

15 August 2011 (Monday)

## Track 2(iii) 2(iv)

**2(iii): Prognostic biomarkers**

**2(iv): Biomarkers based on Cancer Types**

### Session Chair

**Dr. Jimmy Efird**

Brody School of Medicine, USA

### Session Co-Chair

**Dr. Shyamal Dilip Desai**

LSU Health Sciences Center, USA

## Session Introduction

**Title:** Season-of-Birth as a prognostic factor of survival time follow a diagnosis of cancer

Dr. Jimmy Efird, Brody School of Medicine, USA



**Title:** Molecular screening for Lynch syndrome population based approach using immunohistochemistry and methylation analysis

Dr. Lars Henrik Jensen, University of Southern Denmark, Denmark



**Title:** Gold nanoparticles and nanotechnology for cancer biomarker discovery and research

Dr. Qun Huo, University of Central Florida, USA



**Title:** Combination of Notch1 and Notch2 as prognostic marker on Patients with colorectal cancer

Dr. Dake Chu, The Fourth Military Medical University, China



**Title:** Novel role for orphan receptor PXR in Cancer

Sridhar Mani, Albert Einstein College of Medicine, USA



## Season-of-Birth as a prognostic factor of survival time follow a diagnosis of cancer

**Jimmy T. Efir**

Brody School of Medicine, USA

Evidence of an association between survival time and date of birth would suggest an etiologic role for a seasonally variable environmental exposure occurring within a narrow perinatal time period. Risk factors that may exhibit seasonal epidemics include diet, infectious agents, allergens, and antihistamine use. Typically data has been analyzed by simply categorizing births into months or seasons of the year and performing multiple pairwise comparisons. This paper presents a statistically robust alternative, based upon a trigonometric Cox regression model, to analyze the cyclic nature of birth dates related to patient survival. Disease birth-date results are presented using a sinusoidal plot with peak date(s) of relative risk and a single P value that indicates whether an overall statistically significant seasonal association is present. Advantages of this derivative-free method include ease of use, increased power to detect statistically significant associations, and the ability to avoid arbitrary, subjective demarcation of seasons.

### Biography

Dr. J. T. Efir completed his Doctorate in Epidemiology at Stanford University School of Medicine. He currently is an Associate Professor at Brody School of Medicine, East Carolina University (ECU) and has a joint appointment as Epidemiologist/Chief Statistician in the Center for Health Disparities Research. Prior to joining ECU, Dr. Efir was Director of the Biostatistics Facility at the John A. Burns School of Medicine (Honolulu, Hawaii) and an Associate Member of the Cancer Research Center of Hawaii. Dr. Efir's research interests include brain tumours, soft-tissue sarcomas, and HPV-related cancers.

## Molecular screening for Lynch syndrome. population based approach using immunohistochemistry and methylation analysis

Lars Henrik Jensen

Department of Oncology, Vejle Hospital and University of Southern Denmark, Denmark

Microsatellite instability (MSI) in colorectal cancer is one of the few prognostic markers and markers of cancer biology that have made it from bench to bedside. MSI tumors have a better prognosis and may respond differently to chemotherapy, but here we will focus on MSI and screening for the hereditary cancer syndrome, Lynch syndrome, which affects 2-5 % of all colorectal cancer patients.

MSI is variable length mutations in tumor DNA caused by deficiency of DNA mismatch repair. Dysfunction of this repair system is caused by inactivation of any of the repair enzymes MLH1, MSH2, MSH6, or PMS2. It can be measured either on the DNA level as MSI or on the protein level with loss of expression of the affected protein. Lynch syndrome is caused by hereditary mutations in any of the four mismatch repair genes. About 15 % of all colorectal cancers have MSI, but not more than one in three of these are caused by germline mutations. The rest is caused by a sporadic phenomenon, promoter hypermethylation of MLH1.

Based on an exploratory study and a validation study, we have established a strategy for molecular screening for Lynch Syndrome with initial immunohistochemistry and in the case of MLH1 deficiency also promoter methylation analysis. The strategy is now implemented in our region and will be followed prospectively.

Several obstacles and challenges have to be met to bring knowledge from the laboratory to the patients. Molecular screening for Lynch syndrome may serve as a template for how to do this successfully.

### Biography

Lars Henrik Jensen is a medical doctor from University of Aarhus. He completed his Ph.D in 2007 from University of Southern Denmark and has been an exchange visitor at University of Southern California. His primary areas of research are gastrointestinal cancers, clinical trials, and molecular markers.

## Gold Nanoparticles and Nanotechnology for Cancer Biomarker Discovery and Research

**Qun Huo**

Nano Science Technology Center, University of Central Florida, USA

Nanotechnology is bringing ground-breaking tools and new capabilities to biomolecule research and medical diagnosis. Gold nanoparticles as one of the most extensively studied nanomaterials, have many interesting and unique optical properties. These properties make gold nanoparticles as excellent optical probes for biomolecular imaging and assay applications. Based on the light scattering property of gold nanoparticles, our group has recently developed a nanoparticle-enabled dynamic light scattering assay (NanoDLSay) technology for biomolecular detection and analysis. This technique detects proteins, DNAs and other biomolecular targets by monitoring the size change of the gold nanoparticles caused by target analyte binding. In the last few years, we have investigated heavily on the use of NanoDLSay technique for cancer biomarker research. From our study, we made several new findings: (1) a prostate cancer biomarker, prostatic acid phosphatase (PAP), is significantly more complexed or aggregated in prostate cancer tissue than in the normal and BPH (benign prostate hyperplasia) tissue; (2) the concentration of certain serum protein-complexed VEGF (vascular endothelial growth factor) in blood serum is decreased in prostate cancer compared to normal and benign prostate conditions; and (3) we discovered a new protein complex from the nucleus of a pancreatic cancer cell line, *Panc-1*. In this talk, we will explain the principle of NanoDLSay technology and its broad applications in cancer biomarker research.

### Biography

Qun Huo received her Ph.D. from University of Miami in Chemistry in 1999. After completing a two-year postdoctoral work at University of Miami, she joined North Dakota State University as an assistant professor in 2001. In 2005, she became an associate professor in the NanoScience Technology Center at University of Central Florida. She has published more than 60 peer-reviewed papers and her research focus is gold nanoparticles and nanotechnology for biomedical applications. She received the prestigious National Science Foundation CAREER award, NIRT (Nanotechnology Interdisciplinary Research Team) award and she is currently a New Florida 2010 Boost Scholar award recipient.

## Combination of Notch1 and Notch2 as Prognostic Marker on Patients with Colorectal Cancer

**Dake Chu**

The Fourth Military Medical University, China

**Background:** Aberrantly activated Notch signaling has been shown to play a key role in carcinogenesis and progression of various human malignancies. However, the prognostic roles of Notch1 and Notch2 are still uncertain. In this study, we investigated the expression of Notch1 and Notch2 in colorectal cancer to determine their prognostic value.

**Methods:** The protein expression of Notch1 and Notch2 was examined by immunohistochemistry in 1003 clinical colorectal cancer specimens. Statistical analysis was carried out to assess associations of Notch1 and Notch2 expression with survival of patients with colorectal cancer.

**Results:** Significantly negative correlation between Notch1 and Notch2 was found in colorectal cancer ( $P < 0.001$ ). Notch1 and Notch2 were proved to be inversely correlated with tumor differentiation, depth of invasion, lymph node metastases, distant metastasis, TNM stage and survival of patients, suggesting opposite function of the two receptors. Notch1 and Notch2 were proved to be adverse independent prognostic predictors ( $P < 0.001$ ). Moreover, a synergistic effect of positive Notch1 and negative Notch2 coexpression on predicting poor overall survival was proved.

**Conclusion:** Notch1 and Notch2 may be independent adverse prognostic predictors for patients with colorectal cancer. These results would contribute to identify more efficient prognostic predictors and therapeutic targets.

## Novel Role for orphan receptor PXR in Cancer

**Sridhar Mani**

Albert Einstein College of Medicine, Bronx, NY

The nuclear receptor pregnane X receptor (PXR) is activated by a range of xenochemicals, including chemotherapeutic drugs, and has been suggested to play a role in the development of tumor cell resistance to anticancer drugs. PXR also has been implicated as a regulator of the growth and apoptosis of colon tumors. Here, we have used a xenograft model of colon cancer to define a molecular mechanism that might underlie PXR-driven colon tumor growth and malignancy. Activation of PXR was found to be sufficient to enhance the neoplastic characteristics, including cell growth, invasion, and metastasis, of both human colon tumor cell lines and primary human colon cancer tissue xenografted into immunodeficient mice. Furthermore, we were able to show that this PXR-mediated phenotype required fibroblast growth factor (FGF) 19 signaling. PXR bound to the FGF19 promoter in both human colon tumor cells and “normal” intestinal crypt cells. However, while both cell types proliferated in response to PXR ligands, the FGF19 promoter was activated by PXR only in cancer cells. Taken together, these data indicate that colon cancer growth in the presence of a specific PXR ligand results from tumor-specific induction of FGF19. These observations may lead to improved therapeutic regimens for colon carcinomas.

### Biography

Sridhar Mani (Shri) is a Professor of Medicine and Genetics at the Albert Einstein College of Medicine, Bronx, NY. He was the Founding Director of the Phase I Experimental Therapeutics Program at the Montefiore/Einstein Cancer Center. He received his MD degree (1990) from the Mount Sinai School of Medicine, New York, NY followed by further postdoctoral training in Internal Medicine (Board Certified)(1990-1992) and Hematology/Oncology (Board Certified, Onc 1992-1995) at Yale-New Haven Hospital, Yale University School of Medicine, New Haven, CT. Subsequently, he was the program leader for gastrointestinal oncology at the University of Chicago, Chicago, IL. During his tenure as a medical student, he did summer work at Rockefeller and then as a postdoctoral fellow at Yale, he studied under Dr. Eric Fearon on the role of DCC in colon cancer. In 1998, he returned to NY (Albert Einstein College of Medicine) to develop a Phase I Program in Oncology and a laboratory effort on drug metabolism. He is the recipient of the Clinical Investigator Award from the Damon Runyon Foundation (New York) and presently is an NIH funded Investigator on the role of orphan nuclear receptors in metabolism. He is a permanent member of the Developmental Therapeutics Study Section of NCI and serves as an editorial board member for Cancer Research, Clinical Cancer Research and Molecular Cancer Therapeutics (AACR). He has more than 100 peer-reviewed papers in journals like Science, Cancer Research, Clinical Cancer Research, Molecular Pharmacology, Molecular Endocrinology, Molecular Cancer Therapeutics, and Journal of Clinical Oncology.