

Epigenetics in Cancer Prevention: Early Detection and Risk Assessment Workshop

Agenda

Mission: The goal of the Workshop is to evaluate the state of science and determine the future research needs to stimulate research on implications of epigenetics in early detection, risk assessment and prevention of cancer. The objectives of the workshop include, but are not limited to, the following:

- define epigenetic changes- terminology
- development of technology for high-throughput assays
- epigenetic mechanisms in cancer
- epigenetic changes: clinical correlates

Day One

8:30 AM	Welcome Address	<i>Peter Greenwald</i>
8:40 AM	Charges to Participants	<i>Mukesh Verma</i>
8:50 AM	Significance of the Topic	<i>David Sidransky</i>

Basic Concept

9:20 AM	Basic mechanisms underlined in alterations of DNA methylation in cancer. <i>Stephen Baylin</i>
9:45 AM	Epigenetic variation in normal and neoplastic tissues - implications for risk assessment and disease prevention. <i>Jean-Pierre Issa</i>
10:10 AM	Chromatin and cancer epigenome. <i>Fyodor Urnov</i>
10:35 AM	Coffee Break

Technology

10:55 AM	Methylation specific PCR in early cancer detection. <i>James Herman</i>
11:20 AM	Technology advancement in epigenetics and cancer. <i>Peter Laird</i>

Applications

11:55 AM	A challenge of early detection of primary brain tumors: where to start? <i>Waldemar Debinski</i>
12:20 PM	Gastric carcinogenesis associated with <i>Helicobacter pylori</i> involves loss of clooxygenase-2 promoter methylation. <i>Keith Wilson</i>
12:45 PM	Lunch

2:00 PM - 5:00 PM Sessions I - IV

Session I	Define epigenetic changes - terminology
Session II	Epigenetic mechanisms in cancer
Session III	Development of technology for high-throughput assays
Session IV	Epigenetic changes: clinical correlates

General Issues:

- How can we use our knowledge of epigenetics for early cancer detection and risk assessment?
- What are the mechanisms of acetylation and methylation regulation?
- Is DNA methylation an initiating event in gene silencing or consolidating mechanism that comes into play once a gene has become inactive through other mechanisms?
- What is the role of pericentric hypermethylation and translocation (protection against viruses and transposable elements) in epigenetics?
- What is the role of non-CpG methylation in mammalian cells?
- How are cell-type specific DNA methylation patterns established and maintained?
- What are the factors that provide stability to the maintenance enzymes of acetylation and methylation?
- Are epigenetic changes inherited? What are the mechanisms?
- Are there other mechanisms of epigenetic regulation of gene expression?

2:00 PM

Session I: Defining epigenetic changes - terminology

Chair: Peter Jones

Co-Chair: Jean-Pierre Issa

Moderator: Waldemar Debinsky

The objective of this session is to define the terminology used in epigenetics and to come to a consensus for future definitions. There exists a concern about the hereditary aspects of gene regulation mediated by methylation and/or acetylation.

Specific Issues:

- Genomic imprinting and epigenetics
- Epigenetics and X-chromosome

- Epimutations and epimutagens
- Chromatin modeling and epigenetics

2:50 PM

Session II: Epigenetic mechanisms in cancer

Chair: David Sidransky
 Co-Chair: Benjamin Tycko
 Moderator: Max Costa

The objective of this session is to identify and prioritize research in the -epigenetics area and understand the mechanisms involved. Exogenous factors such as radiation, smoke, free reactive oxygen, free radicals (nickel, arsenic, cadmium etc.) and endogenous factors such as stress and hormones affect gene regulation via epigenetics.

Specific Issues:

- Genomic imprinting and disease susceptibility
- Cancer-associated infectious agents and epigenetics
- Pericentric hypermethylation and translocation
- Demethylase/deacetylase and methylase/acetylase transferase regulation
- DNA repair mechanisms and epigenetics
- DNA methylation in mitochondria

3:30 PM

Coffee Break

3:40 PM

Session III: Development of technology for high-throughput assays

Chair: Stephen B. Baylin
 Co-Chair: Tim Huang
 Moderator: Peter Laird

Although the field of epigenetics is growing rapidly, technological advancement in quantitation of methylation and high-throughput assays has yet to be developed. The objective of this session is to discuss cutting edge technology in the epigenetics field.

Specific Issues:

- Methylation-specific PCR
- Sensitivity of current technologies
- Methylation sensitive RDA (Representational Difference Analysis)
- Technology in RNA methylation
- Public database of methylated genes

4:20 PM	Session IV: Epigenetic changes: clinical correlates
<p>Chair: James Herman Co-Chair: Timothy Bestor Moderator: Keith Wilson</p> <p>Application of epigenetics in early cancer detection and risk assessment is the major focus of this workshop. The focus of this session will be on clinical correlates and epigenetics as they exist today and as they should exist in future.</p> <p>Specific Issues:</p> <ul style="list-style-type: none"> • Implication of epigenetics in clinical studies: heritable vs. sporadic (breast/ovarian cancer, HNPCC) • Colon, lung, gastric, breast, esophageal, prostate cancer and epigenetics: examples • Epidemiology and epigenetics • Pharmacoepigenetics • Gene therapy and methylation of retroviral vectors 	
5:00 PM	Adjourn

Day Two

8:30 AM	Keynote Address: How DNA methylation impacts mammalian epigenetics and cancer. <i>Peter Jones</i>
9:15 AM	Cancer genomics and epigenetics. <i>Timothy Bestor</i>
9:45 AM	Prevention wrap-up: perspectives and prospectus. <i>Andrew Feinberg</i>
10:30 AM	Coffee Break
10:50 AM	Reports and Recommendations: Session I Reports and Recommendations: Session II Reports and Recommendations: Session III Reports and Recommendations: Session IV
11:45 AM	General Discussion Discussion on publication of the workshop proceedings
12:00 PM	Adjourn