

# **24th Annual Cancer Progress Conference**

## A Few Remarks on Chemoprevention of Cancer

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**New York, NY**  
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# A New Approach to Control of Cancer is Badly Needed

## Total Cancer Deaths in Men, USA

Site	1971	2013
Lung	53,000	87,000
Colorectal	22,000	26,000
Prostate	17,000	30,000
Pancreas	10,000	19,000

## Total Cancer Deaths in Women, USA

Site	1971	2013
Lung	11,000	72,000
Colorectal	24,000	25,000
Breast	31,000	40,000
Pancreas	8,000	19,000
Ovary	10,000	14,000

Deaths for 2013 are estimated. These are total deaths, not rates which are adjusted for population. Data from Siegel, R.L. et al., CA Cancer J Clin 63: 11-30, 2013.

# **Can Chemoprevention really work?**

- **Does it work in experimental animals?**
- **Does it work in real people?**

# Chemoprevention **Works**

- **Basic science** in support of chemoprevention
  - What is chemoprevention?
  - Proof of principle in animal studies
    - Lung
    - Breast
    - Colon
    - Prostate
    - Brain...total failure!
    - Pancreas
    - Liver
    - Bladder
    - Ovary

# **Clinical evidence for cancer chemoprevention**

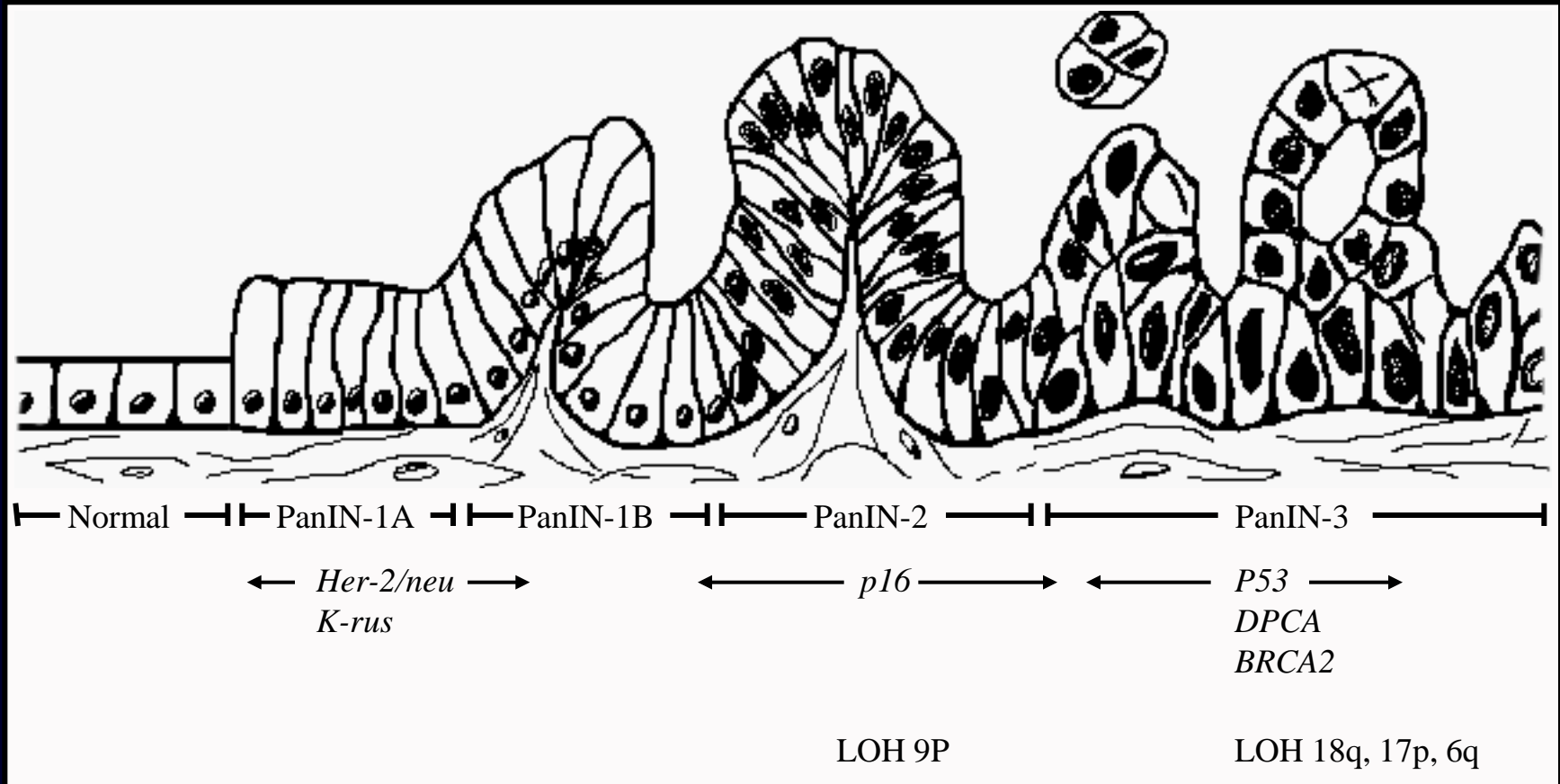
- **Breast cancer**
  - **SERMS**
    - Tamoxifen
    - Raloxifene
    - Lasofoxifene
  - **RETINOIDS**
    - Fenretinide (pre-menopausal women)

# Clinical evidence for cancer chemoprevention

- **Prostate Cancer**
  - **Finasteride**
  - **Dutasteride**

- The disease is **carcinogenesis**,  
**NOT cancer**
- What is carcinogenesis?
  - **Carcinogenesis** is a **process** that extends over a long time, **not a static event**

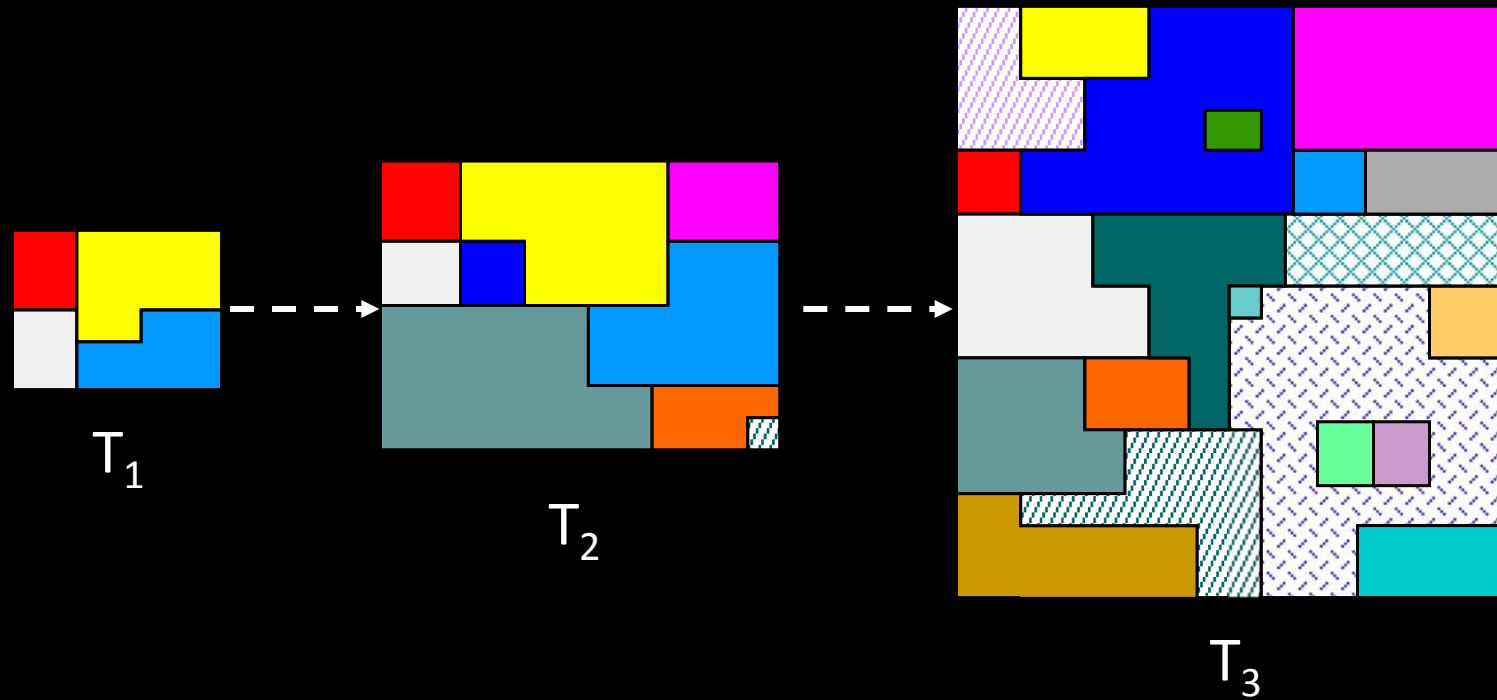
# Progression Model for Pancreatic Cancer



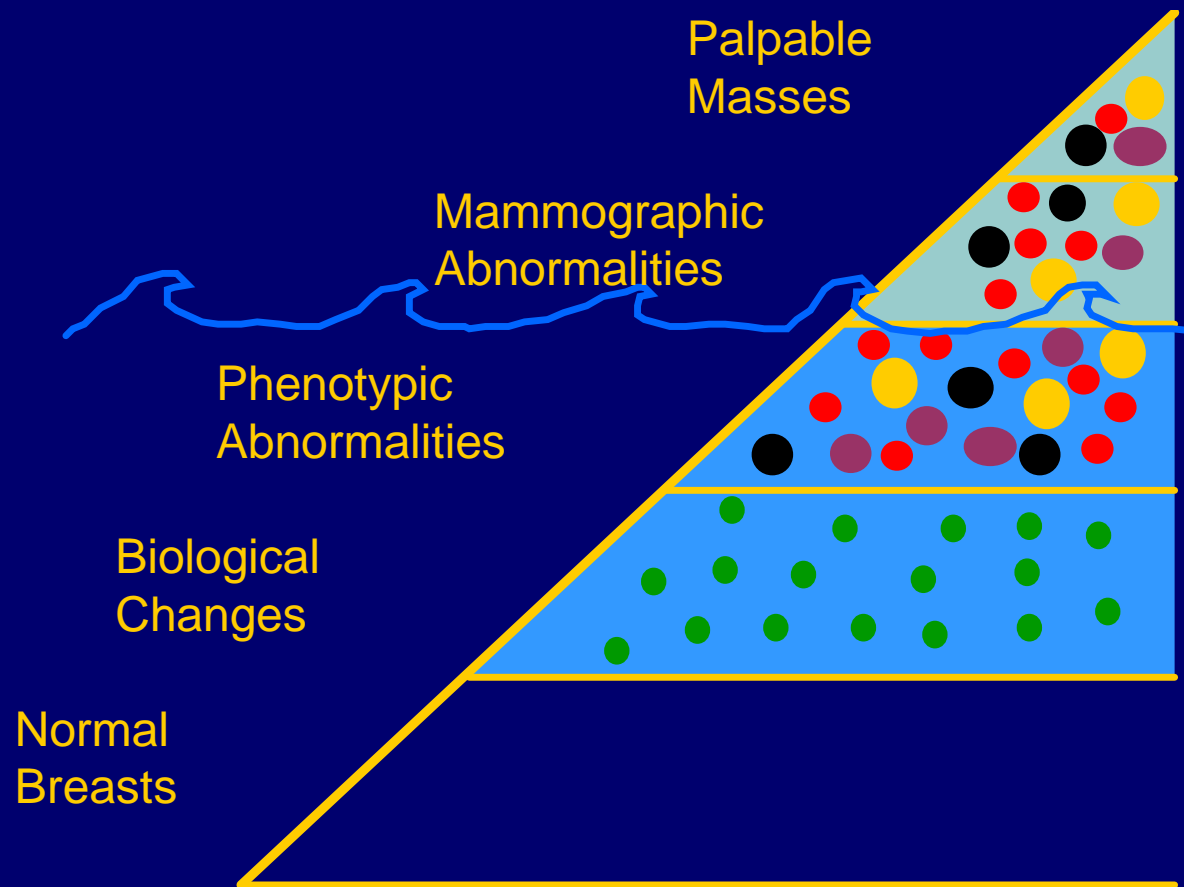
Progression model for pancreatic cancer. The progression from histologically normal epithelium to low-grade PanIN to high-grade PanIN (left to right) is associated with the accumulation of specific genetic alterations (Hruban et al., Am. J. Pathol., 156:1821, 2000)



# Changes in the Cellular Composition of Tumors During Tumor Progression



# The Iceberg



- Invasive Cancer
- Non-invasive Cancer
- Biological Changes
- Hyperplasia
- Benign

**The goal is to melt the iceberg  
before it surfaces**

# My Personal #1 Priority

- **Development of new drugs for chemoprevention**
  - High degree of **EFFICACY**
  - High degree of **SAFETY**
- **Development of effective combinations**

# Conceptual Negativity

- Inadequate conceptions of a “healthy person”
- Benefit vs. risk arguments - side effects of drugs
- “You need to treat thousands of people to prevent one cancer death”
- “Don’t tamper with our bodies”
- Poorly designed clinical trials

# **Inadequate** conceptions of a **“healthy”** person

- The bizarre notion that people are “healthy” until they have actual symptoms of disease
  - Is there a **smoldering fire** in the **barn** before it bursts into **flames**?

**The young man with his head on the block is a metaphor for the patient with pancreatic cancer, shortly before diagnosis**

**A HEALTHY PERSON?**



# Misperception of the Concept of Risk

- It's really **“risk vs. risk”**, not **“benefit vs. risk”**
  - It's the **risk of doing nothing** vs. the **risk of taking** a chemopreventive **drug** for a long period of time.
- Need for development of a **“Scorecard”** of risk for cancer



# European Society of Cardiology Scorecard for 10-year risk of fatal cardiovascular disease

		Non-smoker					Smoker					Age
Systolic blood pressure	180	14	16	19	22	26	26	30	35	41	47	65
	160	9	11	13	15	16	18	21	25	29	34	
	140	6	8	9	11	13	13	15	17	20	24	
	120	4	5	6	7	9	9	10	12	14	17	
	180	4	4	5	6	7	7	8	10	12	14	50
	160	2	3	3	4	5	5	6	7	8	10	
	140	2	2	2	3	3	3	4	5	6	7	
	120	1	1	2	2	2	2	3	3	4	5	
		4	5	6	7	8	4	5	6	7	8	
												Cholesterol mmol

# High Risk Groups

- **Restrict chemoprevention trials to people of exceptionally high risk**
- **Small cohort of patients would yield valuable data -- no need to treat thousands of people**
  - **BRCA mutation**
  - **Pancreatic incidentaloma**
  - **Advanced dysplasia of lung epithelium**

# It's all about quality of life

- Are we here only to treat advanced disease?

OR

- Are we really here to keep people healthy?