood pressure, heart rate, physical function (6- min walking test), handgrip strength, arm volume and psychological condition (Life Satisfaction Inventory and Beck Depression Inventory) were evaluated before and after the exercise program. The results showed significant increases of 19.9% for physical function, 24.3% for right handgrip strength, 26.1% for left handgrip strength, 36.3% for life satisfaction and also a decrease of 35% for depressive symptoms in the experimental group after the training program. Significant reductions of 9% for left hand and 13.7% for right hand arm volume were also found in the experimental group. Consequently, a combination between aerobic exercise with Greek traditional dances and upper body training could be an alternative choice of physical activity for breast cancer survivors, thus promoting benefits in physical function, strength and psychological condition. Dr. Antonia Kaltsatou has studied Sports Sciences in Aristotle University of Thessaloniki in Greece. Her doctoral dissertation is entitled "Functional and psychosocial effects of exercise training with Greek traditional dances in chronic heart failure patients". Dr. Kaltsatou is member of the Sports Medicine Laboratory of Aristotle University of Thessaloniki for the last 8 years.

#### 10. Quality of life and rectal cancer surgery.

Antonio Amato, Unit of Coloproctology, Dept. of Surgery, Hospital of Sanremo, Italy. Summary: In rectal surgery, the statement that the quality of life for patients with a permanent colostomy after abdomino-perineal excision (APE) was poorer than for patients undergoing an operation with a sphincter-preserving technique has represented a kind of surgical dogma. In the past decades, as published studies demonstrated that the oncologic results after APE operation and anterior resection (AR) are comparable, it has become the state of the art, that whenever feasible, rectal cancer should be treated by a sphincter-preserving technique, which is also regarded as a criterion of success. In 2010 a Cochrane reviews on 26 selected studies don't allow firm conclusions whether the OoL is different comparing permanent stoma and no stoma patients. Some of the included studies challenge the assumption that AR patients fare better. In a prospective study, we have analyzed the patient reported outcomes in a series of 149 eligible patients submitted to neoadjuvant chemoradiotherapy and surgery for rectal cancer. Data were collected at T0 (baseline), 2-3 weeks after CRT (t1), 6 months (t2) and 12 months (t3) after surgery. FIS (Fecal Incontinence Score) significantly get worse over time and only 14% of patients had optimal continence; in all investigated areas, the percentage of patients reporting bowel function problems at 1 year after surgery was higher than that of baseline levels. However, there were no correlation with the Health related-QoL scales and no clinically meaningful changes were registered except for future perspective that shows clinically meaningful improvements. The definition of Health related-QoL incorporates the subjectivity as main aspects. Individual patients with the same objective health status can report dissimilar scores due to the differences in expectations and coping. Furthermore, it is focused on multidimensionality, combining features of 3 categories: physical, mental and social health. Studies that only take into account intestinal functioning scores could bring about misleading conclusions.

#### 11. Ovarian cryoopreservation- from SILS to microorgan transplanataion.

Ariel Revel, Professor, Department of Obstetrics and Gynecology, Hadassah Medical Center and Hebrew University-Hadassah Medical School, Jerusalem 91120, Israel. Summary:

# **12.** Genetic variations in mitochondrial DNA and hypoxia pathway genes and clinical outcomes in colorectal cancer.

Asan M. S. Haja Mohideen1, Elizabeth Dicks2, Ban Younghusband1, Patrick Parfrey2, Roger, Green1, Sevtap Savas1,3 1Discipline of Genetics, Faculty of Medicine, Memorial University of Newfoundland, St. John's, NL, Canada. 2Clinical Epidemiology Unit, Faculty of Medicine, Memorial University of Newfoundland, St. John's, NL, Canada. of Oncology, Faculty of Medicine, Memorial University of Newfoundland, St. John's, NL, Canada. 3Discipline Deranged metabolism and energy production are the two hallmarks of cancer progression.

**Summary:** These processes can be promoted by the alterations in the function of mitochondria. Mitochondria are present in variable number of copies in cells depending on the energy requirements. They also have their own genome (mtDNA). In addition, hypoxia (i.e. reduced oxygen levels) is a characteristic of the tumor cells, which

contributes to aggressive phenotype. Therefore, in this study we hypothesized that genetic variations in mtDNA and hypoxia pathway genes may be correlated with disease progression and thus survival in colorectal cancer patients. To test this hypothesis, we investigated the correlation of a large number of mtDNA and hypoxia pathway gene variations with outcome in patients recruited to the Newfoundland Colorectal Cancer Registry (NFCCR). Six mtDNA polymorphisms (mitoT479C, mitoT491C, mitoT10035C, mitoA13781G, 10398A/G, and 16189T/C) as well as 77 polymorphisms from 7 hypoxia pathway genes (HIF1A, HIF1B, HIF2A, HIF2B, HIF3A, LOX and CXCL12) were investigated in 537 patients. Genotype data for these polymorphisms were obtained by TaqMan® SNP genotyping assays and by a genome wide SNP genotyping method. In addition, the mtDNA copy number change in tumor tissues (colon or rectum) with respect to non- tumor tissues was estimated using quantitative polymerase chain reaction in 279 patients. The associations of these markers with overall survival (OS) and disease free survival (DFS) were tested using the Cox proportional hazards model. As a result, associations of none of the mtDNA polymorphisms with OS or DFS were detected in our cohort. The mtDNA copy number change (the decrease versus increase in the mtDNA quantity in tumor tissue with respect to non-tumor tissue) was not associated with outcome, either. However, out of 77 hypoxia pathway polymorphisms, two polymorphisms (HIF2A rs4953352 and HIF2B rs12593988) were associated with both OS and DFS in multivariable models when adjusted for other clinicopathological variables. Briefly, in the case of the HIF2A rs4953352 polymorphism, patients with the TT genotype had better prognosis when compared to patients with the CC and CT genotypes. In the case of the HIF2B rs12593988 polymorphism, patients with the GG genotype had poor prognosis when compared to patients with the GA and AA genotypes. In conclusion, while remain to be confirmed in other patient cohorts, our results suggest the associations of HIF2A rs4953352 and HIF2B rs12593988 polymorphisms with outcome in colorectal cancer patients.

# **13.** Neural network intelligent diagnosis system to classify normal, pre-cancerous and cancerous cervical cells based on pathological cell images.

Babak Sokouti, Department of biomedical engineering, Tabriz Branch, Islamic Azad University, Tabriz, Iran.

**Summary:** Pathological level diagnostics based on morphological technologies can propose a precise methodology for cervical cancer classification. Artificial neural networks (ANNs) as a scientific fact which is constructed based on artificial brains' highly interconnected neurons. ANNs are trained according to features extracted from cervical cell images to obtain a logical based output. From the past years neural networks are used as a helpful mean along with clinical diagnosis. In our research, a feed forward neural network was trained on numeral linear plots of cervical cells of 100 actual patients and then correctly classified normal cervical cells from pre-cancerous and cancerous cells without diagnostic errors. The proposed artificial neural network was trained in MATLAB using the backpropagation feed forward model, levernberg-marquardt learning algorithm and two hidden layers on an Athlon Thunderbird 1200 Mhz personal computer. Our ANN learned from thirty extracted morphological features from cervical cells in 100 patients (368 normal, 366 pre-cancerous, and 366 cancerous) at Alzahra hospital. By

using a two fold cross validation, the trained ANN was validated and performed without error on all unseen cases which were not in the data used for training.

#### 14. Environmental Estrogen Mixtures Signaling Via Nongenomic Mechanisms.

Cheryl S. Watson, Biochemistry & Molecular Biology Dept., University of Texas Medical Branch, Galveston, USA. **Summary:** Pending

# **15.** Addressing fear of cancer recurrence: A pilot test of a 6-week cognitive existential group intervention with breast and ovarian cancer patients.

Christine Maheu, Ingram School of Nursing, McGill University, Cancer Survivorship Program, PMH, ELLICSR: Health, Wellness & Cancer Survivorship Centre, Toronto General Hospital, Canada.

Summary: Background: Fear of cancer recurrence (FCR) is one of the most frequently cited unmet needs among cancer survivors. Moderate to high levels of FCR affect 33 to 56% of cancer patients and can persist for several years after diagnosis. FCR is associated with impairment in functioning, psychological distress, stress-response symptoms, and lower quality of life, as well as increased use of health care resources. Despite these factors, few manualized interventions exist to address FCR among cancer survivors. Objectives: The goals of the present study were to develop, describe, standardize, and do preliminary testing of a 6-week cognitive-existential group intervention to address FCR in women with breast or ovarian cancer. Secondary goals of the intervention are to reduce cancer-specific distress, improve quality of life, and promote optimal coping and screening behaviors. It is hypothesized that the group intervention will result in lower FCR, better psychological functioning, better coping, enhanced quality of life, and better adherence to screening guidelines. Methods: The development of the cognitive-existential intervention was theoretically guided by Leventhal's Common Sense Model, Mishel's Uncertainty in illness theory, and cognitive models of worry. The earlier sessions focus on the acquisition of skills such as cognitive restructuring and relaxation techniques. The latter ones focus on exploration of each participant's specific fears about FCR and exposure to these fears. We have completed 6 groups consisting of 5-8 women with either breast or ovarian cancer. They were recruited from the Breast Cancer Survivorship Program in Toronto and The Ottawa Hospital. Women were asked to complete the following questionnaires before beginning the group, after completion of the group, and at a 3-month follow-up: The Fear of Recurrence Questionnaire, the Impact of Event Scale, the Brief Cope, the Mishel Uncertainty in Illness Scale, and the Impact of Cancer Scale. Some participants also completed exit interviews where they provided detailed feedback on the intervention. Results: We found a moderate effect of the intervention in reducing FCR, cancer-specific distress, and maladaptive coping strategies and improving quality of life. Most of the improvements were sustained at the 3-month follow-up. Interviews with patients after completion of the study revealed satisfaction with the intervention. Patients also made some suggestions for improvement such as increasing the number of sessions to get more time to process difficult emotions. Conclusionrelevance: This brief intervention has shown promising results in addressing FCR among women with breast or ovarian cancer and in providing substantive evidence to support testing of this intervention in a RCT format. Future directions for the intervention will be

presented. We hope this presentation will inform future research and interventions to address this common concern among cancer survivors, and provide concrete examples of tools to achieve this goal.

### 16. Breast cancer and internal ionising radiation exposure.

# Christopher Busby, Dept of Physical Chemistry, Wellcome Research Laboratory, Langley Park, Beckenham.

**Summary**: The principle cause of breast cancer in the last and current century is exposure to internal radionuclides from anthropogenic sources. The breast cancer epidemic which began in the 1980s and is now flattening out or reversing in trend was caused by exposure of women who were passing though puberty at the time of peak fallout exposures in the period 1959-1963 to mainly Strontium-90 and Uranium in food, air, water and milk products. This is shown by cohort effects in breast cancer mortality and incidence in the period 1955-1995 presented in this contribution. There is additional supporting evidence. The rates of breast cancer are higher in those who have a higher intake of dairy produce, which was the principal vector for Strontium-90; this also contributes to an explanation of the higher rates in high socioeconomic groups although late age at first pregnancy is also a contributor to this effect. A similar high rate of incidence in high socioeconomic groups is found in the case of childhood leukemia and the source is probably the same, dairy produce contaminated with Sr-90 and other radioactive Group II elements, also Uranium. Further support comes from comparison of high and low rainfall/fallout areas in the UK. A comparison of Wales and England, differentially contaminated by Sr-90 show a large difference in breast cancer rates which developed in the 1980s from a situation where the rates were comparable. Additional support comes from the low breast cancer rates in populations with low dairy intake, e.g. the Japanese and in the USA the Shaker communties. In the last 10 years I have studied two groups with high risk of breast cancer. The first is nuclear site downwinders. In three separate nuclear sites in the UK, Hinkley Point, Bradwell and Trawsfynydd there have been statistically significant breast cancer incidence and mortality excess found in several studies carried out by my research group. In the case of Hinkley Point in Somerset the 2fold excess mortality risk 1994-2004 was independently confirmed by an incidence study which also found excess leukemia in the downwind town of Burnham on Sea. Associated with this was a significant excess infant mortality rate in the same town. In a recent study of Fallujah Iraq published in 2010 my group found a very high excess rate of breast cancer (9-fold relative to Egypt). Also present was an increase in child leukemia, in infant mortality and congenital malformation at birth. Examination of the hair of women in the town revealed high levels of Uranium, presumably from weapons. Other studies in the USA by Gould and Sternglass support the conclusion that the principal cause of breast cancer in 1980-present is exposure to man made radionuclide contamination in the environment. The effects of Chernobyl can already be seen in Sweden, Wales and the ex Soviet territories contaminated by Chernobyl fallout. I predict large increases in breast cancer in Japan in the next 15 years, beginning in the next 5 years. Calcium supplements may have a protective effect.

# **17.** Ten Years Experience of the Glasgow Prognostic Score Relating to Cancer Outcomes.

Clem Imrie, Lister Dept of Surgery, Royal Infirmary, Glasgow, UK. **Summary:** Increasingly teams in different countries have consistently demonstrated that simple markers of the systemic inflammatory response (SIR) such as neutrophil/lymphocyte ratio (NLR) and C-reactive protein (CRP) have prognostic significance in common cancers. Patients with an NLR >5, or a CRP >10 mg/l have a poorer prognosis, with standard therapies less effective. A simple and useful prognostic score is achieved by adding hypoalbuminaemia (<35g/l) to CRP. This Glasgow Prognostic Score (GPS) has a max score of 2 = CRP > 10mg/l + Albumin < 35g/l (those patients fare poorly). The intermediate score of 1 = CRP > 10 mg/l + Albumin > 35g/l, while those with a CRP < 10mg/l score 0 and exhibit in all the common cancers significantly better survival. This GPS score is more accurate in comparison studies than other measures of SIR. Originally described from the UK, the results have been confirmed in multiple international clinical studies. The intake of oral anti inflammatory drugs have been associated with longer survival in non resectable cancers; and the follow up data from large prospective studies of aspirin therapy (mainly used in the treatment of vascular disease) have shown both reduced new adenoma and colon cancer development. All prospective studies of cancer therapy should record the SIR status of patients. Simple low cost anti inflammatory drugs appear to have considerable potential benefit to those patients in the poorest prognostic group with GPS 2. An undervaluation of certain therapies has ensued from the inclusion of patients with the poorest outlook in many studies.

# **18.** Cancer Testis (CT) Antigens: an immunotherapic perspective in Advanced Squamous Cell Carcinoma of the Larynx.

David Livingstone A Figueiredo, National Institute of Science and Technology in Stem Cell and Cell Therapy/Pharmacy Department UNICENTRO/ Department of Otolaryngology, Ophtalmology and Head and Neck Surgery, Ribeirao Preto-Sao Paulo University, Brazil, Titular member of Brazilian Head and Neck Surgery Society. Summary: Pending

# 19. Regional heterogeneity of glioblastoma and its MRI, PET and in vitro correlates.

David Schiffer, Neurology, University of Turin, Neuro-Bio-Oncology Center of Policlinico di Monza Foundation (Vercelli), Italy.

**Summary**: Glioblastoma (GBM) is a heterogeneous tumor. It has been recently studied from this point of view by different MRI procedures, such as DWI (diffusion), DSC (perfusion), Spettroscopy and PET which have been compared with regional phenotypes and genotypes in order to give them a biological significance. Multiple samples of the tumor and its periphery can be obtained by stereotactic procedures or by means of a surgical navigation workstation. Interesting results have been achieved especially concerning peritumor areas where the distinction among tumor cell infiltration, edema and normal tissue is of paramount importance for prognosis and therapeutic post-surgical strategies.Enhancing and non-enhancing areas correspond to aggressive and more quiescent tumor, respectively. DWI, DSC and spectroscopy aspects correspond to combination of infiltration of different degree, edema and normal tissue with their relevant phenotypic and genetic asset. This inquiry is important since it has been demonstrated that the prognosis improves with removal of infiltrated tissue. Our

experience in this field is presented. Another important issue is to verify by the use of different sampling of the tumor and its periphery, where cancer stem cells are located or generated in the tumor. Since current opinion is that these cells should be the real target of therapies, the sites of staminality in the tumor became a real target of diagnosis. The literature discusses the tumor niches of cancer stem cells. Growing in culture cells from different tumor samples, neurospheres and adherent cells, expression of cancer stem cells, are differently generated and with different growth rate, clonogenicity and tumorigenicity according to the tumor sample they originate from. In this regard the difference between "tumor initiating cells" and "tumor stem cells" must be discussed, as well as the opposition between malignancy phenotype and that of cell migration and motility. Adherent cells which show a differentiated phenotype could be considered as contributing to the solution of the problem. Cancer stem cells can be considered as representing a functional status regulated by microenvironments in the tumor.

# 20. Extra-mammary Inferior Approach in Breast Conserving Surgery for Cancer.

Domenico Gerbasi, Breast Unit, Department of Surgery, A.O. "Bolognini" Seriate, Italy.

**Summary:** The aim of this study is to demonstrate that it is possible to make a breastconserving surgery yet oncologically radical for cancer, if not locally advanced with the oncoplastic surgery technique that we propose, avoiding the excision of the skin overlying the tumor and the scar on the breast, exploiting an "extra-mammary" access through an incision made immediately below the inframammary fold. In fact, the purpose of each type of surgical procedure on breast-conserving therapy for cancer is to complete the wide excision of the tumor with a minor a cosmetic alteration as possible of the breast profile, because the change of the body image affects the psychological aspects related to social relations and sexuality. The indications for this technique, according to TNM classification, are: T1 and T2 breast cancer without the involvement of the skin and unifocal ductal carcinoma in situ. After ultrasound-guided drawing of the anterior projection of the tumor on the skin, the surgical incision is made 2 mm below and parallel to the inframammary fold with a variable length, in relation to the need for exposure of the operative field. The dissociation of the posterior face of the mammary gland from the pectoralis major muscle fascia facilitates the localization of the tumor by bimanual palpation and his wide excision, regardless of his location, with a posterior approach, preserving the skin overlying the lesion. The reconstruction of the residual breast parenchyma with plastic flow of glandular flaps can be easily performed. The resulting surgical scar is hardly visible on standing, because hidden from the natural breast ptosis. Radioguided sentinel lymph node biopsy can be easily performed through a small axillary incision. In accordance with the current international protocols related to breastconserving therapy, surgical treatment will be followed by radiotherapy and chemotherapy in due cases, into a standardized treatment regimen. With a four-year follow-up in our personal experience, no cosmetic alteration of breast profile and no clinical or radiological signs of recurrence of disease were observed. Additional research needs to be conducted to evaluate long term results and effectiveness of the proposed technique, presented for the first time at 5th Annual World Cancer Congress in Beijing in may 2012.

#### 21. The relationship of coagulation with cancer.

Ernesto de Meis, the Federal University of Rio de Janeiro and Gama Filho University; the committee of thrombosis and hemostasis -National Cancer Institute in Rio de Janeiro, Brazil.

#### Summary: Pending

#### 22. Ovarian tissue cry preservation in oncological patients: state of the art.

Fabbri R., Parazza I., Vicenti R., Macciocca M., Magnani V., Venturoli S., Gynecology and Pathophysiology of Human Reproduction Unit, S. Orsola-Malpighi Hospital, University of Bologna, Italy. Raffaella Fabbri, Assistant Professor, Human Reproductive Medicine Unit, Obstetrics and Gynaecology, S. Orsola Hospital, University of Bologna, Italy.

**Summary:** In recent years, advances in the diagnosis and treatment of childhood, adolescent and adult cancer have significantly improved the survival rate and life expectancy of cancer patients. However, chemotherapy and radiotherapy treatments are gonadotoxic and may induce the loss of ovarian function and fertility with consequent premature ovarian failure (POF). A number of factors determine the level of ovarian damage caused by chemotherapy: the type of drug, administration protocol (duration and dosage) and the patient age. Cyclophosphamide and other alkylating agents are the most toxic factors for the ovary, producing a decline in primordial follicle density which is exponential as the dose increases. Moreover the effect of chemotherapy on female gonadal function is related to the patient's ovarian reserve: younger patients are less likely to experience severe POF. Ovarian damage from radiotherapy depends on the dosage and irradiation field. In particular more than 30 Gy hypothalamic/pituitary radiation produces impaired secretion of gonadotropins, 2-5 Gy ovarian/uterine radiation results in half of follicles being lost with consequent impaired gonadal function and more than 5 Gy abdominal radiation causes irreversible ovarian failure. Different options are available to preserve fertility in cancer patients and give them the opportunity to restore fertility and also to become mothers when they have recovered from disease. The choice of the most suitable strategy for preserving fertility depends on the type and timing of therapy, the type of cancer, patient age and the partner status. Ovarian tissue cryopreservation is an important strategy for conserving both steroidogenic and gametogenic functions and it is the only option available for pre-pubertal girls, women with hormone-dependent tumours and women who cannot delay the start of chemotherapy. Cryopreservation of ovarian tissue could be applied in different malignant diseases (systemic, extra-pelvic and pelvic) and in benign haematological, autoimmune or genetic diseases. Other benign diseases, such as ovarian endometriosis or recurrent ovarian cysts are also indications for ovarian tissue cryopreservation. Ovarian tissue can theoretically be frozen using two different approaches: as fragments of ovarian cortex or as an entire ovary with its vascular pedicle. To date, human ovarian tissue cryopreservation has so far been almost exclusively limited to avascular cortical fragments. The cryopreservation of ovarian tissue is a complex procedure because the heterogeneous cytological composition (oocytes, granulosa and stromal cells) of the ovarian tissue makes the adaptation of protocols for ovarian tissue cryopreservation difficult. Many factors influence the effect of ovarian cryopreservation, such as cryoprotectant, frozen carrier, cortical sample size and freezing procedure. The standard

method for ovarian tissue cryopreservation is slow freezing/rapid thawing. This results in good preservation of all types of follicles and is the method of choice for the cryopreservation of ovarian fragments. Another method, albeit experimental, is the vitrification of cortical fragments. Vitrification is technologically promising. It is simpler and one cryocycle is less time-consuming and cheaper than the conventional freezing method. However, results have shown that vitrification can guarantee the storage of viable follicles after warming, but conventional freezing is more effective. Moreover during the vitrification procedure the tissue is cooled at an extremely rapid rate, because it is brought into direct contact with liquid nitrogen, particularly when specific "open carrier" for ultrarapid cooling are used. There is also a hypothetical risk of disease transmission through contact with accidentally contaminated liquid nitrogen. Therefore, for cryopreservation of human ovarian tissue, conventional freezing is more promising than vitrification at present. The main aim of ovarian tissue cryopreservation is to reimplant cortical ovarian tissue after thawing. Tissue is re-implanted into the pelvic cavity (orthotopic site) or a heterotopic site such as the forearm or the abdominal wall once oncological treatment is completed and the patient is disease-free, in order to restore ovarian function and normalize levels of gonadotrophins. The advantage of orthotopic transplantation is that follicles are in their natural micro-environment and can develop with fewer problems. Moreover, it allows for a natural pregnancy to occur. To date worldwide, 20 children have been born as a result of orthotopic transplantation of frozen/thawed ovarian tissue. Until now all pregnancies obtained after transplantation of cryopreserved ovarian tissue were observed in adult patients at the time of harvesting. However there is no reason to doubt the capacity of pre-pubertal ovarian cortex to develop and function correctly after re-implantation. To date, only two experiences of puberty induction have been reported after orthotopic and heterotopic autotransplantation of human cryopreserved ovarian tissue. For heterotopic transplantation there are many unresolved issues. One of them is the optimal site for transplantation. In theory, the optimal site should be vascularised, because the rapid revascularization of the graft is crucial for the survival of ovarian follicles. In addition the site of re-implantion should be easily accessible without any invasive procedure, because repeated ovarian transplantation and/or egg retrieval may be necessary if early graft exhaustion is expected. Another concern related to transplanting ovarian tissue to the heterotopic site is the environmental factors that can affect the follicular development such as temperature, pressure, space for follicular growth, peritoneal fluid, cytokines, angiogenic factors, and hormonal milieu, so the oocyte maturation process appears to occur differently than in the orthotopic environment. The main drawback of the cryopreservation of ovarian cortical strips is the ischemia that occurs at the time of ortho/heterotopic transplantation. Because these small cortical pieces are grafted without any vascular anastomoses, they are completely dependent for their survival on the time necessary for establishment of neovascularization after grafting. Therefore, the reduction of the ischemic interval between transplantation and revascularization is essential for maintaining the viability and functional lifetime of the graft. To this end, cryopreservation of the whole ovary with an intact pedicle and vascular supply could potentially overcome this problem because reperfusion will occur immediately upon re-transplantation and anastomosis. This strategy is still experimental and no human studies of whole ovary transplant after cryopreservation have been performed to date. Ovarian tissue cryopreservation offers real

hope for fertility preservation to young cancer patients and it should be offered before gonadotoxic chemotherapy in all cases where there is a high risk of POF.

### 23. Melanoma Stem Cells and *B-RAF* Mutations are Mutually Exclusive Markers of Melanoma Severity.

Farid Menaa, R&D, Fluorotronics, Inc. San Diego, CA, USA.

**Summary:** Introduction: Malignant melanoma is associated with genetic heterogeneity and a complex etiology. In contrast to other skin cancers, melanoma affects a younger population and has a strong tendency to metastasize with a consequently extremely poor overall survival. Oncogenic B-RAF and N-RAS mutations are respectively the most frequent genetic alterations. B-RAF mutation (V600E) is considered as the most critical genomic alteration with regards to melanoma malignancy and maintenance. Nevertheless, the new model of carcinogenesis involving cancer stem cells is also believed to be responsible for initiation and progression of melanoma to metastasis as well as for disease recurrence after cytoreductive therapy. Here, we explored the possible relationship between the mutational status of tumor genes B-RAF and N-RAS and the presence or absence of melanoma stem cells (aka melanoma initiating cells or melanoma propagating cells) in a cohort control-case study which involved patients diagnosed with metastatic melanoma. Material and Methods: Patients with primary ocular melanomas were excluded. All tumor samples (metastatic melanoma stage IV biopsies) and clinical data were collected with Institutional Review Board approval and patient's informed consent. Half-part of the frozen solid tumor tissue samples was used for genomic DNA isolation by RNase and proteinase K digestion and subsequent phenol/chloroform extraction. Established cell lines derived from the other half-part of the biopsy, were maintained in RPMI 1640 supplemented with 10% fetal calf serum, 5 mM L-glutamine, 100 U/ml penicillin and 100 mg/ml streptomycin at 37 degrees Celcius in a humidified 5% CO2 atmosphere. Detection of mutation(s) was performed by single strand conformation polymorphism (SSCP). Fluorescent capillary SSCP technique was used to detect mutations the B-RAF and the N-RAS genes. Direct DNA sequencing was used to identify and confirm mutations detected in the B-RAF and N-RAS genes by SSCP. Identification of a side population (SP) of melanoma stem-like cells (MSCs), previously isolated and characterized, was assessed routinely by Hoechst exclusion assay. Regression analyses as well as statistical analyses were performed. Differences with a pvalue inferior or equal to 0.05 were considered statistically significant. Results: We found a strong inverse correlation between the presence of B-RAF mutations and the presence of MSCs. However, a strong positive correlation was observed between the presence of N-RAS mutations and the presence of MSCs. Further, we confirmed that B-RAF and N-RAS mutations are mutually exclusive and so, both N-RAS mutations and MSCs could be then found in melanoma. Eventually, we found that mutations were well preserved between biopsies and established-biopsy derived cell lines. Conclusion: This pioneered study reports the presence of MSCs as a strong marker of melanoma severity and, underlined the absolute need of a systematic search for MSCs in "B-RAF negative" melanoma cells. Indeed, this discovery represents a precious tool for more reliable diagnosis, prognosis and, more efficient personalized therapy. Financial Support: F.M. was awarded and supported with a DFG grant (German Foundation) for this study. Keywords : Melanoma, Melanoma Stem Cells, B-RAF mutations, N-RAS mutations,

Cancer Theranostics, Cancer Prognosis, Cancer Metastasis. Selected References: [1] Menaa F et al. Melanoma Stem Cells and B-RAF Mutations are mutually exclusive markers of melanoma severity. Submitted. [2] Menaa F, Houben R, Eyrich M, Broecker EB, Becker JC, Wischhusen J. Stem cells, melanoma and cancer stem cells: The good, the bad and the evil? G Ital Dermatol Venereol., 2009, 144:287-296 (special issue). [3] Menaa F, Synwoldt P, Houben R, Wischhusen J, Schrama D, Broecker EB, Ugurel S and Becker JC. Identification of melanoma cells with stem cell properties. Proc. Journal of Tissue Engineering (Part A), 2009, 15:721-722. [4] Baumann R, Ritter R.C, Menaa F, Houben R, Synwoldt P, Wischhusen J, Schrama D, Ugurel S, Becker JC. Melanoma cells with cancer stem cells characteristics. Proc J Dtsch Dermatol Ges., 2009, 7(9):825-854. [5] Menaa F, Synwoldt P, Houben R, Wischhusen J, Broecker EB, Becker JC. Populations of melanoma cells with stem cells features. Proc Gordon Research Conference (GRC) "Stem Cells and Cancer", 2009 - Les Diablerets, Switzerland. [6] Houben R, Wischhusen J, Menaa F, Synwoldt P, Schrama D, Bröcker EB, Becker JC. Melanoma stem cells: Targets for successful therapy? J Dtsch Dermatol Ges., 2008, 6:541-546. [7] Menaa F, Synwoldt P, Houben R, Wischhusen J, Schrama D, Broecker EB, Ugurel S and Becker JC. Isolation and characterization of melanoma initiating cells. ProcJ Dtsch Dermatol Ges., 2008, 6(9):788-789.

### 24. SSEA-5 and L1CAM are pluripotent markers expressed in both human retinoblastoma cells and induced pluripotent stem cells.

Gail M. Seigel<sup>\*</sup>, Rui Chang<sup>#</sup>, Linda Cassidy<sup>\*</sup> Meerim Choi<sup>\*</sup> and Jason Meyer<sup>\*\*</sup> \*University at Buffalo, Buffalo, NY, #Mount Sinai School of Medicine, NY, NY, \*\*Indiana University, Indianapolis, IN, USA.

Summary: Purpose: Induced pluripotent stem cells (iPSCs) show great promise for ocular cell replacement therapies through directed differentiation to mature retinal cell types. However, there remains a risk of uncontrolled growth caused by undifferentiated cells that persist after differentiating treatments The goal of this study was to identify potential markers that could be used to monitor pluripotency in iPSCs during retinal differentiation to promote controlled cell growth of iPSCs in vivo. Methods: We chose to identify potential candidate pluripotent markers based on differential expression between stem-like and non-stem-like cells in retinoblastoma. Magnetically enriched stem-like ABCG2+ and ABCG2- cells from the human RB143 retinoblastoma cell line underwent microarray analysis using the Agilent platform. We used ensemble based statistical models to predict key marker genes that were differentially expressed between ABCG2+ and ABCG2-. The larger list was filtered and condensed into genes with biological relevance to the behavior of iPSCs and hESCs. One of these genes was L1CAM, a neural cell adhesion marker. In addition, we chose SSEA-5 for analysis based on promising published data as a novel marker of pluripotency. We analyzed retinoblastoma cells, retinoblastoma xenografts, iPSC- derived teratomas, as well as iPS cells before and after retinal differentiating treatment to determine whether these markers would be useful for monitoring pluripotency. Results: We found that retinoblastoma cells and xenografts contained cells that were immunoreactive to L1CAM and SSEA-5. In iPS-induced teratomas, we saw immunoreactivity to both markers, with some areas of co-localization. Undifferentiated iPSCs exhibited strong immunoreactivity to SSEA-5 and L1CAM, with a few positive cells remaining even after 20 days of retinal differentiating treatment.

Conclusions: Both SSEA-5 and L1CAM are cell surface markers that show promise as indicators of pluripotency in iPSCs. Further studies will reveal their usefulness in actively mediating controlled cell growth in iPSCs.

### 25. Practical aspects of digital mammography.

Gary J. Whitman, Radiology with Tenure and Radiologist, Department of Diagnostic Radiology, Division of Diagnostic Imaging, The University of Texas MD Anderson Cancer Center, USA. Summary: Pending

### 26. Endometrial cancer screening – is it necessary?

Gina Opolskiene, Vilnius University Hospital Santariskiu Klinikos. Summary: Endometrial cancer is one of the most common forms of gynaecological cancer in the developed countries and the incidence is rising (Amant et al, 2005). Endometrial cancer usually affects elderly, postmenopausal women. The normal postmenopausal endometrium is thin, uniform and less than 1 mm thick anatomically (Parsons, 1998). Sonographic transvaginal measurement of endometrium have a slight tendency to overestimate the anatomical endometrial thickness (Saha et al, 2004), but normal postmenopausal endometrium does not exceed 4-5 mm in thickness when measured with ultrasound (Parsons, 1998). Women with thick endometrium and postmenopausal bleeding must undergo endometrial sampling because of high risk of endometrial cancer (Smith-Bindman et al, 1998). Women with asymptomatic postmenopausal endometrial thickening present a management dilemma because endometrial cancer can not be ruled out in these cases (Wolfman et al, 2010). Earlier (only five years ago) all postmenopausal women with thick endometrium, symptomatic and asymptomatic, underwent endometrial sampling (Dilatation and curettage or hysteroscopy) in our institution. In my presentation I will analyze management and compare histological diagnoses of symptomatic and asymptomatic postmenopausal women with thick endometrium, will discuss examples and will draw some conclusions.

### 27. Advances in the management of castration-resistant prostate cancer.

*Guru Sonpavde, Medicine, Urologic Oncology UAB Cancer center, Birmingham, AL, USA.* 

**Summary:** The therapeutic landscape of castration-resistant prostate cancer has been revolutionized by the arrival of multiple novel agents in the past 2 years. Immunotherapy in the form of sipuleucel-T, androgen axis inhibitors including abiraterone acetate and enzalutamide, a chemotherapeutic agent, cabazitaxel, and a radiopharmaceutical, radium-223, have all yielded incremental extensions of survival. A number of other agents appear promising in early studies, suggesting that the armamentarium is likely to continue to expand. Emerging androgen pathway inhibitors include androgen synthesis inhibitors (TAK700), androgen receptor inhibitors (ARN-509, ODM-201), AR mRNA inhibitors (EZN-4176), AR DNA binding domain inhibitors (EPI-001), selective AR down-regulators or SARDs (AZD-3514) and agents that both inhibit synthesis and the receptor (galeterone). Promising immunotherapeutic agents include poxvirus vaccines, CTLA-4 inhibitors (ipilimumab) and PD-1/PD-L1 inhibitors. Biologic agents targeting molecular drivers of the disease are also being investigated as single agents including cabozantinib

(Met and VEGFR2 inhibitor) and tasquinimod (angiogenesis and immune modulatory agent). Despite the disappointments with the combination of docetaxel with antiangiogenic agents (bevacizumab, aflibercept, lenalidomide), endothelin receptor antagonists (atrasentan, zibotentan) and high-dose calcitriol (DN-101), the results of the combination of dasatinib (targeting Src) and custirsen (clusterin antagonist) with docetaxel are eagerly awaited. New therapeutic hurdles consist of discovering optimal sequencing and combinations, as well as biomarkers predictive for benefit. Novel agents targeting bone metastases are being developed following the success of zoledronic acid and denosumab. Finally, all of these modalities do not appear curative, suggesting that enrollment on clinical trials and better understanding of biology remain of paramount importance.

### 28. Genome chaos and rapid cancer evolution.

Henry H.Q. Heng, Center for Molecular Medicine and Genetics, and Department of Pathology, and Karmanos Cancer Institute, Wayne State University School of Medicine, Detroit, USA.

**Summary:** Cancer progression represents a typical somatic cell evolutionary process where genome replacement rather than specific gene mutation serves as a driving force. Recently, rapid genome re-organization has become a hot topic following various sequencing projects that revealed the common existence of genome chaos in cancer patients. One subtype of genome chaos, named chromothripsis, has been reported from various cancer types. Both the biological meaning and the mechanism are less clear, however. Based on the evolutionary mechanism of cancer, and the new synthesis that system inheritance is preserved by the karyotype, we propose that genome chaos represents an effective survival mechanism for cancer cell evolution and especially under crisis conditions. Clearly, how to avoid triggering genome chaos is of clinical importance in order to reduce drug resistance.

# **29.** Potential Effects of Angelica Sinensis on Breast Cancer Treatment and Prevention.

Hong-Hong (Helen) Zhu, the Department of Public Health, College of Human and Health Sciences, Western Kentucky University, Bowling Green KY, 42101, USA. Summary: This study was to determine potential effects of Angelica Sinensis on breast cancer treatment and prevention. The MTS Assay was used to compare the effects of Angelica Sinensis on human breast cancer cells (MCF-7 and CRL-7368) with its effects on normal fibroblasts (HTB-125). A revised Ames test was used to test for antimutagenicity. The standard strains of Salmonella typhimarium (TA) 100 and 102 were used in the test. Methyl methane sulfonate (MMS) and UV light were used as positive mutagen controls and ethanol and double distilled water (DDW) as controls. The SAS statistical software was used to analyze the data. Angelica Sinensis was found to be much more toxic to all cancer cell lines tested than to normal fibroblasts. There was a significant negative dose-effect relationship between Angelica Sinesis and cancer cell viability with a P trend < 0.0001. Half maximal inhibitory dose (ID50) of Angelica Sinensis for cancer cell lines MCF-7, and CRL-7368 was 0.10 and 0.07 ug/ul, respectively. For the normal fibroblasts, ID50 was 0.58 ug/ul. Revertants per plate of TA 100 decreased with the introduction of increasing doses of Angelica Sinensis extracts

with a P trend < 0.0001 when UV light was used as a mutagen. There was no difference in revertants per plate between ethanol and DDW control groups. In conclusions, Angelica Sinensis could be used as a safe and effective adjuvant therapy to prevent and treat breast cancer. Angelica Sinensis needs to be investigated as a potential adjuvant anti-cancer therapy for breast cancer treatment and prevention of recurrence.

#### **30. Image-guided personalized anti-EMMPRIN therapy.**

Hyunki Kim, Departments of Radiology and Biomedical Engineering, Comprehensive Cancer Center, University of Alabama at Birmingham, USA.

Summary: Pancreatic cancer yields the highest fatality rate among all cancers and is the fourth leading cause of cancer death in the United States. A monomeric monoclonal antibody targeting extracellular matrix metalloprotease inducer (EMMPRIN) has a great potential as a novel agent for pancreatic-cancer treatment. EMMPRIN is a membranebound glycoprotein, highly expressed on pancreatic adenocarcinoma, which stimulates the production of matrix metalloproteinases (MMPs) from stromal tissue surrounding tumor cells. MMPs play a critical role to degrade extracellular matrix components, leading to the tumor-cell invasion and metastasis. Furthermore, EMMPRIN promotes tumor angiogenesis via stimulating VEGF and cytokines production by both the autocrine and paracrine pathways. Therefore, anti-EMMPRIN therapy can suppress tumor angiogenesis, while preventing tumor metastasis. However, care must be taken when applying anti-EMMPRIN antibody in combination with chemotherapeutic agents. If anti-EMMPRIN antibody is used for hypervascular tumors, its antiangiogenic effect may induce vascular normalization, reducing the interstitial pressure, and thereby improve the drug-delivery efficiency. In contrast, for hypovascular tumors, the antiangiogenic effect may excessively decrease the tumor vasculature, reducing the drug delivery while increasing tumor hypoxia. We demonstrated that anti-EMMPRIN therapy enhanced the drug-delivery efficiency in a hypervascular pancreatic tumor model, while reducing microvessel density, and it showed synergy when used with gemcitabine. However, an antagonistic effect was produced when anti-EMMPRIN antibody was used in combination with chemotherapies in a hypovascular model. Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) is an ideal method to measure tumor vascularity in order to aid the decision of personalized anti-EMMPRIN therapy, and we proposed a specific clinical protocol to implement it based on DCE-MRI.

### 31. Surgical management of ovarian cancer.

Ignacio Zapardiel, European Network Young Gyn Oncologists - Executive board member, Consultant. Gynecologic Oncology Unit, La Paz University Hospital. Madrid. Spain.

**Summary**: Ovarian cancer has one the highest case-ratio mortality among female malignancies, partially due to ist late diagnosis. Near 75% of cases are diagnosed in advanced stage disease when overall survival rate is around 25%. Ovarian cancer treatment is based on to pillars surgical cytoreduction and platinum-based chemotherapy. The primary treatment for advanced disease between surgical maximal effort or neoadjuvant chemotherapy is still controversial, and may impact on oncological outcomes (overall survival and disease-free survival).

# **32.** The Benefit of Centralized Healthcare System - It's Role in Re-establishing a Community Hospital Pathology Service Using Telepathology and Supportive Service Corridors.

I.W. Kuzmarov MD FRCS(c)<sup>1</sup>, S Trifiro MD FRCPC<sup>2</sup> and Bich N. Nguyen MD FRCPC<sup>3</sup> <sup>1</sup>Direction of Professional and Hospital Services, Santa Cabrini Hospital, <sup>2</sup>Department of Pathology, Santa Cabrini Hospital, <sup>1,2</sup> McGill University; <sup>3</sup>Department of Laboratory Medicine, University of Montreal Hospital Centre

Summary: Santa Cabrini Hospital is composed of 369 acute care beds, with a separate pavilion providing services for 100 long term care patients. The hospital is situated in the northeastern part of Montreal, a major city in Canada and provides services to an area that encompasses approximately 750,000 people. Santa Cabrini Hospital is also a trauma centre and a primary (local) cancer centre. The hospital has functioned with two pathologists for many years. The two were highly efficient and produced a large volume of pathologic units that could have easily necessitated three full-time pathologists. The two pathologists resigned abruptly for personal reasons leaving no one to replace them. The manner, in which they were replaced, reflects on both the organisation of the Quebec health and social services system and the collaborative effect of the many players in the social. Healthcare is universal in Canada, administered by the provinces but under the federal umbrella via the Canada Health Act, which describes the conditions to be met by the provinces in order to receive the transfer payments that help support it. It must be accountable and portable from one province to another. The presentation will cover the organisation and governance of health care services in Quebec and how this structure permits the rapid implementation of service corridors to make up for the manpower shortage in pathology. In addition the presentation will deal with the installation of digital pathology to complete the service corridor. The presentation will demonstrate the overall ability of the system to adapt to change. The crisis in pathology will be used to demonstrate how models of integrated universal healthcare systems with centralized pyramidal or longitudinal structures can meet many challenges. This model, in Quebec can deal with issues that range from emergency management, to resource distribution, to the establishment of critical care pathways in all sectors.

# **33.** Colorectal Cancer Inherited Susceptibility in the Brazilian population: the first replication study in Latin America.

# Israel Gomy, AC Camargo Cancer Hospital in Sao Paulo. Cancer geneticist at Sao Paulo State Cancer Institute.

**Summary:** Background: Colorectal cancer (CRC) is one of the most prevalent cancers worldwide, including in developing countries where lifestyle and dietary factors are more industrialized. Its genetic contribution in the etiology is well known since risk is twice when there is one first degree affected relative. Genome-wide association studies (GWAS) have revealed approximately 10% of the excess familial risk through genotyping SNPs with strong linkage disequilibrium with functional variants in individuals from European population. Only 20 common SNPs have been discovered by GWAS, however, there are few replication studies in more heterogeneous populations. Here we show preliminary data of the first study of CRC inherited susceptibility performed in Latin America in the Brazilian population and tried to replicate European

studies. Methods: We genotyped 1,467 individuals (740 cases and 727 controls) for 10 tagSNPs (rs6983267, rs4939827, rs4779584, rs16892766, rs10795668, rs4444235, rs9929218, rs10411210, rs961253, rs3802842) using TaqMan® SNP Genotyping Assays and SDS2.3 software (Applied Biosystems®). We exclude from the analysis genotypes with poor call rates and SNPs with significant deviation from Hardy-Weinberg equilibrium. Statistical analyses were performed through SNP&Variation Suite 7 (Golden Helix). Results: Significant association (p?0.05) was found between five out of ten SNPs and CRC risk for most genetic models. One SNP (rs10411210) was associated with a lower risk of CRC. Conclusions: Despite we did not adjust for population stratification by ancestry, this study partially replicated European GWAS in a population with heterogeneous genetic background. Therefore, it is necessary to study other admixed populations which certainly would aid to uncover the missing heritability of CRC and help to build the genetic architecture of CRC susceptibility.

### **34. Prediction and Tracking of Moving Tumors can Result in Significant Reduction in Dose to Critical Organs and Tissue.**

Ivan Buzurovic, Department of Radiation Oncology, Thomas Jefferson University, Philadelphia, USA.

Summary: In external beam radiotherapy (EBRT), one of the major challenges is to compensate for target motion that is induced by a patient's respiration. To accommodate possible organ movement in any condition and ensure that the prescribed radiation dose to the treating volumes is achieved during the treatment, current procedure in treatment planning includes a large margin around the clinical target volume (CTV), delineating the planning target volume (PTV). This method, however, undesirably allows substantial dose to be delivered to healthy tissue as well as to adjacent critical organs. Respiratory and cardiac motions have been found to displace and deform tumors in the lung and other organs. Because of this, radiation oncologists must expand the margin during radiotherapy, and consequently a large volume of healthy tissue is irradiated, and critical organs adjacent to the tumor are sometimes difficult to spare. Target motion during radiation and motion compensation are interesting topics studied by many research groups. Several methods for tumor motion compensation, such as breath holding, gating, and active tracking and dynamic delivery (ATDD) have been reported so far. Among these methods, ATDD is most effective, but challenging. Recently, it was found the novel tumor tracking technologies can be integrated onto treatment couches and validated the tumor tracking system capabilities to follow desired trajectories. When the active tracking system was applied, irradiated PTV (i.e. the area set for treatment) was 20 to 30 percent less for medium size tumors and more than 50 percent for small size tumors. Implementation of active tracking techniques and dynamic dose delivery can minimize irradiation to healthy tissues and improve sparing of critical organs. Consequently, quality of patient treatment potentially can be improved.

### **35.** Acupuncture for the treatment of hot flashes in breast cancer patients, a randomized, controlled trial.

*Jill Brook Hervik, Physical therapist/acupuncturist, Pain Clinic, Vestfold Hospital, Norway.* 

Summary: Objective: To investigate the efficacy of acupuncture in women with breast

cancer suffering from hot flashes as a result of anti-estrogen medication. Methods: In a prospective, controlled trial, 59 women suffering from hot flashes following breast cancer surgery and adjuvant estrogen-antagonist treatment (Tamoxifen) were randomized to either 10 weeks of traditional Chinese acupuncture or sham acupuncture. Number of hot flashes day and night were recorded prior to and during treatment, and 12 weeks following treatment. A health score was conducted at baseline, at the end of 15 treatments and after 12 weeks. Results: Mean number of hot flashes day and night was reduced by 50 and almost 60% respectively from baseline to the end of treatment in the acupuncture group, and further reduced by 30% day and night during the next 12 weeks. A marginaly significant reduction in hot flashes in the day was seen during treatment, but was completely reversed during the following 12 weeks in the sham group. No reduction was seen in hot flashes at night. Health scores were improved by 50% from baseline to the end treatment in the acupuncture group, and maintained 12 weeks after treatment ended. No corresponding changes were seen in the sham acupuncture group. Conclusion: Acupuncture treatment provided effective relief from hot flashes and an increased health related quality of life in women operated for breast cancer, medicated with Tamoxifen.

#### 36. Breast cancer progression in old mice is delayed with exercise training.

Jorming Goh and Warren Ladiges, University of Washington, Seattle, WA, USA. **Summary:** Cancer is an age-associated disease, with advancing age a primary risk factor. This observation is supported by an increase in the age-specific incidence of breast cancer in women until menopause and then a slower rate of increase thereafter. Up to 80% of women diagnosed with breast cancer are over 50 years of age. This stratification necessitates an individualized approach in cancer prevention and treatment tailored to women of different ages. Pre-clinical animal models are useful and necessary to address the molecular and cellular complexities of age-dependent breast cancer and response to physical activity and chemotherapy. There is a need to recapitulate the physiological changes due to aging and consider the critical molecular and cellular targets that are expressed differently between the young and old. We used the 4T1 mouse breast cancer cell line orthotopically implanted into the fourth breast fat pad of 18-month old female Balb/c mice, as a model of invasive breast cancer for older women. Average daily distance ran on voluntary running wheels was  $4.89 (\pm 1.73)$  km prior to tumor implant, and 2.38 (± 1.51) km after tumor implant. Running distance was negatively correlated with tumor volume measured 28 days after tumor cells were implanted (1 x 104 cells). Increased distance ran was also correlated with increased whole body VO2 uptake (Pearson's r = 0.81, P = 0.04), and decreased mitotic index (Pearson's r = -0.85, P = 0.03) and increased necrotic index (Pearson's r = -0.74, P = 0.05) of primary tumor cells. In conclusion, the further distance each old mouse ran, the greater the protection against tumor progression in association with increased metabolic rate. The results suggest that 4T1 breast cancer in old Balb/c mice represents an excellent model to investigate the mechanisms involved in the anti-tumor effects of exercise training in older women with invasive breast cancer.

# **37. Basal/ Squamous cell carcinomas induce differential expression of Bcl-2 and Bax molecules in tumor infiltrating lymphocytes of xeroderma pigmentosum patients.** *Kalthoum Abid, Immuno-Histology Lab, Medicine University of Tunis, Tunisia.*

**Summary:** It is widely recognized that the inflammatory microenvironment of tumors may contribute to cancer growth and spread and to the immunosuppression associated with neoplasia. It is also known that TIL (tumor infiltrating lymphocytes) are primed for apoptosis and that their death seems to be responsible for inadequate anti-tumor defense. The anti-apoptotic Bcl-2 protein and its proapoptotic homolog Bax, are crucial regulators of apoptosis. Here, we present two situations where TILs are doomed or not to die in XP (xeroderma pigmentosum) patients, that are deficient in repair of UV-induced DNA damage and whose tumors are UV-induced. Immunohistochemistry was performed on tissue sections derived from skin biopsies of XP patients, using antibodies against Bcl-2, Bax, CD3, CD8 and CD56 molecules. We calculated the percentages of T cells expressing Bcl-2 and Bax proteins and also the Bax/ Bcl-2 ratios, for each biopsy. Our results showed that TILs in BCCs (basal cell carcinomas) have significantly greater apoptotic index than those of SCCs (squamous cell carcinomas). The lower propensity to undergo apoptosis of SCC TILs, in comparison with those of BCC, is likely to be associated with more aggressive tumor behaviour mediated by inflammation.

#### 38. Breast Cancer Screening & Diagnosis in 2013.

#### Kevin M. Kelly, SonoCiné, USA.

Summary: As Dr. Tabár showed in his 30 year study screening mammography by finding breast cancer at an average diameter of 1.8 cm instead of the average diameter of 2.6 cm when the cancers are found physically the long term reduction in mortality from breast cancer was about 30%, because of the 2/3 reduction in the average volume of the cancers at discovery. With automated whole breast ultrasound (AWBU), MRI, PET or BSGI occult cancers average about 1cm which is an 80% decrease in volume compared with mammography alone. Consequently, it is theoretically possible to reduce the present death rate perhaps up to half or more by using a consistent reproducible, affordable nonrisk method of ancillary screening. MRI and the nuclear procedures are inherently more expensive and have some risk related to the contrast injections. Ultrasound is clearly the most satisfactory as the secondary screen in large populations. An automated system designed for optimum detection of small cancers has been successful in our initial study of 6400 mammograms with and without AWBUs. The number of cancers found doubled from 23 to 46 and the number of invasive cancers  $\leq$  1cm tripled from 7 to 21. A subsequent reader study with 12 radiologists who used breast ultrasound in their clinical practices had a 63% increase in cancer detection and 150% increase in detection of invasive cancers  $\leq 1$  cm. The impact of the dense breast laws," Over-Diagnosis", and a strategy to raise the low PPV of biopsy ultrasound lesions will be discussed.

# 39. Targeting of PDGFR $\beta$ with an RNA-aptamer inhibitor inhibits glioma cell survival, growth, invasion and enhances antitumor activity of an anti-EGFR aptamer.

### Laura Cerchia, Istituto per l'Endocrinologia e l'Oncologia Sperimentale del CNR "G. Salvatore", Italy.

**Summary:** The platelet-derived growth factor receptor (PDGFR) is an important member of receptor tyrosine kinase (RTK) family. The activation of PDGFR $\beta$  signaling pathway induces various cellular responses, including cell proliferation, migration and angiogenesis. Preclinical studies have not only shown a central role for the

overexpression and deregulated activation of PDGFRβ- mediated signaling in development of many tumors, including glioma, and the maintenance of the malignant phenotype, but have also demonstrated that the targeted inhibition of signaling cascades has significant anti-cancer effects. Also, several studies have reported that EGFR crosstalk with PDGFR<sup>β</sup> potentially leads to glioblastoma resistance to anti-EGFR therapy and that EGFR transactivation contributes importantly to PDGFRß signal transduction. Overall these data indicate that PDGFR<sup>β</sup> represents a valuable target for tumor therapeutic development. A number of tyrosine kinase inhibitors under development as anti-tumor agents have been found to inhibit the PDGFR<sup>β</sup>. However, these compounds are not selective and have multiple tyrosine kinase targets. Aptamers are single-stranded oligonucleotides able to bind with high affinity to specific protein or non-protein targets by folding into complex tertiary structures. Their high specificity and low toxicity render them a valid alternative to antibodies for in vivo targeted recognition as therapeutics or delivery agents for nanoparticles, small interfering RNAs, chemotherapeutics and molecular imaging probes. Here we report a novel PDGFR<sub>B</sub>-specific antagonist that is a nuclease resistant RNA-aptamer, named Gint4. The aptamer, generated by a cell-SELEX approach on malignant glioma target cells, specifically binds to the extracellular domain of the human PDGFRB (Kd, 10.4 nM). Following binding, the aptamer inhibits liganddependent receptor activation, including Erk and Akt phosphorylation, cell growth, migration and invasion. Further, we demonstrated that the stimulation of glioma cells with the PDGFRß specific ligand, PDGF-BB, caused EGFR transactivation that was hampered by treatment with both the Gint4 aptamer as well as with CL4, the RNA aptamer that we have previously generated as an high affinity inhibitor of EGFR. Interestingly, the combined treatment of glioma cells with the anti- PDGFRß Gint.4 aptamer together the anti-EGFR CL4 aptamer strongly cooperates in inducing inhibition of cell survival and growth. Moreover, we demonstrated that Gint4 rapidly and specifically internalizes within the target cells thus it can be used as cargo for tissue specific internalization.

#### 40. What is the brain-cancer connection?

#### Lei Cao, Nuclear Engineering, Department of Mechanical and Aerospace Engineering, The Ohio State University, USA.

**Summary:** A focus of much cancer research is at the molecular and cellular level. In contrast, the effect of lifestyle, social interactions and psychological state is less investigated. Our recent work demonstrates that living in an enriched environment with complex physical, cognitive, and social stimulation leads to improved cognitive and metabolic health, and reduced tumor growth and increased remission. Furthermore, the enriched environment decreases adiposity; increases energy expenditure; causes resistance to high fat diet induced obesity; and induces a genetic, morphological, and functional transformation from white fat to brown fat and subsequent energy dissipation. These robust effects on peripheral cancer and adipose tissues are mediated by the activation of a specific neuroendocrine brain-adipocyte axis: the hypothalamic-sympathoneural-adipocyte (HSA) axis. The enriched environment triggers brain-derived neurotrophic factor (BDNF) gene expression in the hypothalamus of the brain increasing sympathetic tone to fat tissues. The selective sympathoneural modulation of white fat induces brown fat genetic program and subsequent increased thermogenesis and lean

phenotype. This brain-adipocyte axis also suppresses leptin production in fat via betaadrenergic signaling leading to a reduction in cancer proliferation.

# 41. Role of the PI3K/AKT/Mtor pathway in the regulation of glioma cancer stem cells.

# LIAS EL HABR, INSERM U894 Glial Plasticity Team, Psychiatry & Neurosciences Center, St Anne Hospital, Paris, France.

**Summary:** Gliomas are primary brain tumors that remain of dismal prognosis due to a lack of effective treatment. The presence of CSCs (cancer stem cells), which combine stem properties and therapeutic resistance with the ability to regenerate tumors, has been recently ascertained in several types of solid tumors including gliomas. Glioma CSCs are distinct from the other cells within the tumor mass because of their ability to grow as neurospheres in defined medium, to maintain a cellular hierarchy, to self-renew, and to share common molecular markers with neural stem cells (NSCs). Remarkable progress has been made in identifying the signaling pathways implicated in the regulation of glioma CSCs. Aim of this review is to summarize the findings of several recent reports dealing with the role of the PI3K/AKT/mTOR pathway in the behavior of glioma CSCs.

### 42. Tumors Bank of the National Cancer Institute of Mexico.

Luz Ma. Ruíz Godoy Rivera, National Cancer Institute of Mexico (INCan), Mexico City, Mexico.

**Summary:** A tumor bank (TB) is an ordered collection of neoplastic samples, normal tissue, and/or fluids preserved under optimal conditions, as well as storing patients clinical information. The objective of this conference is talk about the sample collection, preservation, and histological and molecular quality control, medical structure, functioning and perspectives how platform of the medical cancer research and translational medicine. One crucial element of institutional interest will be the transfer of these concepts to the different oncological centers, integrating in this manner a network that enables. The exploration of the different kinds of tumors as pathologies from therapeutic, epidemiological, and molecular research. The tumor bank was able to create a database of the four most common malignancies: breast cancer, colon adenocarcinoma, renal cell carcinoma and ovarian adenocarcinoma. The database is housed electronically on INCaNet, and provides information with regard to age, gender, topography, histopathologic diagnosis, clinical stage, treatment and monitoring. INCaNet continuously updates the patient's clinical information and allows researchers and physicians to see the scanned and signed letter of informed consent. The tumor bank is not keeping its achievements to itself, however, and recognizes that creating a network of tissue banks will allow Mexico's cancer research to further increase its contributions. We want to realese some information about the our samples for external protocols in the other Contries.

### 43. The real cause of a severely anaemia syndrome original case report.

Manuela Stoicescu, Internal Medicine Department, University of Oradea, Faculty of Medicine and Pharmacy, Medical Disciplines Department, Romania. **Summary:** Objectives: The main objective of this clinical case presentation was to detect the real cause of a severely anaemia syndrome (Hb=5g/dl) in a young women patient

aged 25, former athlete for 12 years within a athletics class. Material and method: I will present the clinical case of a young women patient, aged 25, former athlete, who went to a sports highschool - followed a athletics class - for 12 years, which clinically presented: asthenia, adynamic, dizziness, fatigue from exertion. Also the patient admitted the daily consumption of oral contraceptives for the last 7 years. On the physical examination, the following are observed: pale skin, brittle nails, koilonychia, with pale hands and pale palm creases, fine glossy, brittle hair, innocent murmur heart, in rest in normal limits. After conducting a series of mandatory tests in school, the following results are detected: Hb=5g/dl, Red blood cells=3 040 000/mm3, Ht=24,6%, MCV=61,0 fL, MCH=17,6pg, MCHC=28,8 g/dL, RDW=18,1%. Blood plates=395 000/mm3, White blood cells= 6 230/mm3, Leukogram: neutrophils=64, 37%, Lymphocyte=27,29%, Monocytes=6,24%, Eosinophils=0,71%, Basophils=1,40%. I want to mention that she did not presented clinical symptoms of bleeding, reason for which she is immediately hospitalized with this severely anaemia syndrome within the Hematology Department. After the following investigations are performed: gastroscopy, gynecological examination, MRI-scan, sternal puncture, all hematological tests, all laboratory tests complete, the results were within normal values and no cause of the anaemia was found. The patient was treated with isogroup, iso-Rh blood transfusions and with injectable iron supplements until the values returned to a Hb=11g/dl level. The patient was discharged from the hospital with the diagnose of an unknown anaemia syndrome and was to follow a treatment with iron supplement tablets. After about 6 months, she repeated the blood tests, the Hb value being low again - 6g/dl, reason for which the patient is hospitalized again within the Hematology Department and all investigations are carried out again, including the sternal puncture, but this time as well the results are within normal limits, the anaemia cause being still undetermined. The patient is treated with iso- group, iso-Rh blood transfusions and with injectable iron supplements until the values returned to Hb=10g/dl, after which the patient is discharged from the hospital again with the diagnose of an unspecified anaemia syndrome and was to follow at home an iron supplement tablets treatment. After about 7 months, after repeating the analysis the value was Hb=7,1g/dl, she was immediately commited to hospital, this time within the Internal Medicine Department. I mention this was my first directly consultation of the patient. After repeating the tests, appeared low value of reticulocytes - 0,3% (at the two previous hospitalization in Hematology Department were within normal limits-1,3% and 1,1%) and sternal puncture confirmed now a marrow suppression only in the red blood cell line.Because she was performance athlete in this moment I suspect anabolic steroids consum and after determination in urine the test for use of anabolic steroids, this being determined as positive Final diagnosis was: marrow failure syndrome on red blood cell line after anabolic steroids consumption. Results and discussions: After much detailed and complex investigations following repeated hospitalizations, the cause of the severe anaemic syndrome of the young patient aged 25, athlete was still undetermined, after performing the blood transfusions and the injectable iron treatment, the Hb values raised to a 10 or 11g/dl value, and after a variable period of time, the Hb values relapsed to a level of 5, 6 or 7g/dl, with the cause remaining undetected for a long period of time. Only in moment when was suspected anabolic steroid consum appeared the reality. Conclusions: 1. The use of anabolic steroids in young athletes is a known practice. 2. Perhaps, currently their side effects are not completely recognized, a fact that implies

even more risks since young people are concerned, in which cancer evolution is faster and more risky, due to the increased cell turnover of young people. 3. A warning sign should be alerted against these extremely dangerous practices and the consumption among the young athletes should be stopped. 4. Information programmes should be conducted among young people, about the risks that they are taking when consuming anabolic steroids. 5. Also, the women have a higher risk than men, because most of the times, they have the disadvantage of consuming both oral contraceptives and anabolic steroids, in most cases in an undeclared, unadmitted and unknown manner, thus being even more difficult to diagnose, whose side effects being probably far less known and insufficiently studied. 6. These issues should be given a greater importance than they are given in the present throughout the world and the legislation should not be so permissive in this regard. 7. The carcinogenic risk of anabolic steroid consumption in young atheletes, is currently less known and insufficiently studied in the context of hematologic diseases, but the presented case above is suggestive in this regard and probably not unique. 8. It is possible, that after a constant consumption, a syndrome of bone marrow suppression should occur, especially on erythrocyte line combined with a accentuated haemolysis, due to the excessive physical effort, which leads to severe anaemia, just like in the presented case above.

#### 44. Sentinel lymph node biopsy in selected cas of ductal carcinoma in situ.

#### Marcinova Marta., Vrzgula A., Krajnikova S., III. Clinic of Surgery - l. Private Hospital, Košice - Šaca, Slovakia.

Summary: Introduction: Seninel lymph node biopsy (SLNB) is a minimaly invasive, accurate method of evaluating axillary lymph nodes in patients with invasive breast cancer. The technique has also been successfully applied in patients with a cor cut biopsy (CCB) diagnosed ductal carcinoma in situ (DCIS). The treatment of DCIS still represents a hotly debated issue and wide variations in surgical management have been recently reported. Material and methods: Case report of a fourtyone year old women (possitive family history, after four births, using a hormonal anticonception for five years) with a breast tumor (size 2cm), CCB diagnosed DCIS. Results: Lymphoscintigrapy showed one lymph node. SLNB was performed and histologically determined as negative for metastases and microinvasion. Surgical tecnique was quadrantectomy with histological negative margins resection. But definitive histological study shoved components of ductal invasive carcinoma, grade 1, low nuclear grade, proliferative index Ki-67 score 10%, possitive estrogen (Eg) - progesteron (Pg) receptor expression and intraductal papilomas in the sorrounding tissue, typical and atypical ductal hyperplasia. Conclusions: The role of SLNB in pure DCIS remains controversial. SLNB can be performed accurately in patients with a biopsy diagnosed of DCIS. The rate of metastatic axillary involvement in patients with pure, completely ressected DCS is low (1.7%). An extensive and accurate deffinitive histologic examination of the DCIS tumor is compulsory to exculde microinvasive foci, that are in fact responsible for axillary lymph node metastasis. We have to take account to biological tumor features: size, grade, histological subtypes, finding of microinasion or isolated tumor cells, diffuse or multicentric microcalcifications, sex hormone receptor status, proliferative index; according to radicality of surgery - free margins resection and to the menopausal status; which are associated with the risk of lymph node metastases. Beause of a high rate of invasive

breast disease on the final pathology of patients with DCIS diagnosed by CCB, these patients chould be offered SLNB. If the SLNB detects micrometastases a complete axillary dissection is not always unavoidable. SLNBs should be considered as a standard rutine procedure in treatment of all patients with DCIS.

# 45. Exploring patients' needs in a Surgical Oncology unit - The contribution of the social worker.

Maria Trigoni, Department of Social Work, University Hospital of Crete, Greece. Summary: Introduction: Each patient reacts uniquely to the disease experience, while at different stages of the disease process and hospitalization, patients exhibit a range of psycho-social needs.. Stress- induced anxiety and disruption of everyday routine are the most common emotional reactions. The presence of a supportive family and social environment, the opportunity for face-to-face communication and close interpersonal relations are important prerequisites for emotional relief. Another important factor that affects the patient, is the hospital context, and the quality of nursing care. Communicating with health professionals, being actively involved in decision-making about treatments and the nursing care plan as well as being adequately informed are all essential components for maintaining a sense of 'normalcy' and a more positive attitude. The purpose of this study was to investigate and record the self-reported psycho-social needs of patients in a surgical oncology clinic after the diagnosis of their disease. Study Population - Method: A descriptive study was designed and used the method of interview in 40 patients (men and women) who were admitted to the Surgical Oncology Clinic at the University Hospital of Heraklion (PAGNH) Crete, from November to December 2010, from a social worker. All surveyed by a standardized list of questions about their feelings because of the illness and the needs they identify. The data sectioned into thematic sections, followed recording and content analysis. Results: Of 40 patients, 14 were men and 26 women, from 30 to 95 years. The majority were married, with children, and all patients were insured. The 35 patients reported that they had supportive environment. The majority (n = 35) reported feelings of anxiety and insecurity which related to disease progression, a new day faced, but despite their health problems reported that they felt calm and safe for the medical - nursing clinic. Most had a positive assessment of the services provided but there were but 6 patients where they would like more information to feel safe. The majority of participants were distressed because of the surgery and treatments and those who had chronic health problems were constantly stress, anger and despair. Emotions usually alternated in different phases of hospitalization related to the problem of health. Positive relationships with family seemed to be a source of strength for patients. Feelings of frustration were individual incidents. Conclusions: The majority of patients exhibited strong emotions, requiring further investigation and intervention by a social worker. Patients with a life-threatening disease, such as cancer, are in need of emotional support. Social workers assigned in inpatient oncology units are urged to thoroughly assess patients' needs, providing support and counseling for both the patient and the family. Systematic, on-going collaboration of unit staff with the Social Service department, using an interdisciplinary team approach, is highly recommended.

### 46. Identification of Amplified Oncogenes with Potential to Modulate Metabolism in

#### **Brain Tumors.**

Marie E. Beckner, Dept. of Neurology, Louisiana St Univ Hlth Sci Cen-Shreveport, USA. Summary: Amplified oncogenes have been found in low and high grade brain tumors. The most malignant brain tumors, glioblastomas, commonly harbor amplified oncogenes and the amplifications with enhanced gene expression levels can be extreme. The functional consequences putatively include increased cellular proliferation and altered metabolism to provide advantages over normal cells and resistance to treatments. In this study we surveyed the literature for reports of amplified oncogenes in brain tumors and assayed 28 glioblastomas and 15 invasive/atypical/anaplastic meningiomas for a group of these oncogenes in multiplex ligation-dependent probe amplification (MLPA) assays based on a PCR technique. The list of amplified oncogenes with potential metabolic consequences in glioblastomas reported in the literature is extensive and includes EGFR, PDGFRA, MET, PIKE, PIK3CA, PIK3C2B, CYP27B1, AKT3, IRS2, etc., with coamplifications often noted. The menu for our assays included most on this list. We detected amplifications (greater than 2-fold) ranging to greater than 70-fold in the glioblastomas with amplifications in the invasive/atypical/anaplastic meningiomas also present but limited to less than 6-fold. Co-amplifications were commonly found in both types of tumors. Therefore, multiplex detection of amplified oncogenes in individual tumors offers a low cost and rapid approach to understanding complex metabolic enhancements in individual tumors with the potential for developing targeted therapies.

### **47.** In pursuit of fascination: exploring the contribution of Attention Restorative Theory to address fatigue in palliative care.

### Marilyn N Kirshbaum, University of Huddersfield, UK.

**Summary:** Background: Fatigue can be distressing and devastating to individuals who have long term, incurable conditions. Aim: This study investigates a uniquely cognitive approach, based on Attention Restorative Theory (ART), as a novel, yet effective intervention strategy. Objectives were to: identify 'enjoyable experiences' as identified by individuals who have moderate to severe fatigue related to a palliative care condition; analyse reported 'enjoyable experiences' by mapping emergent themes against attributes of restorative activities specified in ART; develop a prototype for an intervention that could be used in clinical practice. Design and Methods: A qualitative approach was used to obtain knowledge about a discrete population who experienced moderate to severe fatigue as a result of a long term, palliative care condition. A consecutive sample of 25 people was selected from the local hospice and community; those with acute mental illness and under the age of 18 were excluded. Semi-structured, narrative interviews lasting no more than 45 minutes were conducted stemming from the question: What do you enjoying doing? Results: Seventy-five examples of 'enjoyable experiences' were identified, including artistic pursuits, voluntary community work, socialising and learning. These activities were organised into five emergent conceptual themes: Belonging (social coherence), Expansion (opportunities for creativity and learning), Restoration (effortless and nurturing), Purposeful (achievement based) and Attraction (beautiful, entertaining). When mapped against attributes of restorative activities specified in ART, there was some congruence, but also some differences. It was clear that the participants expressed a great need to be safe and in a nurturing environment. Some participants placed a high value in and received great joy from contributing to the

community, which was not noted in previous ART literature. A prototype due to be piloted as an intervention has been developed in the form of a Guide to Restorative Energy Management, comprising a short interview, an analysis of activities and a coplanning section. The guide is intended to be used to address fatigue through exploring, discovering and promoting experiences which engage interest, excite, nurture and challenge the person.

#### 48. Breast conservation in breast cancer patients with cardiac pacing devices.

Mark Trombetta, Clinical Program Development, Allegheny General Hospital Dept. of Radiation Oncology, Radiation Oncology, Drexel University College of Medicine, Temple University School of Medicine, USA.

Summary: Introduction: Patients with implantable pacemakers and defibrillators who develop localized breast cancer have historically been considered better candidates for mastectomy than breast conservation due to the risk of device malfunction even though many of these patients are desirous of breast preservation. The disruptive potential to the pacing device resulting from either the primary radiation beam or electromagnetic fields that develop during delivery of megavoltage irradiation has been a major impediment to breast preservation. Since the use of pacing devices is growing rapidly and newer treatment techniques involving the use of accelerated partial breast radiotherapy (APBI) have changed the breast cancer paradigm, we developed a systematic strategy at the Allegheny General Hospital for patients with early-stage breast cancer and implanted cardiac pacing devices who desire breast preservation. Materials and methods: From 9/2007-10/2012, Thirty -four patients previously implanted with either a cardiac pacemaker [dependent and non-dependent) or an automated implantable cardioverterdefibrillators (AICD) and affected by with early-stage breast cancer (21 ipsilateral to the device) were treated with APBI or whole breast radiotherapy (WBRT). Eligibility criteria included patients with operable TIS-T2 (<3.0 cm) tumors with negative surgical margins and a surgical axillary evaluation that revealed three or fewer metastatic lymph nodes. All patients were evaluated by a surgical breast oncologist and a radiation oncologist for eligibility and treatment planning. A computed tomography scan was acquired for radiation treatment planning and to determine a predicted radiation dose to the implanted device before offering breast conservation. Patients chose between 3 dimensional conformal radiation therapy (3D-CRT; 3850 cGy in twice daily fractions of 385 cGy: 16 patients) using external beam radiation or high-dose rate balloon brachytherapy (HDR; 3400 cGy in twice daily fractions of 340 cGy: 9 patients) when eligible, or were offered WBRT if they were not APBI candidates (5040 cGy + 1000-1260 cGy tumor bed boost: 9 patients). Results: All patients were able to complete their treatment without interruption. In three of the WBRT patients, the superior border of the tumor bed margin required shaving by 0.5 cm on average to avoid excessive dose to the device, but the coverage was felt to be adequate since the most superior areas of the chest wall are least susceptible to chest wall motion and target miss. Only one patient (treated with ABPI) developed a pacer parameter change which was clinically manifest by a perception of electrical impulses in her chest which correlated with an increased electrical signal output of the device. This was remedied by resetting the device parameters. There was no negative clinical impact otherwise. Interestingly, the device was 25 cm from the tumor bed (contralateral to the involved breast) suggesting that the electromagnetic field flux

was the cause of the malfunction. No other problems were manifest. Conclusion: Breast preservation is feasible and preferable in patients presenting with early stage breast cancers who also have implanted cardiac devices in the contralateral or ipsilateral breast as long as both the limits of cardiac device tolerance and reasonable target volume coverage can be achieved. Breast conservation should be considered for these patients who meet appropriate conservation criteria. Keywords: Radiation, Pacemaker, Defibrillator, APBI, Breast, Lumpectomy.

### 49. Prognostic/Diagnostic Biomarkers in Melanoma.

# Martin C. Mihm, Melanoma Program, Department of Dermatology, Brigham and Women's Hospital, Harvard University, USA.

**Summary:** The discussion will include biomarkers that effect both prognosis and/or therapy. The specific markers that allow for identification of the radial and vertical growth phase will be presented. The importance of uncomplicated radial growth phase will be discussed, as well as the various aspects of the vertical growth phase. The latter will include markers of proliferative activity of T-cells and their subtypes, as well as markers that allow for identification of vessels and their importance in prognosis. Furthermore, the morphologic clues supported by biomarkers will be reviewed, especially with emphasis on increased vascularity. Therapeutic markers that will be discussed include the presence of CTLA-4, the presence of PDL-1 and NPDL, the significance of beta endothelin expression, as well as the significance of the beta3 integrin group. Melastatin and its relationship to prognosis will be reviewed. The importance of the C-kit mutation, the BRAFT mutation and the GMAQ mutation will be reviewed with emphasis on their importance in prognosis as well as their therapeutic significance.

# 50. Combined approach of Fine Needle Aspiration Cytology and Ultrasonography in the Diagnosis of Breast Lump.

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**Summary:** Breast carcinoma is the most common malignant tumour and the leading cause of death from cancer in women. A large number of patients in Bangladesh have been suffering from breast cancer. Now-a-days, Fine needle aspiration cytology (FNAC) is performed as a pre-operative test to evaluate breast lump. But erroneous diagnosis is also noted with FNAC when compared with histopathology. In many situations ultrasonography (USG) provides unique information. If FNAC is combined with USG, the rate of correct diagnosis may be increased. The aim of the present study is to see the accuracy of FNAC and USG in the diagnosis of breast lumps and to see whether combination of the methods increase the diagnostic yield. 222 female patients with palpable breast lump were included in this study. USG was done in 220 patients and FNAC was done in all the 222 patients. Histopathology was done in 89 cases. FNAC and USG in combined approach showed 100% sensitivity, 94.62% specificity, 75% PPV, 100% NPV and 95.49% accuracy. Ultrasonography was found to be less sensitive, but specific and accurate in the diagnosis of breast lump though there is highly significant

(P<0.001) correlation. However, the study has shown a much higher performance of FNAC. Key words: Breast lump, FNAC, ultrasonography.

### 51. New Emerging Therapies in Colorectal Cancer.

Minsig Choi, Karmanos Cancer Center, USA. **Summary:** Pending

### 52. Surgery for locally advanced and metastatic renal cell cnacer.

M Hammad Ather, Associate Prof and Director Urology residency, Aga Khan University. Summary: Radical cystectomy in patients with bladder cancer includes regional LN dissection.Extended bilateral PLND may confer a survival benefit for patients with node positive and node negative bladder cancer. Besides pathological tumor stage, lymph node status is the strongest prognostic factor in patients with bladder cancer. The dissection of the pelvic lymph node during radical cystectomy for muscle invasive bladder cancer is now standard of care. However, the optimal extent of the lymphadenectomy (LND) remains dubitable. Some recent work from the mapping studies and retrospective analyses, has shown that the extended LND up to the mid-upper third of the common iliac vessels appears to provide further prognostic and therapeutic benefit and therefore should be defined as standard LND. The extent of LND suggested is applicable to all form surgical extirpation of the urinary bladder i.e. open surgery, minimally invasive approach (laparoscopic and robot assisted). The concept of total lymph node count is now not considered a quality criterion because nodal yield is overly influenced by the individual patient's anatomy, surgical technique, template applied and pathological workup. Lymph node density is thought to be a superior prognostic factor, but it is similarly influenced by the above-mentioned factors. Concerning molecular techniques to improve the sensitivity of postoperative nodal staging further research is necessary. There are few ongoing prospective randomized trials will potentially help to further define the optimal LND template. Current body of evidence strong support optimal lymphadenectomy during radical cystectomy not only for staging accuracy but also for its therapeutic benefit.

### 53. Insulin-like growth factor-1 and childhood cancer risk.

Mohamed ahmed badr, Pediatrics hematology and oncology, Zagazig University, Egypt. **Summary:** Overexpression of growth factors and/or their receptors is a common event in malignancy and provides the underlying mechanisms for one of the hallmarks of cancer, uncontrolled proliferation. Mounting evidence suggests that IGF-1 is involved in the pathogenesis and progression of different types of human cancer such as colon, breast, prostate and lung. However, only a few studies have investigated the association between IGF-1 levels and childhood cancer risk. We aimed to compare the IGF-1 serum level in children with de novo malignancies to healthy children, and to assess its relationship with cancer type, stage, metastasis and different disease characteristics. The study was carried out on 100 children; 50 children with de novo malignancies and 50 healthy children of matched age and gender as a control group. The patients were subjected to a routine work-up for their cancers according to our local standards. Estimation of the serum level of IGF-1 was carried out in the two groups using ELISA. Our results showed that children with cancer had significantly higher levels of IGF-1 than healthy controls of the same age and gender. No association was found between IGF-1 and tumor type, stage, metastasis and other disease characteristics. In conclusion, the IGF-1 serum level is an important indicator of risk for the most prevalent forms of childhood cancer. It may be used to identify children at the highest risk for these cancers and aid in determing who may benefit most from preventive strategies. Given the small number of children in our study, studies with larger populations are required to confirm these results.

# 54. Targeting Breast Tumor Imaging With 99mTc Radiolabeled PR81 and Its F(ab')2 Fragment in Nuclear Medicine.

# Mojtaba Salouti, Zahra Heidari, Mojtaba Salouti, Biology Research Center, Zanjan Branch, Islamic Azad University, Iran.

**Summary:** Objective: Compared to intact IgG, F(ab')2 and Fab exhibit significantly improved tumor specificity and intra tumor penetration in animal models. Generally, lower molecular-weight agents provide better target to non target ratios due to their rapid background clearance. In this study, we compared the biodistribution and localization characteristics of 99mTc labeled intact PR81 and its F(ab')2 to identify potentially more useful radiopharmaceutical for diagnosis of breast cancer. Methods: Purified monoclonal antibody PR81 was digested with 5% (w/w) pepsin for 28 h at 37°C in 0.1 M sodium acetate buffer at pH 4.2. The F(ab')2 fragments were purified by protein A column chromatography followed by elution with pH 8. The purity of F(ab')2 preparation was evaluated by SDS-PAGE under non reducing conditions and proved to be more than 95%. 99mTc Radiolabeling of PR81 and F(ab')2 fragment were performed using the HYNIC as a chelator and tricine as a co-ligand. The immunoreactivity of the complexes was assessed by radioimmunoassay using MCF7 cells. Biodistribution and imaging studies were performed in female BALB/c mice with breast tumor xenograft after 4, 8 and 24 h after the preparations injection. Results: Labeling of PR81 and F(ab')2 fragment with 99mTc resulted in a specific activity of 89.2%±4.7 and 70.1%±5.2, respectively. The immunoreactivity of 99mTc-HYNIC-PR81 and its 99mTc labeled fragment was 83.2%±4.7 and 65.2%±5.1, respectively. The tumors were visualized with high sensitivity after 4 and 24 hrs injections of radiolabeled fragment and intact antibody, respectively (figure 1). Conclusion: Our comparative study showed that F(ab')2 fragment of PR81 is much more suitable, rapid and reliable than intact PR81 for diagnosis of breast tumors.

# 55. Initiating a Regional Comparative Breast Cancer Research Program in the Eastern Mediterranean Region.

*Nada Alwan, Iraqi National Cancer Research Center, Baghdad University.* **Summary:** Breast cancer: is the commonest malignancy among women in countries within the Eastern Mediterranean Regions (EMR). In Iraq, it comprises approximately one third of the registered female cancers. Other features that justify increasing efforts for breast cancer control in the EMR include the obvious rise in the incidence rates, the higher frequencies of younger ages and advanced stages at the time of presentation and the likely prevalence of more aggressive tumours resulting in high mortality/incidence ratios. At the level of national registration, most of the cancer registries of those countries lack data regarding tumour staging and mortality rates. In fact, within the hospital records, there is no proper documentation on critically important risk factors and clinical characteristics of the disease including stage distribution at the time of initial diagnosis, hormonal receptor status, proportion of women presenting with distant metastases, treatment modalities and survival rates. In an attempt to address the aforementioned information needs on the clinical profile of breast cancer patients, and emphasizing the role of research as one of the basic pillars in the adoption of the cancer control strategy, a "National Breast Cancer Research Program-NBCRP" was established in Iraq in 2009. In collaboration with the International Agency for Research on Cancer (IARC) and WHO, the Iraqi researchers developed a comprehensive information system for Iraqi patients diagnosed with breast cancer. Thereafter, that data base model was utilized to compare the demographic characteristics, clinicopathological presentations and management outcomes of breast cancer patients inhabiting selected countries in the EMR (so far Iraq, Jordan, Lebanon and Egypt are included). In January 2012, the World Health Organization Regional Office for the Eastern Mediterranean (EMRO) in collaboration with the Iraqi National Cancer Research Program, IARC, Susan G Komen for the Cure and IAEA/PACT - organized a Consultative Meeting to discuss the plan of action for implementing a "Regional Comparative Breast Cancer Research Program" ((Sharm Al-Sheikh, Cairo). The roles of the international collaborating agencies in that project were clearly defined and the expected outcomes of the program were illustrated. The online informaton system data base, supervised by the Screening Group of IARC, is curently operating in a major cancer facility within each of the four countries participating in that project; i.e., Iraq (National Cancer Research Center), Egypt (National Cancer Institute of Cairo), Jordan (King Hussein Cancer Center) and Lebanon (Lebanese Cancer Society).

#### 56. Metronomics: bringing target tretments to low income countries.

Nicolas ANDRE, Inserm, UMR911, Aix Marseille University, Pediatric Oncology and Hematology Unit Children Hospital of La Timone, AP-HM, Metronomics Global Health Initiative, Marseille, France.

Summary: Over the last 10 years, metronomic chemotherapy (MC)-defined as the chronic administration of chemotherapy at relatively low, minimally toxic doses on a frequent schedule of administration, with no prolonged drug-free breaks— turned out to be a potential alternative medical strategy to treat refractory cancer. Although, MC was originally thought to be an anti-angiogenic treatment, new mechanism of action have also been reported (restoration of the immune system, induction of tumoral dormancy...). Nowadays, more than 70% of cancer deaths occur in low and middle income countries where survival rates are also much lower than in our high income countries. Many patients do not have access to any treatment or cannot afford treatment. They are eventually sent home to die. New constraint adapted strategies are mandatory. MC is a very attractive therapeutic option in low- and middle-income countries because of its low cost, because it is well tolerated and easy to access. Moreover, combined with drug repositioning, modern anticancer effects can also be obtained with the metronomic approach. Here, we will see how metronomics (the combination of MC and drug repositioning) allows to foresee the potential new developments of cheap, non toxic targeted treatments in countries with limited resources.

### 57. Cancer Survivorship: Myth or Reality.

Pam McGrath, B.Soc.Wk., MA., Griffith University, Australia.

**Summary:** Recent advances in the care and treatment of cancer mean that more patients are now achieving a cure, or at least substantial lengths of time in remission. The perspective for supportive care in this area has now changed from responding to the psychosocial needs associated with acute illness to supporting individuals to live with a chronic condition. Indeed, the notion of 'survivor' has now been mainstreamed and accepted in oncology, supportive care and in the media. The assumption is that this is a positive term embraced by individuals diagnosed with cancer. This presentation challenges many of the assumptions associated with the term 'survivor', discussing findings from a recent study on survivorship in relation to haematological malignancies funded by the Leukaemia Foundation of Queensland. The findings indicate caution is needed in the use of the term as the majority of haematology patients interviewed did not identify with the term because it creates too much focus on the disease and interferes with the major coping strategy of 'getting on with life'.

#### 58. Primary Hepatic Neuroendocrine Tumor: An Unusual Cystic Presentation.

*Prasad K Shetty, Bhagwan Mahaveer Jain Hospital, Bangalore, India.* **Summary:** Neuroendocrine tumors can be found throughout the body and 90% occur within the gastrointestinal tract. They preferentially metastasize to the liver and occasionally cause the carcinoid syndrome by secretion of serotonin and its precursors. Primary neuroendocrine tumors of the liver are exceedingly rare, with only about 60 cases reported in the current literature. We present a case of a 57-year-old male with a primary hepatic neuroendocrine tumor successfully resected. The case presented required meticulous radiological, histopathological and immunohistochemical work-up to rule out an occult extrahepatic malignancy with hepatic metastasis to confirm the primary nature of hepatic tumors. Here we intend to put forward a review of the current literature regarding the diagnosis, pathology and management of this disease.

### 59. Myofibroblast presence in histologically normal mucosa adjacent to oral squamous cell carcinoma: evidence for field cancerisation.

### Punnya Angadi, Department of Oral Pathology and Microbiology, KLEVK Institute of Dental Sciences and Hospital, Belgaum, Karnataka, India.

**Summary:** Objectives: Field cancerisation is induced by carcinogens that act on a large area of tissue and cause molecular alterations that may not be obvious clinically and histologically but can increase the risk of development of malignancy. Myofibroblasts are considered primary cellular components of activated tumor stroma. Their stromal accumulation has been associated with increased tumor aggressiveness and poor prognosis in oral squamous cell carcinoma (OSCC). However, their role in field cancerisation has not been addressed. The present study aims to evaluate the presence of myofibroblasts in histologically normal mucosa adjacent to oral squamous cell carcinoma (HNMAOSCC) and patient matched OSCC tissues. Materials and Method: 50 patient matched tissues of OSCC and HNMAOSCC were subjected to immunohistochemistry using  $\alpha$ -SMA antibody for detection of myofibroblasts. 15 normal oral mucosa specimens were also stained as controls. Results: The number of  $\alpha$ -SMA stained myofibroblasts in OSCC and HNMAOSCC were significantly increased as compared to that of the normal controls (p<0.001). A statistically significant increase in the myofibroblasts population between OSCC and HNMAOSCC was observed (p=0.000). Further, a significant

correlation was established for the presence of myofibroblasts in the stroma of OSCC and the adjacent histologically normal mucosa. Conclusions: Myofibroblasts presence was demonstrated in the stroma of OSCC and also in the HNMAOSCC. This suggests that myofibroblasts could be an early stromal change in the histologically normal mucosa adjacent to OSCC highlighting the possible role of myofibroblasts as likely mediators for field cancerisation and it potential use as a field effect marker.

### 60. Affibody molecules for HER2 imaging and targeted drug delivery.

Rafal Zielinski, Department of Experimental Therapeutics, The University of Texas M.D. Anderson Cancer Center, USA.

Summary: The amplified HER2/neu gene and/or the overexpressed protein have been identified in approximately 20% of invasive breast and non-small lung carcinoma, as well as in ovarian carcinomas and B-cell acute lymphoblastic leukemia. Particularly in breast cancer, elevated HER2 is associated with increased proliferation and survival of cancer cells and, thereby, contributes to poor therapy outcomes and unfavorable prognoses. Accurate evaluation of HER2 status in breast cancer patients is a key factor in determining their further treatment. Women with HER2-positive tumors qualify for antibody-based targeted therapy (trastuzumab) alone, or in combination with chemotherapy. Clinical evaluation of HER2 expression is based on IHC or FISH staining of biopsied tissue. Both methodologies are ex vivo techniques and, due to tumor heterogeneity, often deliver false-positive or -negative results. Affibody molecules constitute a unique class of artificial ligands. They are relatively small (~7 kDa) highaffinity proteins, structurally based on a 58-amino-acid scaffold derived from the Z domain of the Staphylococcus aureus protein A using combinatorial protein engineering. HER2-specific Affibody molecules strongly bind extra cellular domain (ECL) of human HER2 (Kd=22 pM), without affecting the receptor activation status. Importantly, HER2-Affibody molecules recognize epitope distinct from that one targeted by trastuzumab or pertuzumab. As such, Affibody molecules have great potential to be used as tracers for non-invasive determination of HER2 status both in primary tumors and metastatic lesions. Specifically, in our studies we labeled Affibody molecules with Fluorine 18 or Near Infrared Beacons and used them as contrast agents for Positron Emission Tomography (PET) and NIR Optical Imaging respectively. Affibody molecules were successfully used for determination of HER2 status in different mouse xenografts, but also to monitor response to the therapy. Furthermore, we used HER2-Affibody as a targeting module for specific delivery of cytotoxic agent to HER2-overexpressing tumors. The resulting compound-Affitoxin, reduced the size or significantly delayed the growth of breast, ovarian and gastric xenografts with high levels of HER2 while was inactive against HER2-negative tumors.

# **61.** An Ecological Study of Associations between Cancer Rates and Quality of Air and Streams.

*Raid W Amin, Statistics, Director of the UWF Statistical Consulting Services, USA.* **Summary:** This study illustrates the use of the software SaTScan for a spatiotemporal cluster analysis of cancer rates in Florida. The pediatric cancer data are obtained (at the zip code level) from the Florida Association of Pediatric Tumor Programs, while the adult cancer rates (at the county level) are obtained from the Florida Cancer Data System. This study aims at identifying geographic areas that display high cancer incidence rates, in addition to testing for a space-time interaction. In addition to the geospatial analysis of cancer rates, we will also analyze air quality data obtained from the Environmental Protection (at the zip code level), and data on the quality of streams. The software ArcGIS is used to match cancer, air, and water samples based on their geographical coordinates. A multivariate cluster analysis in SaTScan is used to identify locations over space and time where high cancer rates are associated with high levels of carcinogenic air pollution and low stream integrity. This approach differs from traditional epidemiological methodologies, and it is proposed to use SaTScan as a first round analysis to establish associations.

### 62. Lateral cervical flap for immediate reconstruction of the oral cavity after radical cancer surgery.

### Raja Kummoona, Maxillofacial Surgery, Iraqi Board for Medical Specializations, Baghdad, Iraq.

**Summary:** Lateral cervical flap (LCF) advocated by the author 1994 consist of skin, fascia and muscle is highly vascularised, its thickness is well tolerated by the the oral cavity tissues with less morbidity and deformity of the donor area, been used by the author for the last 3 decades for immediate reconstruction of the surgical defects after radical cancer surgery, for reconstruction of the tongue, floor of the mouth, alveolus and cheek. The flap was tested experimentally on Rabbits to assess the viability of the flap. In this study include 61 patients with oral squamous cell carcinoma and the follow up from 3-5 years,30 female and 31 male, age ranged between 40-70 years (mean 55 years),these cases include 25 cases with well differentiated squamous cell carcinoma,24 cases with moderate differentiated squamous cell carcinoma and 12 cases of poorly differentiated squamous cell carcinoma. These cases were treated by adjuvant chemotherapy with radical surgery and deep X-ray therapy. In 23 cases the LCF was use as an access for radical resection of supra omohyoid neck dissection. I conclusions, the LCF proved to be an ideal and most reliable flap for reconstruction of both oral and prioral defects after radical cancer surgery.

# **63.** Polymorphic variants into angiogenesis pathways and non-small-cell lung cancer: overcoming a challenge.

### Ramon Andrade Mello, Department of Medicine, São João Hospital, Faculty of Medicine, University of Porto, Portugal.

**Summary:** Lung cancer is a highly prevalent disease worldwide. Currently, it is the leading cause of cancer-related death in western nations. Non-small-cell lung cancer (NSCLC) corresponds to 85 % of all histological types. Risk factors are usually associated with Tabaco consumption, occupational exposure, radon and also passive smoking. Lung cancer diagnosis often occurs in advanced stages, IIIB and IV. Thus systemic therapies, such as cytotoxic agents and therapeutically targets, acquired a main role in NSCLC management approach. To date, many factors have influence in NSCLC behavior and therefore in clinical response to target therapies, such as epidermal growth factor (EGF) and its receptor (EGFR) and vascular endothelial growth factor (VEGF) and its receptor of main interest in NSCLC research. Recently, a Portuguese study identified EGF +61 A/G

polymorphism as risk factor for NSCLC advanced patients. Furthermore, others genetic polymorphisms, such as VEGF -2578 C/A and VEGF -1154 G/A, were correlated with increased tumor VEGF expression, vascular density and worse survival. This topic will address the state of art concerning genetic polymorphisms and NSCLC behavior, as well as the related targets therapies in this regard. Key-words: lung cancer; non-small-cell lung cancer; epidermal growth factor; epidermal growth factor receptor; EGFR; EGF; vascular endothelial growth factor; vascular endothelial growth factor receptor; erlotinib; gefitnib; bevacizumab.

### 64. Virtual consultation and spinal cord compression.

Rebecca K.S. Wong, Radiation Oncology, Princess Margaret Hospital, USA. Summary: The diagnosis of spinal cord compression traditionally is associated with a poor prognosis. Rapid diagnosis and commencement of treatment is required for best treatment outcome. The ideal treatment approach requires multidisciplinary input which is not always available at the point of care, as is the case at our institution, where radiation oncologist and spinal surgeons operate in two separate geographic sites. A virtual consultation process was established with the hypothesis that this approach would allow access to multidisciplinary decision-making, and commencement of their treatments. The VCP consist of exchange of a key set of predetermined clinical factors and diagnostic imaging. All images were also retrospectively reviewed by a single investigator (spinal surgeon) and whether the patient is considered a candidate for surgery was recorded. The decision that was made through the virtual consultation process correlated strongly with subsequent in person surgical assessment, as well as retrospective surgical review of the case records and imaging. This was accomplished efficiently without significant delay in the time to radiotherapy and surgery. For the patients who were treated with radiotherapy alone, the median time to radiotherapy was 0 days (range 0-5) while the patients who underwent surgery after VC, the median duration form VC to surgery was 2 days (range 0-69). Treatment starts >1 day can be attributed to subclinical cord compression reducing the clinical urgency to commence treatment or patient preference. This process is now part of standard practice at our institution in facilitating multidisciplinary decision making for patients presenting with spinal cord compression.

# 65. Application of Non-Invasive Serum/Plasma miRNA Markers for Early Detection in Pancreatic Cancer.

Robert-A. Ollar, Neurology, New York Medical College, Molecular Biology Research Program, Biliary and Pancreatic Surgery Division, Comprehensive Digestive Diseases Center of New York, at Beth Israel Medical Center of New York, USA.

**Summary:** Currently there isn't any very sensitivity or specific convenient non-invasive blood specimen type methodology for early detection of Pancreatic Cancer. Initial literature has revealed that miRNA (microRNA) markers from serum/plasma when utilized in connection with micro array chips and Realtime Polymerase chain Reaction Technology offers a quantitative and cost-effective non-invasive diagnostic approach for screening, than currently employed methods in Pancreatic Cancer. This approach, when combined with bioinformatics analysis, and could offer a practical non-invasive

screening test for early-detection in Pancreatic Cancer.

#### **66.** Role of cyclin D1 and molecular pathogenesis of Oral squamous cell carcinoma. *Rohit Moharil, Department of Oral & Maxillofacial Pathology, VSPM's Dental College*

& Research Center, Hingna Road, Nagpur, Maharashtra, India. Summary: Introduction: Oral cancer refers to a subgroup of head and neck malignancies that develop at the lips, tongue, salivary gland, gingiva, floor of the mouth, oropharynx, and other intraroal locations. Oral cancer is estimated by WHO to be eighth most common cancer worldwide. In country like India it is the most common cancer and approximately 90% of all oral malignancies are squamous cell carcinoma [4]. One of the predisposing factors for oral squamous cell carcinoma is genetic alterations; which contribute to cancer growth by altering the normal cell cycle events. Amongst the different cell cycle controlling proteins, one is the family of Cyclins. More than 15 cyclins have been identified such as cyclin D, E A and B. They appear sequentially during the cell cycle.Cyclins regulate the activities of kinases, which have been named cyclin dependant kinases. The activation of specific kinases complex results in cascade of protein phosphorylation that is required for passage through specific cell stages of cell cycle. There are three different forms of cyclin D i.e. D1, D2, D3. Cyclin D1 is believed to control cell cycle transit from G1 in to S phase and it is located on chromosome 11 q 13. Immunohistochemical research studies have correlated abundant expression of cyclin D1 in premalignant lesions and oral cancers and thereby evaluated its role in carcinogenesis. Aims & Objectives: 1, To investigate the expression of cyclin D1, protein in premalignant lesions. 2, To investigate the expression of cyclin D1, protein in oral squamous cell carcinoma. 3, To compare the expression of cyclin D 1 protein between premalignant lesions and oral squamous cell carcinoma and its clinicopathological significance if any. Materials and methods: SELECTION OF STUDY POPULATION, Patients suffering from oral squamous cell carcinoma and premalignant lesions would be selected from out patient department of V.S.P.M'S dental college and research centre Nagpur. Patient's detailed history along with certain parameters like age, gender, site will be recorded. Their diagnosis will be confirmed histopathologically after taking the biopsy with informed consent of each patient. 1, premalignant lersions-a) Sample size - 30 b) will include patients with and without dysplasia. 2, Oral squamous cell carcinoma - a) Sample size - 30 b) will be studied in different grades. Immunohistochemistry technique will be followed for the study. It is the technique used for identifying cellular or tissue constituents (antigens) by means of antigen antibody interactions, the site of antibody binding will be identified by either direct labeling of the antibody or by use of a secondary labeling method. The selection of antibodies for immunohistochemistry technique will be made on the basis of their tumour specificity and hoping that they will react with the tumour under evaluation. Technique: The process of the Immunohistochemistry consists of 1. Preparation of wax sections Surgical specimens will be fixed in 10% neutral buffered formalin and Paraffin embedded blocks will be made. Sections will be cut at 4 um thickness. 2. Sections will be deparaffinized with xylene rehydrated and microwaved for 15 minutes in citrate buffer. 3. Blocking of non-specific reaction. 4. Antigen retrieval. 5. Addition of primary antibody Primary antibody of cyclin D1 (biogenix).

#### 67. Oral carcinogenesis: a pathway-based approach.

Rui Amaral Mendes, Oral Medicine, Oral Oncology and Clinical Pathology, the DMD Program and Clinical Director, The Catholic University of Portugal, University of Michigan, USA.

**Summary:** The progression towards malignancy includes sequential pathological alterations ranging from hyperplasia through dysplasia to carcinoma in situ and invasive carcinoma and is determined by the accumulation of a series of genetic and epigenetic events. Thus, oral carcinogenesis must be seen as a molecular and histological multistage process featuring genetic and phenotypic markers for each stage, which involves enhanced function of several oncogenes and/or the deactivation of tumour suppressor genes, resulting in the loss of cell cycle checkpoints. In cellular carcinogenesis, various genes interact with each other, thus leading to multiple alterations that occur in a rather complex way and in different stages of progression of the disease. Hence, there are several signal transduction pathways frequently altered in cancer, which often produce dramatic changes in cell survival, cell proliferation, morphology, angiogenesis, longevity and other properties known to characterize cancer cells. The underlying pathways governing the progression of oral premaligant lesions and of the molecular changes which antedate the occurrence of invasive malignancy are reviewed and so is the potential use of biomarkers for risk assessment purposes.

#### 68. The multifaceted nature of aptamers.

### Sarah Shidgar, Tao Wang, Jia Lin, Dongxi Xiang, Lei Li, Wei Duan. Sarah Shidgar, Research Fellow at School of Medicine, Deakin University.

Summary: Aptamers, known as chemical antibodies, are short-stranded nucleic acids that bind in a similar manner to antibodies. They have comparable binding affinities to antibodies, are uncomplicated by issues of co-operativity or avidity, possess low toxicity, and lack immunogenicity As they are generated in the test tube, these nucleic acids can be easily modified during chemical synthesis. These modifications can lead to increased stability for in vivo applications, as well as functionalisation for molecular imaging, drug delivery and diagnostic applications. Aptamers are increasingly entering clinical trials, indicating their utility for the treatment of a myriad of diseases. We have generated aptamers targeting two cancer cell markers. These aptamers show specificity and sensitivity to their targets and as they are internalised via receptor mediated endocytosis, these aptamers are highly suited to delivering drug cargoes into the cancer cells. These aptamers have proven suitable for diagnostic applications, such as flow cytometric analysis and histopathological immunohistochemistry. They have also been easily adapted for molecular imaging and they have proven highly effective at drug delivery. As well, because of the small size of the aptamer, these functionalised aptamers rapidly diffuse into tissues and organs, leading to faster drug delivery. We are currently investigating the usefulness of these aptamers in clinical applications.

### **69.** Genetic prognostic research in cancer: What are the promises and current challenges?

Sevtap Savas, Discipline of Genetics and Discipline of Oncology, Faculty of Medicine, Memorial University of Newfoundland, St. John's, NL, Canada. **Summary :** Current prognostic markers used in the clinical management of cancer patients are limited with several clinical and pathological variables, such as disease stage, lymphatic and vascular invasion status, and patient age. While these variables are all related to (the risk of) the disease progression and thus the prognosis in cancer patients, there is a need to identify additional prognostic markers (such as genetic polymorphisms) to make more accurate prognostic estimations. Identification of genetic markers correlated with prognosis may also help elucidate the biological basis of variable prognosis in cancer patients. Because of this clinical and biological relevance of genetic markers in prognosis, an increasing number of studies are investigating them in cancer patient cohorts. On the contrary to other variables used in prognostic research, however, genetic polymorphisms have their own characteristics that need to be considered during the study design and statistical analyses: for example, genotyping errors, possible analysis of genotype data obtained from different tissue resources (e.g. non-tumor and tumor tissues), mode of inheritance (e.g. how many alleles are associated with the effect; is one allele enough or both alleles are required for the effect?), and correlation among the genetic markers. Some of these characteristics of genetic markers simplify our efforts while for others we still need the analysis criteria to be established. In this presentation, both the advantageous and the challenging aspects of analyzing genetic markers in prognostic studies will be discussed together with specific examples from colorectal cancer. I gratefully acknowledge the significant contributions of Dr. Geoffrey Liu and Dr. Wei Xu from the Princess Margaret Hospital, Toronto to this work.

### **70.** The pancreatic cancer serum metabolome: Implications for screening and early detection.

Shawn Ritchie, Discovery Research, Phenomenome Discoveries Inc., Canada. Summary: There are no screening approaches for detecting early stage pancreatic cancer (PC) or increased risk of PC. This presentation will focus on how a non-targeted metabolomics approach based on high-resolution flow-injection Fourier transform ion cyclotron resonance mass spectrometry (FI-FTICR-MS) was used to identify five major metabolic systems (long-chain fatty acids, phosphatidylcholines, lysophosphatidylcholines, sphingomyelins, and plasmenylethanolamines) significantly down-regulated (p<0.00001) in all stages of Japanese PC patients (n=90). These preliminary findings were then confirmed using targeted tandem mass spectrometry (FI-MS/MS) assays for each metabolic system and independently validated in a blinded US Caucasian population (n=60) and the effect of age in a separate random US population sample (n=1000 reference subjects aged 30 to 80) was then performed using a key discriminating metabolite discovered by FI-FTICR-MS (594.4862, p=9.9E-14, PC-594). Disease discrimination using a FI-MS/MS assay was found to be identical in both populations (ROC-AUCs of 0.96 and 0.97) and to the original FI-FTICR-MS results (0.96). In addition, serum PC-594 levels were found to decrease with advancing age, which is consistent with increased risk with advancing age. Our findings demonstrate the power of FI-FTICR-MS for biomarker discovery and the subsequent translation of these findings into clinically useful FI-MS/MS screening assays.

### 71. Presentation Title: Pending

Suman Mallik, Department of Radiation Oncology, Centre for Cancer, Kokilaben

*Dhirubhai Ambani Hospital and Research Institute, India.* **Summary:** Pending

#### 72. Quality of life of patients with lymphoedema post cancer therapy.

TANJA PLANINŠEK RUČIGAJ, University Dermatovenerological clinic, Clinical centre in Ljubljana; Slovenian association for dermatovenerologist, Slovenian Wound Management association and Balkan venous forum. Slovenia.

**Summary:** Lymphoedema is a biger and biger problem in Western countries, because of increasing incidence of malignant diseases and their treatment. Informations for patients are still scope and lymphoedema stay unrecognised among medical staff. Because of that therapy of oedema is not sufficient and quality of life of those patients is not so good that can be. If patients have a lot of informations about their disease and condition and informations about possibilities of different treatment, they can beter manage their condition. They have to know that oedema is chronic and require a daily care. The wearing of compression garment and every day bandaging can be frustrated, especially for younger people because of unfashion look of garments and bandages. The biggest challenges for patients is finding clothes and shoes that can fit limbs who are different sizes. As like at the other chronical disease patients with lymphoedema wich is chronic, time to time feel angry and frustrated and self-pity because of their condition. With questionary of quality of life of our patients we start to recognized patients troubles so we can remove or reduce in near future.

### 73. MicroRNA Biomarkers for Carcinogen Exposure.

### Tao Chen, National Center for Toxicological Research, U.S. Food and Drug Administration, Jefferson, Arkansas, USA.

Summary: MicroRNAs (miRNAs) are small non-coding RNAs that negatively regulate gene expression and control cellular mechanisms. To investigate the potential miRNA biomarkers for chemical carcinogen exposure, we determined miRNA expression profiles from tissues of mice and rats treated with different carcinogens. Generally, a large number of miRNAs in carcinogenic target tissues were significantly altered by treatment of carcinogens while there were only a few of miRNAs that were changed in the nontarget tissues or samples treated with non-carcinogen. Most of these miRNAs altered by carcinogen exposures are involved in cancer-related functions like DNA repair, cell apoptosis and cell growth. Our time-course study using one dose treatment of N-ethyl-Nnitrosourea (ENU) indicated that miRNA could be changed in a few days and the number of differentially expressed miRNAs reached a peak one week after the exposure. In vitro study showed that miR-34a was upregulated after exposure to ENU. Our results demonstrate that most of the altered miRNAs are oncogenic miRNAs and alteration of their expressions may be early indicators of carcinogenic insulation. Thus, these miRNAs can become potential biomarkers for exposure of carcinogens and early indication of carcinogenesis.

# 74. Clinical Trials in Adolescent and Young Adult Oncology: Current Challenges and the Road ahead.

Vivek Subbiah, Division of Cancer Medicine, UT MD Anderson Cancer Center, USA.

### Summary: Pending

# 75. New Biologically Supported Models of Carcinogenesis Involving Hereditary and Non-Hereditary Cancer Cases.

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**Summary:** Many human cancers cluster among family members. These cancers include both pediatric cancers and adult cancers. Important examples of human pediatric cancers include retinoblastoma (child eye cancer), hepatoblastoma (child liver cancer), Wilms tumors (child kidney cancer) and medulloblastoma (child brain tumor). Examples of adult cancers involving hereditary cancer cases include human eye cancer (uveal melanoma), renal cancer (adult kidney cancer), cutaneous melanoma (skin melanoma), and colon cancer, among others. In this paper, we present some new models to incorporate this aspect of human cancers. We will propose new innovative approaches and methods to analyze this type of stochastic models of carcinogenesis. We will use adult human eye cancer (uveal melanoma) as an example to illustrate how to develop this type of stochastic models of carcinogenesis.

### 76. Modeling of tumor growth and immune system interactions: Role of growth model.

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**Summary:** We present our recent investigations in mathematical modeling of the interaction of tumor growth and the innate immune response. Extensive research has been done in this direction by a number of researchers, each representing the tumor-immune dynamics by a system of differential equations. The new perspective we offer is a closer investigation of the model used to represent the rate of growth of the tumor. We focus primarily on two new models, where the first are the hyperbolastic models H1 to H3 introduced in (Theor. Biol. and Med. Model., 2, 2005: 14) and applied to tumor growth in (BMC Cancer, 10 2010: 509). In addition we consider the recently introduced T-model, capable of representing biphasic growth.

# 77. Proteomic Analysis of the Cervicovaginal Fluid Leads to Identification of Biomarkers for Cervix Cancer.

Xaveer Van Ostade, Laboratory of Proteinscience, Proteomics and Epigenetic Signaling (PPES), Department of Biomedical Sciences, University of Antwerp Antwerp, Belgium. **Summary:** Cervicovaginal fluid (CVF) is composed of secretions originating from organs that are part of the female genital tract, including vagina, cervix, endometrium and ovaries. It therefore contains a wealth of information concerning the status of these organs. Cervix cancer is caused by an infection of the cervix with an oncogenic form of human papillomavirus (mostly HPV 16 and 18). Today several screening methods exist, but each has its own disadvantages. Moreover, HPV vaccination so far does not protect for 100% and reaches only part of the female population. All these factors emphasize the need for specific and sensitive biomarkers for cervix cancer. Six CVF samples from healthy women and six samples from precancerous women were run over a 2D-LC-MS/MS proteomics platform and quantified by spectral counting. After comparison, we

identified one protein that was present and absent in all CVF samples originating from precancerous and healthy women, respectively ('qualitative biomarker'). Moreover, we also found four proteins that showed a marked up- or downregulation in one of the two conditions (at least 3-fold; 'quantitative' biomarker). ELISA experiments on 2x9 samples from other healthy and precancerous women confirmed a clear difference in average concentration of the above mentioned 'qualitative' biomarker. Some samples originating from woman infected with HPV types, associated with genital warts, also showed an augmented concentration of this protein. Several ELISA experiments on a series of samples from the same individual (longitudinal) showing progressive infection or clearing are ongoing. Possible applications such as combination with current screening techniques and/or development of a self-diagnosis test could be considered.

#### 78. Updates in diagnosis and management of bone tumors in children.

Youssef AL-Tonbary, Mansoura University Children Hospital, Egypt. Summary: Primary bone cancers are the fourth commonest malignancy affecting teenagers. The average annual incidence rate is 8.7 per million children and adolescents younger than 20 years, making about 6% of childhood and adolescent cancers. Osteosarcoma and Ewing sarcoma are the two types of malignant bone cancer that predominate in children and adolescents representing about 56% and 34% of bone cancers respectively. Their incidence is higher in males than in females and the peak incidence is during the second decade of life. Osteosarcoma can occur in any bone. It most often occurs near the metaphyseal growth plates of the long bones of the extremities. The most common sites are the femur(42%), the tibia(19%) and the humerus (10%). In contrast, Ewing sarcoma commonly occur in the trunkal skeleton (the pelvis, the scapula, vertebral column, ribs and clavicle). In long bones, it tends to arise from the diaphysis rather than the metaphysis. Updates in diagnosis include diagnostic imaging as plain radiography, computed tomography (CT), magnetic resonance imaging (MRI) and nuclear medicine as Positron Emission Tomography (PET) and PET/ CT which allow evaluation of the entire patient in one setting. Tissue biopsy should be performed to confirm the radiographic diagnosis before the initiation of treatment. Open biopsy is the gold standard for diagnosis of a bone tumor. At the molecular level, osteosarcoma is a puzzle of genetic alterations. The application of comparative genomic hybridization to osteosarcoma tissue has disclosed different chromosomal abnormalities, including gains of chromosome 1p, 2p, 3q, 5q, 5p and 6p and losses of 14q, 15q and 16p. Regions of chromosome 21 were absent in 63% of pediatric osteosarcomas. In Ewing sarcoma, the t (11:22)(q24:q12) translocation is detected in approximately 85% of cases. Treatment of bone tumors requires a combination of surgery, radiotherapy and/or chemotherapy. Recently biologically based approaches to treatment were tried as the EWS-ETS family fusion, RNA helicase A, Insulin-like growth factors and type 1 receptor, Rapamycin and analogues and Fenretinide. Also biological reconstruction by autograft and allograft can be used. All updates in diagnosis and treatment of childhood bone tumors will be discussed in addition to a brief summary of the experience of Hematology/Oncology Unit of Mansoura University Children Hospital-Egypt in diagnosis and treatment of these tumors in the last 5 years.

#### 79. "MET" the challenge in non-small cell lung cancer: EGFR crosstalk and the

#### rationale for combinational targeted therapy.

Yu-Wen Zhang, Van Andel Research Institute, Grand Rapids, Michigan, USA. Summary: Non-small cell lung cancer (NSCLC) accounts for 80% of lung cancer, which is the leading cause of death among all human cancers. The receptor tyrosine kinases (RTKs) play important roles in NSCLC development and progression, and are attractive targets for cancer intervention. The hepatocyte growth factor (HGF) receptor MET is one of the RTKs that are frequently activated in NSCLC either by overexpression, amplification or mutation. MET is often co-expressed with epidermal growth factor receptor (EGFR), and its amplification is one of the resistance mechanisms for escaping EGFR-targeted therapy. Previously, we have shown that MET small molecule kinase inhibitor SGX523 synergizes with EGFR inhibitor erlotinib to suppress tumor growth of a NSCLC cell line harboring a MET mutation. To gain further insight into how such combination may benefit NSCLC therapy, we investigated the effects of SGX523 and erlotinib on signal transduction and growth of NSCLC cell lines with different cellular contexts. Overexpressed or amplified MET cross-activated EGFR via hetero-receptor interaction, whereas SGX523 effectively inhibited MET-dependent EGFR crossactivation. When the ligands HGF and EGF were present, only SGX523 and erlotinib combination achieved maximal inhibition on downstream signaling activation and on cell proliferation in vitro. In vivo, SGX523 and erlotinib combination strengthened anticancer activity in a cellular context-dependent manner by enhancing suppression of cell proliferation with or without inducing apoptosis in the xenograft tumors, whereas SGX523 alone achieved near complete regression of MET-addicted tumors. These data provide a good rationale for dual blocking of MET and EGFR to treat NSCLC, even though MET inhibitor alone might be effective against MET-addicted tumors.

# **80.** An ounce of prevention is worth a pound of cure''-The case for and against GnRH-agonist for fertility preservation.

### Zeev Blumenfeld, Reproductive Endocrinology, OB/GYN, Rambam Health Care campus, Technion-Faculty of Medicine, Haifa, Israel.

**Summary:** Decreased secretion of the pituitary gonadotropins, by decreasing gonadal function, may possibly protect against the sterilizing effects of chemotherapy. Although previous suggestions have been made claiming that primordial germ cells fare better than germ cells that are part of an active cell cycle, this hypothesis has not been seriously tested clinically, until recently. A prospective randomized study has found that GnRH-a protected the ovary against cyclophosphamide-induced damage in Rhesus monkeys by significantly decreasing the number of follicles lost during the chemotherapeutic insult. A long-term follow-up of 240 children, 15 years of age or younger, treated for Hodgkin lymphoma [HL] showed azoospermia in 83% of the boys, whereas only 13% of the girls suffered POF. Since ovarian function was preserved in most long-term survivors who were treated prepubertally for lymphoma, but only in about half of similarly treated adult patients, it was clinically logical and therefore tempting to create a temporary prepubertal milieu in women in the reproductive age before and during the chemotherapeutic insult. We have administered a monthly depot IM injection of GnRH- agonistic analogue to more than 250 young patients exposed to gonadotoxic chemotherapy for malignant or non-malignant diseases, after informed consent, starting before chemotherapy for up to six months, in parallel and until the end of chemotherapeutic treatment. Less than 7%

developed irreversible hypergonadotropic amenorrhea. The remaining patients (>93%) resumed cyclic ovarian function, and 53 patients spontaneously conceived 78 times, and were delivered of 63 healthy neonates. These patients were compared to a control group of over 130 patients of comparable age (15-40), who were similarly treated with chemotherapy without the GnRH-a adjuvant. Neither the age, nor the diagnoses, ratio between HD or non-Hodgkin lymphoma differed between the two groups. Similar doses of radiotherapy exposure and ratios of patients treated by radiotherapy in addition to chemotherapy were experienced by the two groups. Moreover, the cumulative doses of each chemotherapeutic agent and the mean or median radiotherapy exposure did not differ between the groups. Our and others' results support the effectiveness of GnRH-a administration also to patients receiving cyclophosphamide pulses for SLE and other autoimmune diseases. Recently we have experienced the first worldwide reported case of spontaneous successful deliveries of THREE healthy neonates after TWO repeated BMT's, concurrently treated with GnRH-a during the gonadotoxic chemotherapy. How can we possibly explain the beneficial effect of the GnRH-a for minimizing the gonadotoxic effect of chemotherapy, in particular that of alkylating agents? Several explanations may be put forward: I. The hypogonadotropic state generated by the GnRH a simulates the prepubertal hormonal milieu. One can conceivably hypothesize that the alkylating agents may bring about an increased rate of destruction/apoptosis of the nonresting follicles, and subsequently a decrease in the secretion of sex steroids and inhibins produced by these follicles, at different stages of maturation and differentiation. The resultant decrease in sex-steroids (estrogen, progesterone, and androgens) and inhibins' secretion will decrease their plasma concentrations and subsequently the negative feedback on the hypothalamus and pituitary, resulting in an increase in FSH secretion. The increased FSH secretion may bring about an increased recruitment of preantral follicles to enter the differentiational one way of maturation, being furthermore exposed to the gonadotoxic effect of the alkylating agents, ending in an increased, exponential rate of follicular apoptosis and degeneration. This vicious cycle may be interrupted by the GnRH-a administration through its ability to prevent the increase in FSH concentrations. II. Another possible explanatory mechanism to the beneficial effect of GnRH-a on decreasing the chemotherapy-associated gonadotoxicity is the decrease in the uteroovarian perfusion due to the hypoestrogenic state, generated by the pituitary- gonadal desensitization. High estrogen concentrations significantly increased ovarian perfusion and the vessel endothelial area, in a rat model of ovarian hyperstimulation, and this effect was significantly and dose-dependently inhibited by administration of GnRH-a. The decreased utero-ovarian perfusion induced by the GnRH-a, may result in a decreased total cumulative exposure of the ovaries to the chemotherapeutic agents as compared to a "control" patient, in a normoestrogenic milieu, thus resulting in decreased gonadotoxicity. III. It has been shown that not only rodents but also primate and human gonads contain GnRH-receptors. In an ovarian carcinoma cell line, GnRH-I and -II receptors' activation may result in decreased apoptosis. Whether the GnRH-a effect is direct on the oocyte cumulus complex, or on the granulosa cell, or possibly on another ovarian compartment in addition to its possible hypogonadotropic effect, is an open question of significant scientific interest. Most recently, a proof of a direct effect of GnRH-a, independent of the hypogonadotropic milieu, has been provided by Imai et al, who have shown a direct, invitro protection from the doxorubicin induced granulosa cell damage, by a GnRH-a. IV.

Another possibility is that the GnRH-a may up regulate an intragonadal anti-apoptotic molecule such as sphingosine-1-phosphate (S-1-P). S1P has been shown to prevent chemotherapy induced gonadotoxicity both in-vivo and in-vitro. Whether the GnRH-a adjuvant cotreatment positive effect is direct or possibly associated with an intraovarian increase in S-1-P is a question of tremendous scientific interest and clinical impact. It obviously awaits further investigation.