Cancer Progress Conference
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Michael B. Sporn, MD
Professor of Pharmacology and Medicine
Dartmouth Medical School
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Statement

Michael Sporn is the founder of a new company, Triterpenoid Therapeutics, whose goal is to introduce new synthetic triterpenoids into clinical use.
Projected Huge Increase in Pancreatic Cancer Deaths, USA

2010 --- 37,000 Deaths, actual

2030 --- 63,000 Deaths, projected

• Pancreatic Cancer is projected to be the second leading cause of cancer deaths in the USA by 2030

Concept 1

The disease is carcinogenesis, not cancer

- Carcinogenesis is a *process*, not a state
Process of Carcinogenesis

Progression takes many years

Progression model for pancreatic cancer. The progression from histologically normal epithelium to low-grade PanIN to high-grade PanIN (left to right) is associated with the accumulation of specific genetic alterations (Hruban et al., *Am. J. Pathol.*, 156:1821, 2000)
Cancer is a polygenic disease

Pancreatic cancers contain an average of 63 genetic alterations
Concept 2

People who are asymptomatic may not be healthy
The concept of ‘health’ needs to consider future events, not just the immediate present.

A healthy person?

I don’t have any symptoms and I’m not feeling any pain!
Concept 3

Use of drugs to suppress carcinogenesis during the latency period after mutagenic initiation
Chemoprevention Works!!!!!
MMTV-neu transgenic mice (Jax Labs) were fed powdered control diet or preventive agents in the same diet, beginning at 7 weeks of age. Mice (numbers shown in parentheses) were palpated weekly for tumors, and none were detected before 20 weeks of age. The experiment was terminated after mice were fed experimental diets for 60 weeks. Liby et al., Clin. Cancer Res. 12: 5902, 2006
Complete Protection against Aflatoxin B$_1$-Induced Liver Cancer with a Triterpenoid: DNA Adduct Dosimetry, Molecular Signature, and Genotoxicity Threshold


_Cancer Prev Res; 7 July 2014_
Complete Prevention of Liver Cancer in Rats by CDDO-Im
Chemopreventive drugs may function more effectively if dosed intermittently rather than continuously
A new paradigm for chemoprevention

M. Rendi, N. Suh, et al., Cancer Res. 64: 3566, 2004
What we need to do
• New Ideas
• New Diagnostic Tools
• New Drugs
• The Old DNA $\rightarrow$ RNA $\rightarrow$ Protein Model is *obsolete*

• A **New World of Network Biology**
Fantasy and Fact in Signaling

It Ain’t So  The Real World

Levy et al., *Science* 328, 983, 2010
New Diagnostic Tools

- Genomic
- Proteomic
- Metabolomic

These will identify people at super high risk
These will be highly profitable for Pharmas
New Drugs
Triterpenoid Scaffolds

- **Oleanane** (olives)
- **Ursane** (apples)
- **Lupane** (birch bark)
- **Dammarene** (ginseng)
- **Friedelane** (cork)
Oleanane Triterpenoid Drugs

CDDO

CDDO-Methyl ester

CDDO-Im

CDDO-Imidazolide

CDDO-EA

Liby, Sporn Pharmacol Revs 2012.
Triterpenoids and suppression of inflammation
Potency of Triterpenoids
CDDO-Im Suppresses iNOS Induction in Macrophages

FemtoMolar Activity of CDDO-Im
To Upset the Apple Cart
“Cancer is Fundamentally an Epigenetic Disease”
“The Key Role of Epigenetics in Human Disease Prevention and Mitigation”
