

# DISTINGUISHED LECTURE SERIES

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On Thursday, Friday and Saturday mornings, plenary sessions designed to interest delegates from all Scientific Groups.

### Thursday, March 4; 9:45 a.m. – 10:30 a.m.



#### David Sidransky

Johns Hopkins University  
Baltimore, Md., USA

#### *Molecular Markers in Personalized Cancer Diagnosis and Treatment*

We aimed to personalize head and neck cancer treatment by generating individual personalized Tumorgrafts generated from a patient's own tumor. Tumor fragments were implanted into nude mice and propagated as tumor fragments to generate cohorts of homogeneously growing tumors suitable for drug treatments. In total, we evaluated 159 different anticancer agents alone or in combination, spanning all currently known classes of anticancer agents and mechanisms of action. Recommended treatments were administered to ten affected individuals, which resulted in a 100% correlation of both positive and negative predictive values. Additionally, molecular studies in these clinically validated Tumorgraft models offer the unique opportunity for the discovery of new biomarkers. For example, we first applied a pharmacologic unmasking approach to detect hypermethylated genes whose inactivation contributes to cisplatin resistance. Utilizing 3 pairs of cisplatin-sensitive and -resistant cell lines, we identified several hundred genes that were down-regulated in each resistant cell line and re-activated by the DNA methyltransferase inhibitor 5-Aza-dC. Among 30 genes, bisulfite sequencing confirmed that 14 genes were hypermethylated in resistant cell lines, but not in the sensitive cell lines. Six of 14 genes were cisplatin-inducible in sensitive, but not in resistant, cell lines. siRNA knockdown of 2 genes, SAT and S100P, increased cell viability with cisplatin treatment in sensitive parental cell lines. Testing of these methylated genes in primary Tumorgrafts correctly predicted cisplatin sensitivity. Methylation-induced gene silencing plays a role in the development of resistance to cytotoxic chemotherapeutic agents. The predictive nature of the personalized models and easy access to tissue support their use in drug development and the discovery of new predictive biomarkers.

### Friday, March 5; 9:45 a.m. – 10:30 a.m.



#### Kenneth Yamada

2008 AADR Distinguished Scientist Award Recipient  
NIDCR/NIH  
Bethesda, Md., USA  
*Cell and Tissue Dynamics in Development and Regeneration*

Recent advances in imaging, three-dimensional tissue culture, and gene expression analysis are revealing how tissues undergo dynamic remodeling in processes as diverse as organ formation and tumor invasion. The mechanisms responsible for these processes include cell adhesion, migration, contractility, signaling, and local gene expression, which can now be visualized or quantified directly. For example, as a result of these advances, we can now visualize mechanisms of salivary gland development involving dramatic tissue rearrangements orchestrated by a variety of matrix and regulatory proteins and genes. The new tools and approaches developed for these studies should be applicable to any field where tissues are remodeled by movements of molecules and cells.

### Saturday, March 6; 10:45 a.m. – 11:30 a.m.



#### Elaine Fuchs

2009 National Medal of Science Recipient  
The Rockefeller University  
New York, N.Y., USA  
*Epithelial Stem Cells: Biology and Clinical Promise*

Elaine Fuchs is the Rebecca C. Lancefield Professor in Mammalian Cell Biology and Development at The Rockefeller University. She is also an Investigator, Howard Hughes Medical Institute. Fuchs has published more than 250 papers and is internationally known for her research in skin biology and associated human genetic disorders, which include skin cancers and life-threatening genetic syndromes such as blistering skin disorders. Fuchs' current research focuses on the molecular mechanisms that underlie how multipotent stem cells respond to external cues, change their program of gene expression, exit their niche and adopt specific fates to make the epidermis, sebaceous glands and hair follicles of the skin. In tackling the biology of normal tissue homeostasis, Fuchs has begun to explore how this process changes during wound repair and in human disorders, e.g. cancers, where tissue development goes awry. Fuchs' lecture will focus on stem cells of the skin and their promise for regenerative medicine.