

Seeing the Unseen: How to Personalize Cancer Screening and Start Winning the War on Cancer

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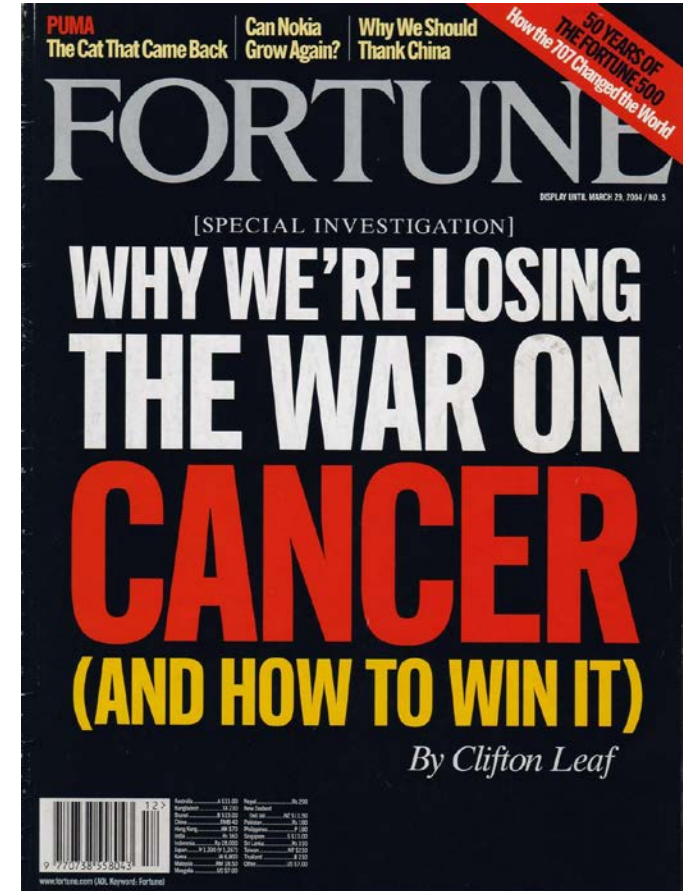
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Program Leader

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- “Each life is precious but in economic terms, >50% of all economic growth over the past 200 years can be traced to increase in life expectancy”
- “Early detection is the only viable strategy to significantly reduce cancer mortality in the foreseeable future”
- Two key issues:
 - *Underdiagnosis*
 - *Overdiagnosis*



LUNG CANCER:

An Example of *Underdiagnosis*

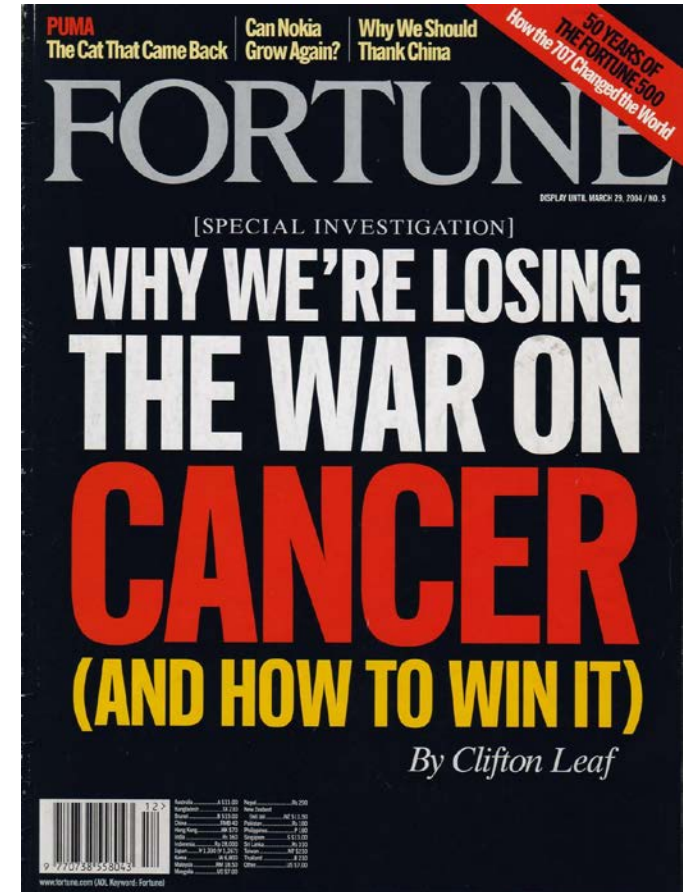
- The 1st major cause of cancer deaths in the U.S.
- 5 year survival is dictated by stage at diagnosis:
 - >90% for stage 1,
 - 49% for localized stage,
 - 16% for regional,
 - 2% for distal metastases.
- Only 16% of lung cancers are diagnosed at a localized stage
- Most patients come to medical attention because of symptoms that are harbingers of advanced, incurable disease

LUNG CANCER:

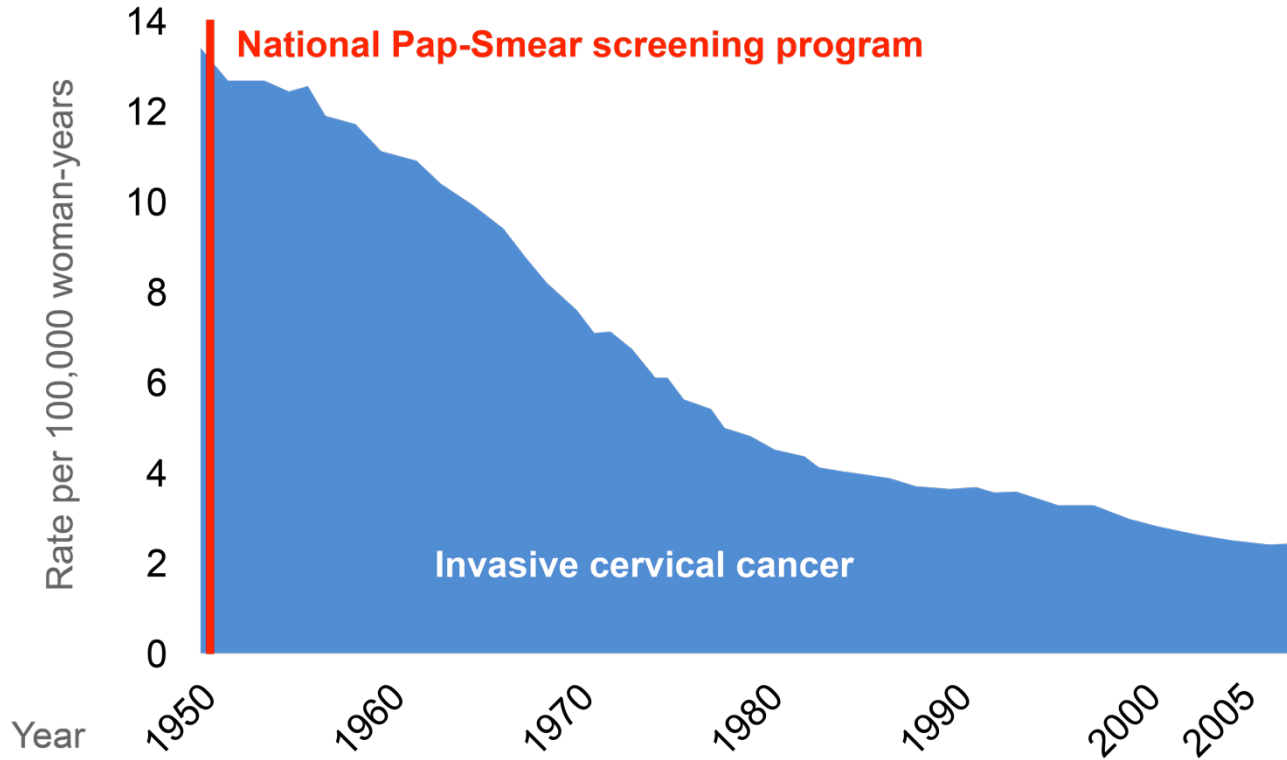
An Example of *Overdiagnosis*

- LDCT has been approved for lung cancer screening in heavy smokers
- PPV for nodules 4 mm or larger identified on baseline LDCT is 3.8%

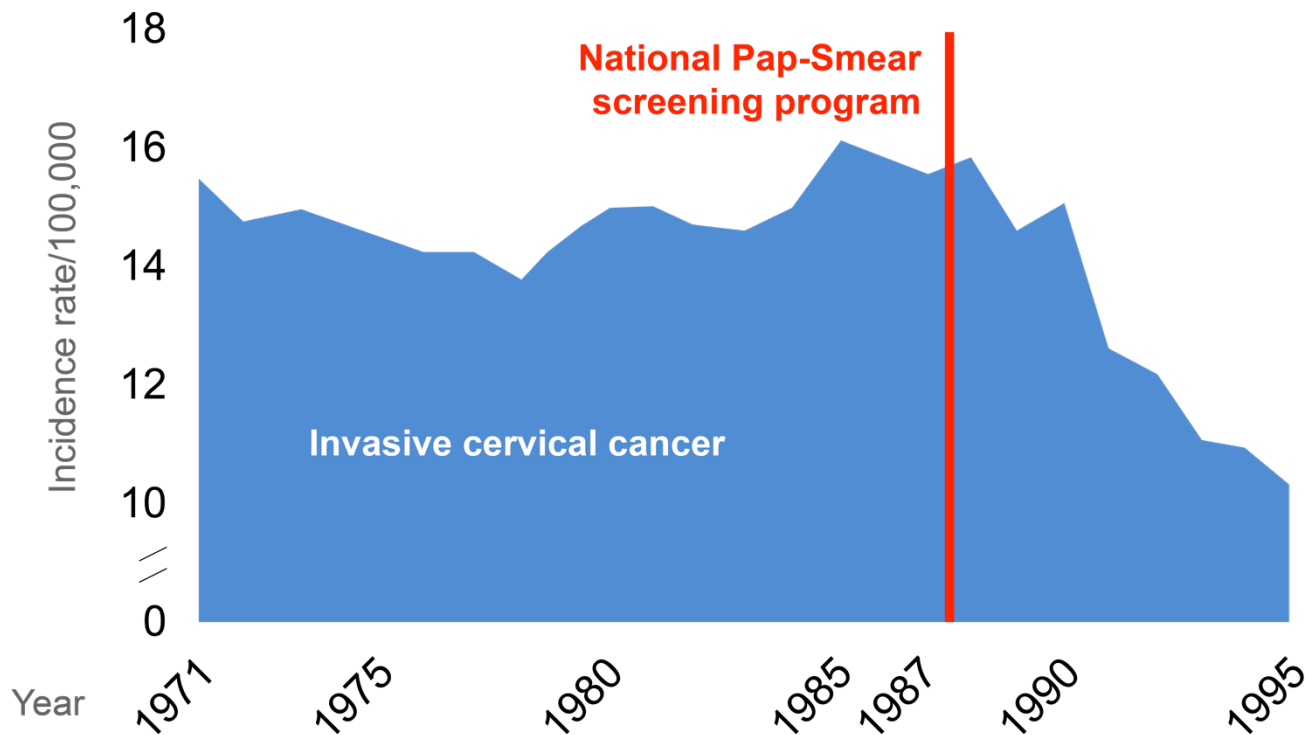
- We don't do “too much” screening
- We do too little screening with imperfect tests.
- Need ‘smart’ screening:
 - Sensitive to **treatable clinically significant** lesions
 - Cost-effective
 - Implementable in population
- Cervical cancer screening is a proven success story!



Effect of screening on death rates from cervical cancer in the United States



Effect of screening on incidence of cervical cancer in England



General Population



**1st Tier
Screening**



- Low-cost
- Primary care setting
- Non/minimally-invasive
- Sensitive to early, curable, clinically significant lesions

**Conventional
Cancer
Screening**



Patient with Early Cancer

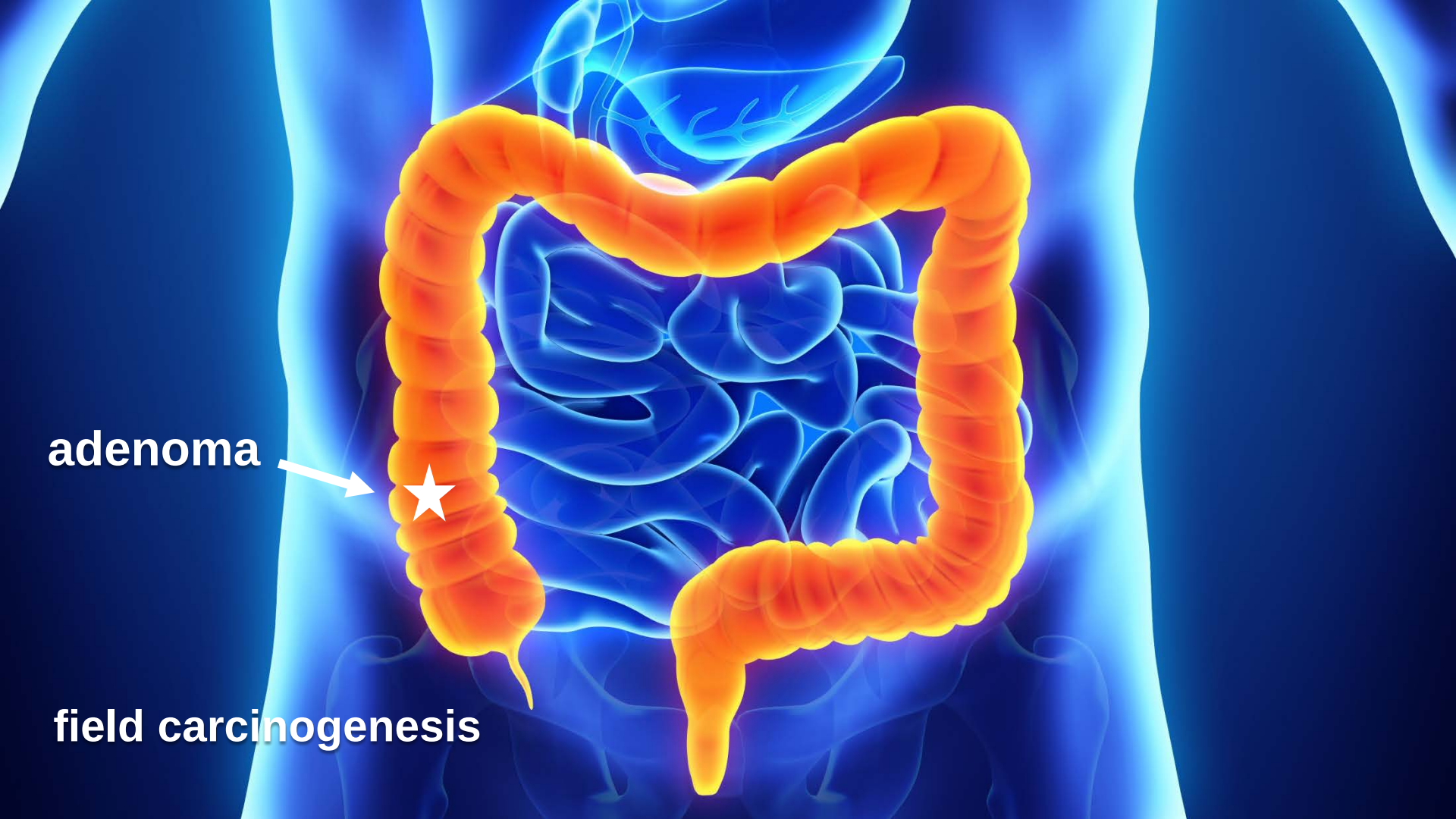


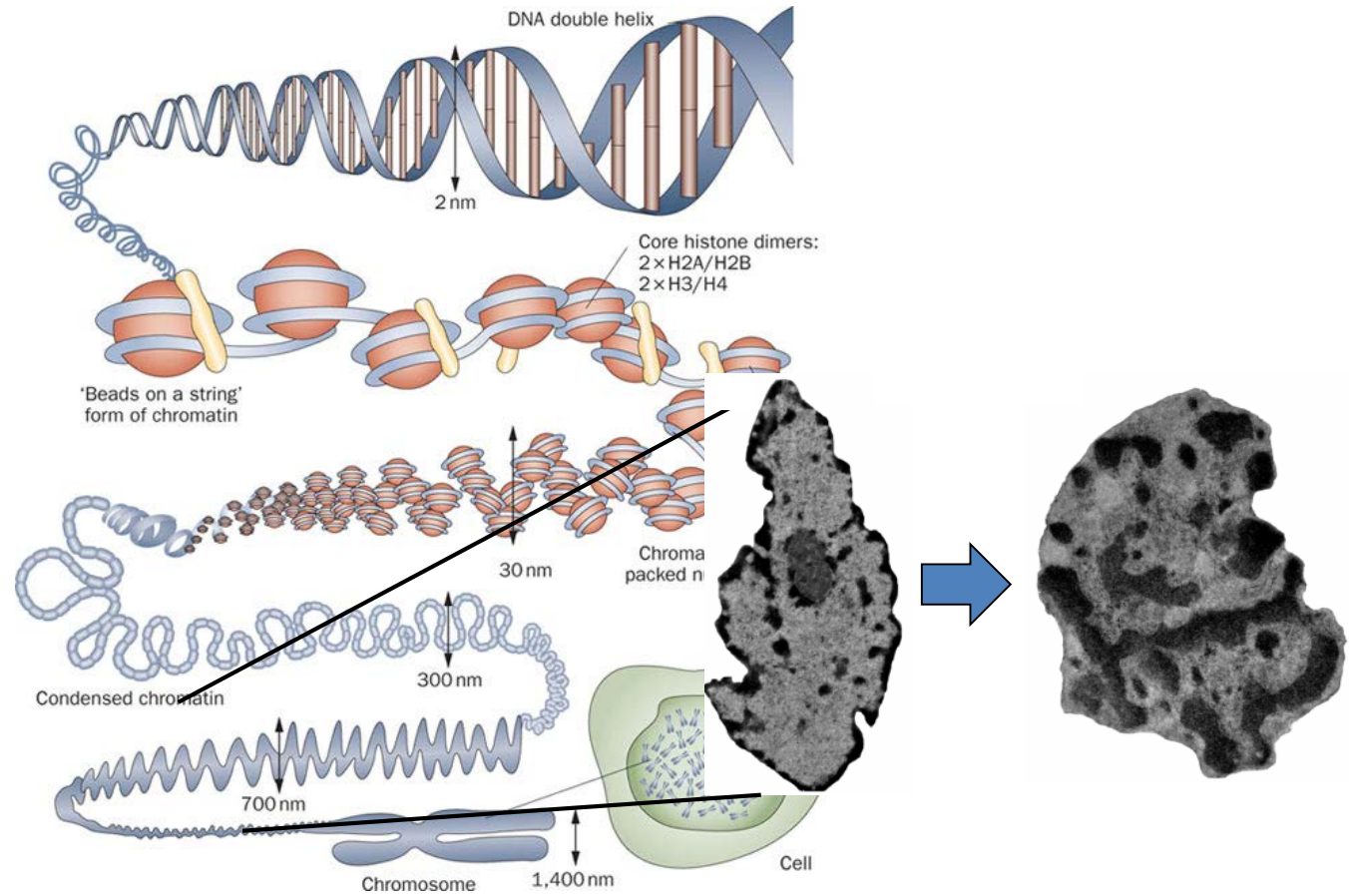


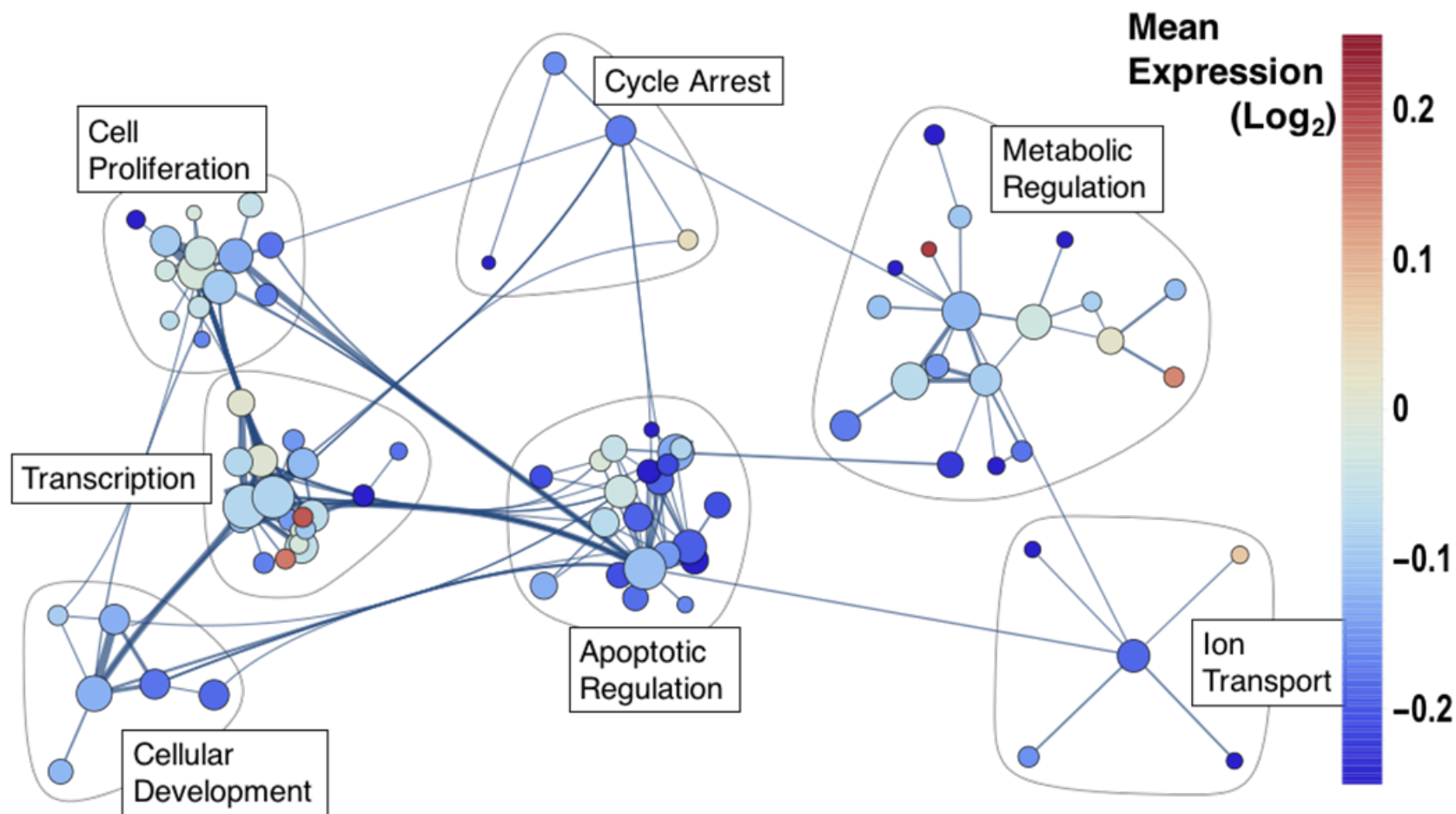
adenoma

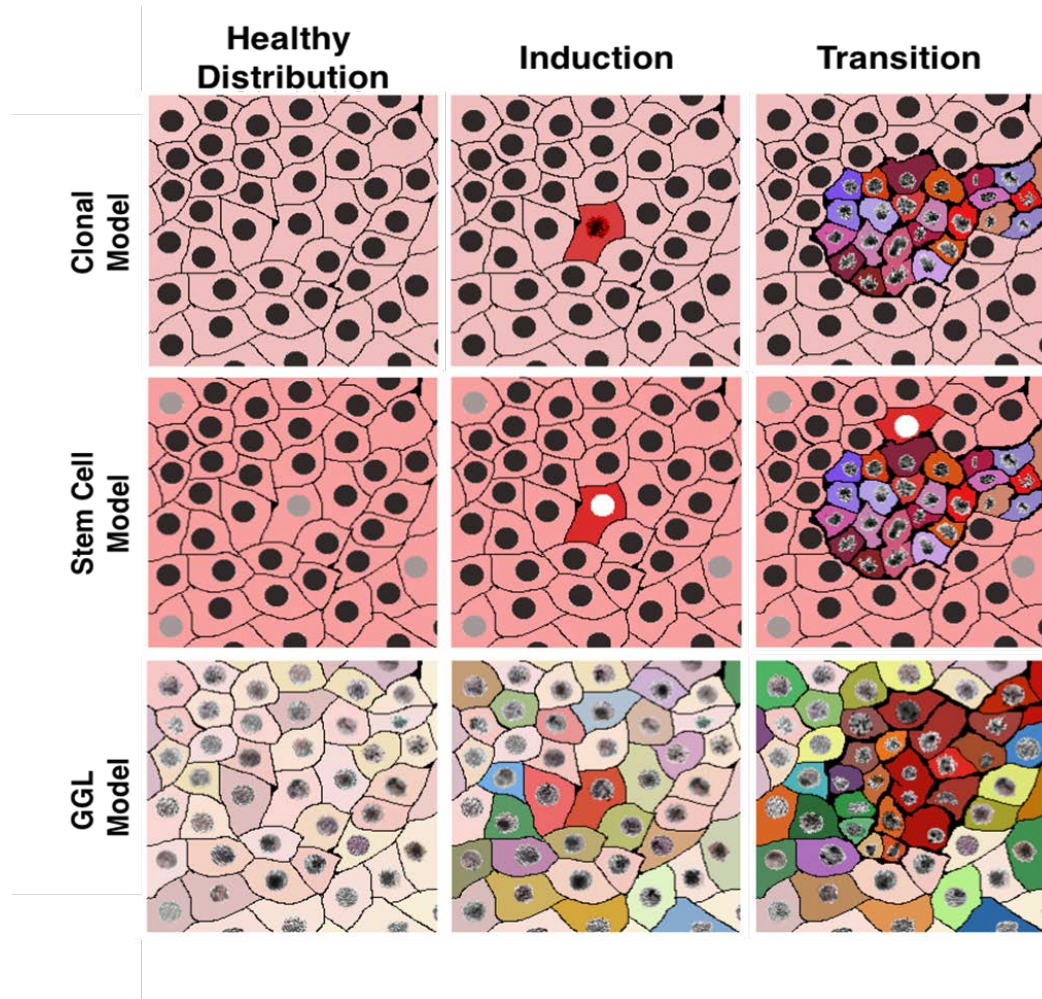
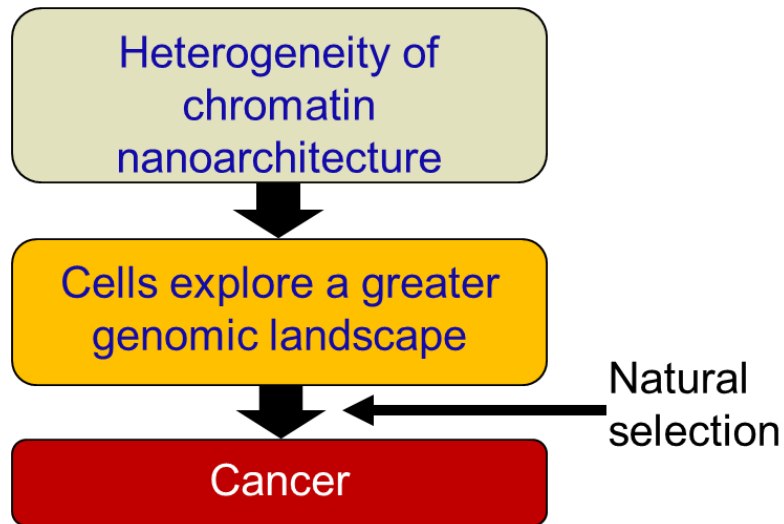


field carcinogenesis

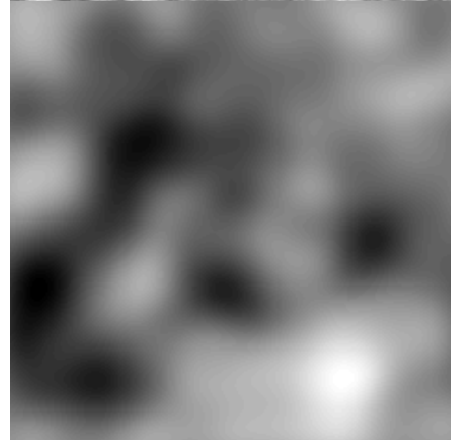
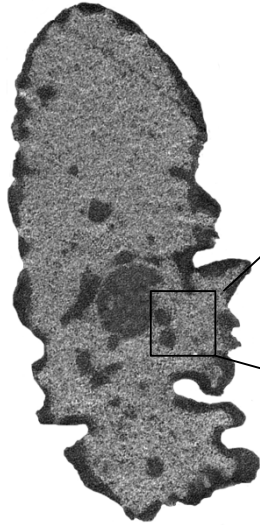


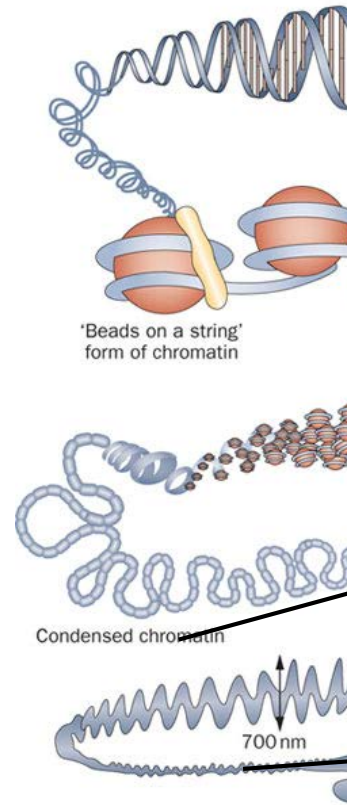




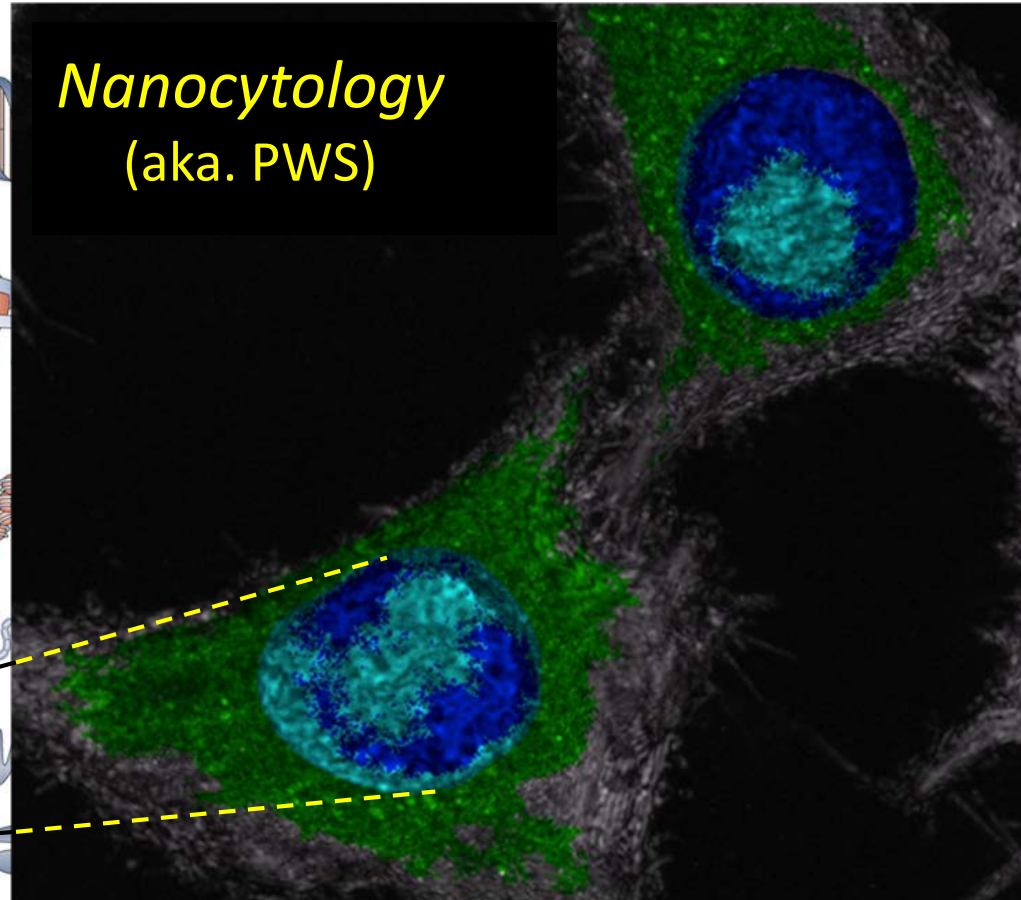


"Defectives shifted"

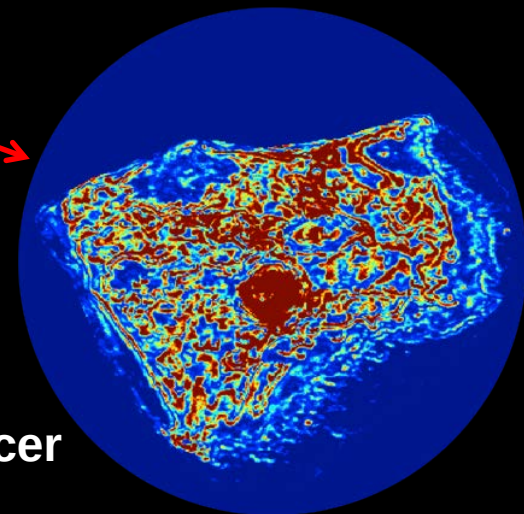
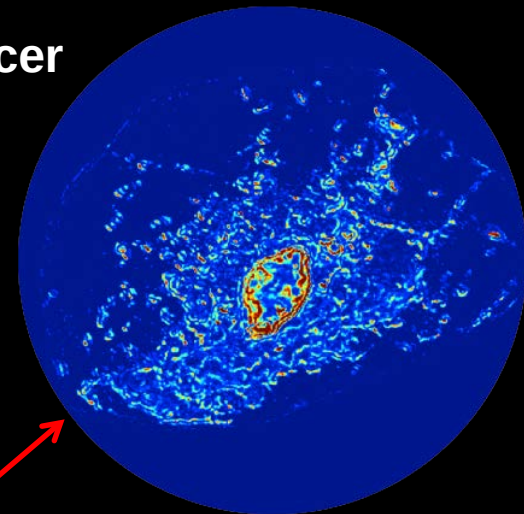
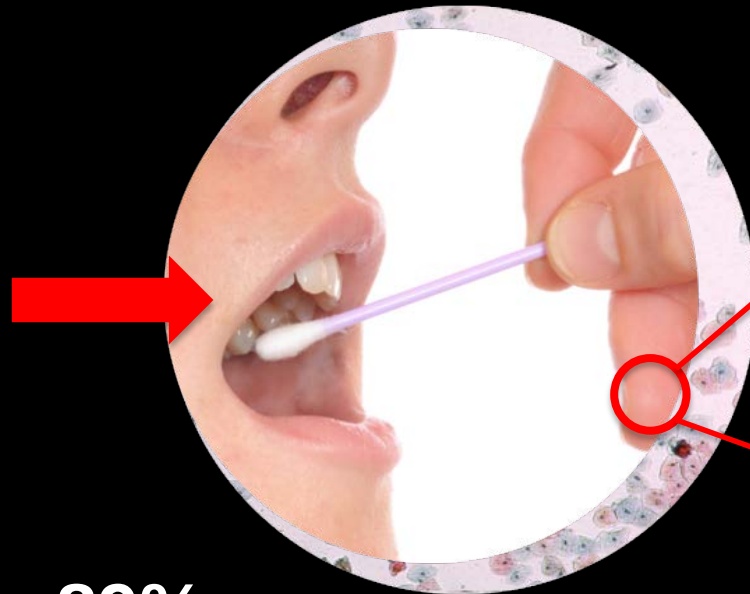




Nanocytology (aka. PWS)



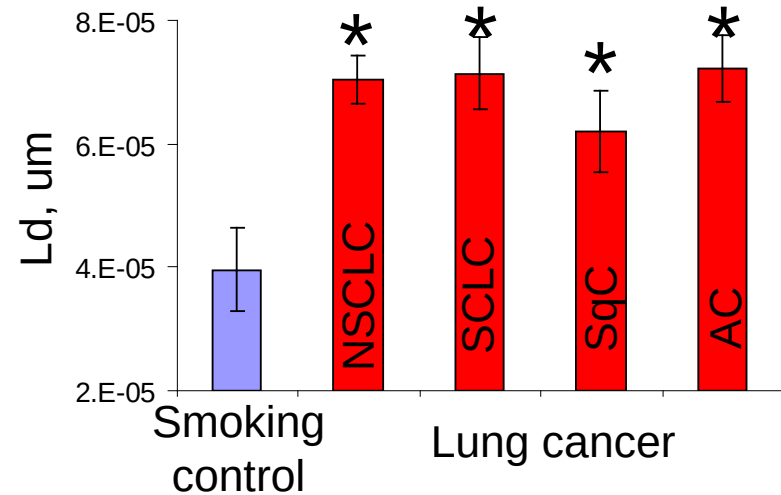
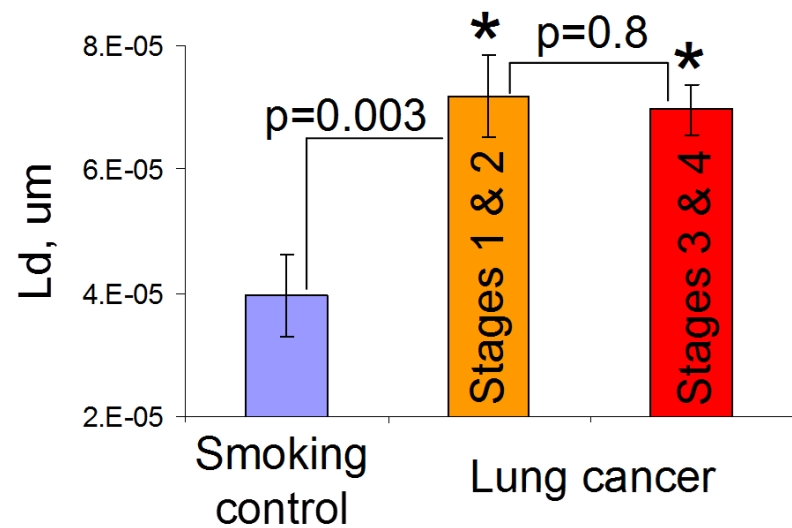
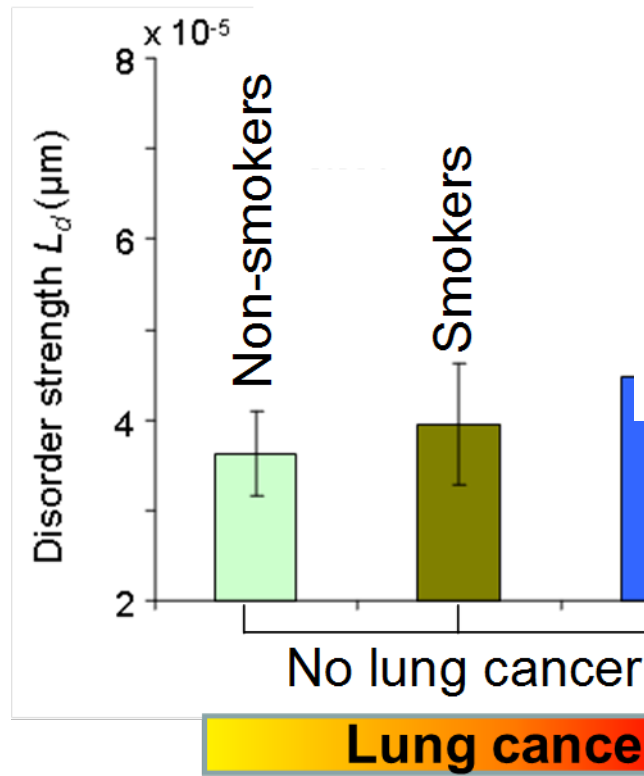
No cancer

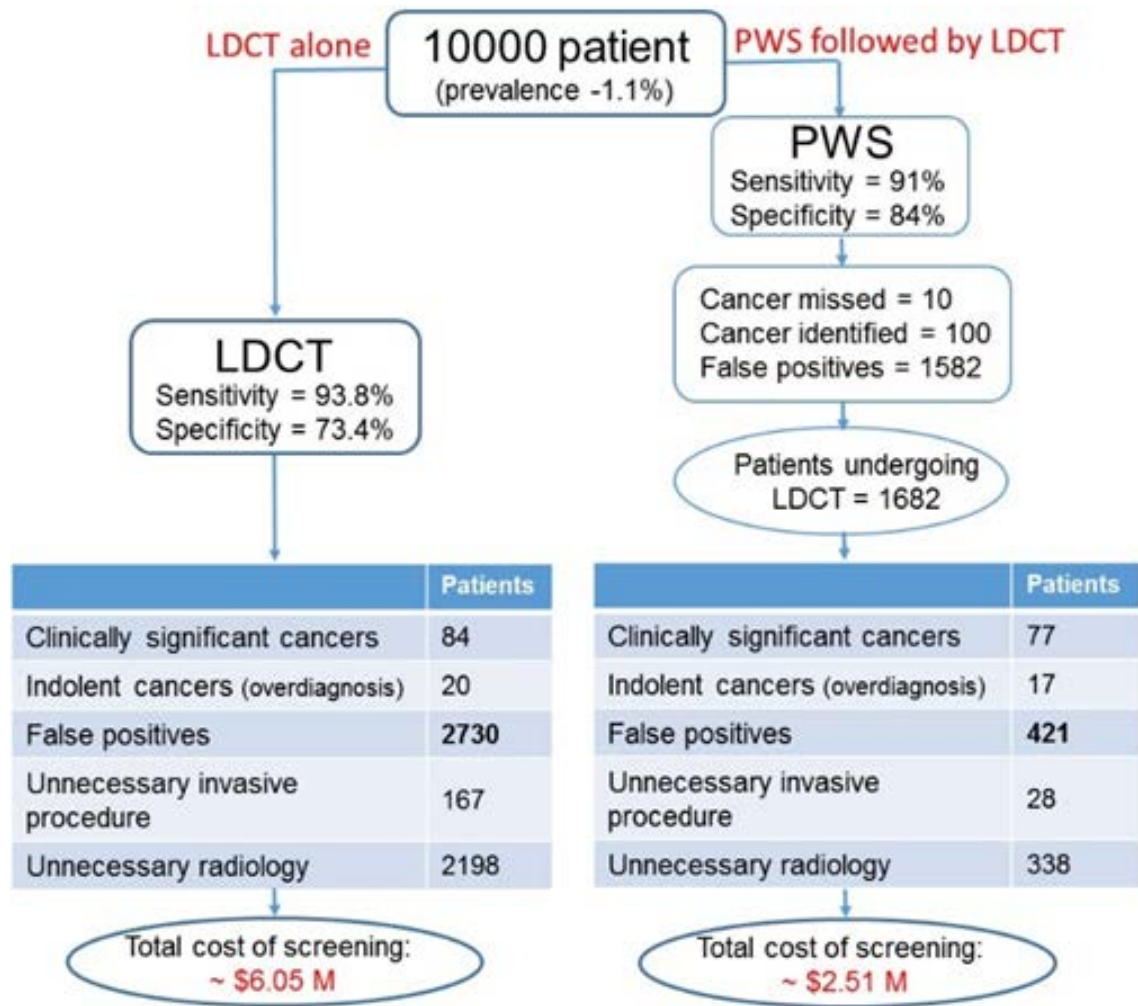


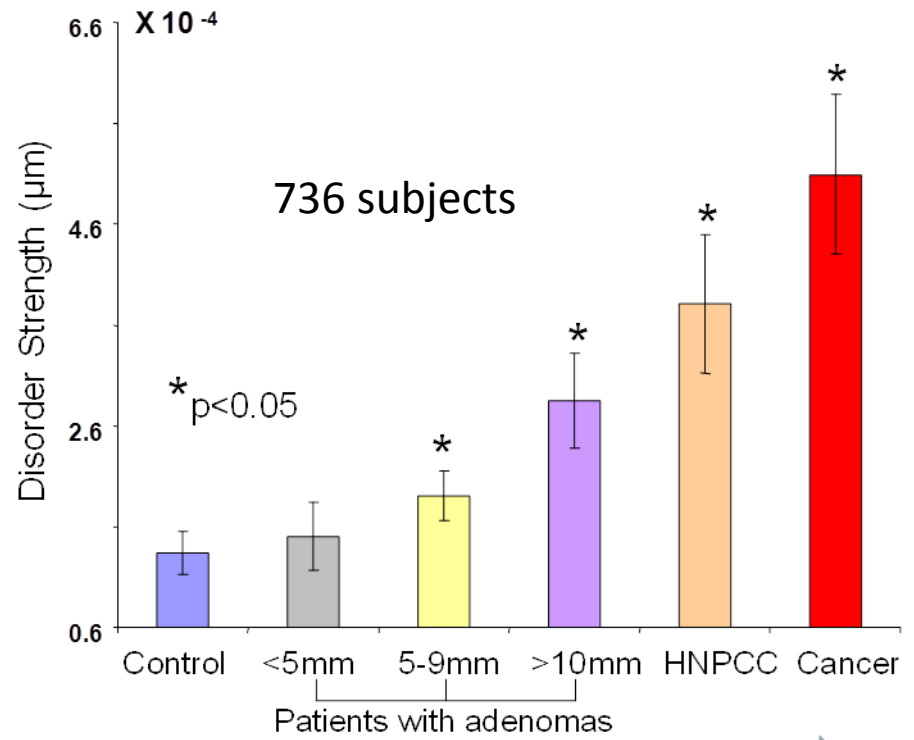
Lung cancer

Sensitivity 89%
Specificity 95%

650 subjects





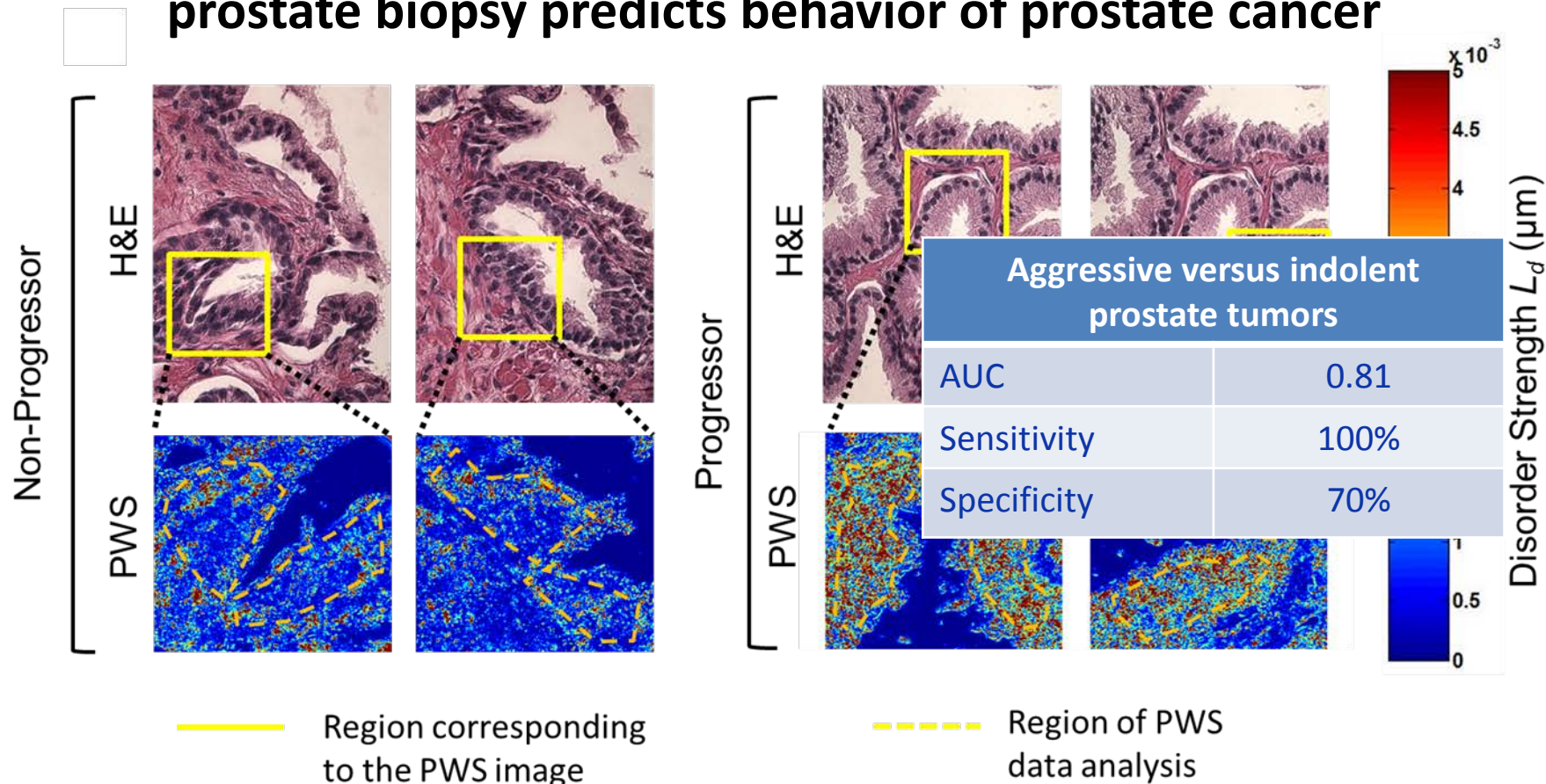


Rectal nanocytology for colon cancer screening

Nanocytology for patients with advanced adenomas	
AUC	0.93
Sensitivity	85%
Specificity	85%

State-of-the-art	FOBT	FIT	Fecal DNA
Sensitivity	11%	34%	44%

Nanocytological analysis of histologically-normal Gleason 6 prostate biopsy predicts behavior of prostate cancer



Nanocytology: a ubiquitous marker of carcinogenesis

Cancer	Cell source	End-point
Lung	Buccal mucosa	Early-stage lung cancer
Colon	Rectum	Advanced adenomas
Prostate	Histologically-normal biopsy (active surveillance)	Aggressive vs. indolent cancers
Ovarian	Endocervix	Serous ovarian cancers
Esophageal adenocarcinoma	Upper esophageal segment (squamous epithelium)	High-grade dysplasia and adenocarcinoma
Pancreatic	Periampullary duodenum	Pancreatic adenocarcinoma
Thyroid	Indefinite FNA cytology (archival)	Thyroid cancer

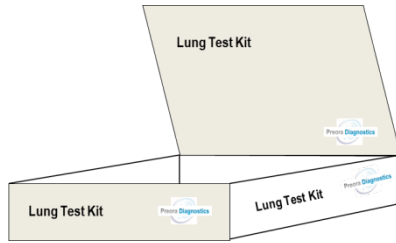
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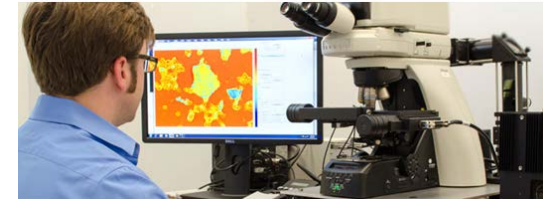
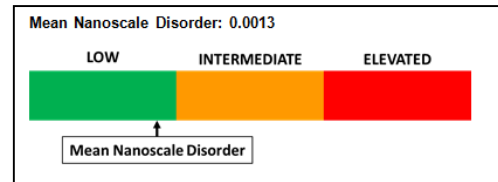
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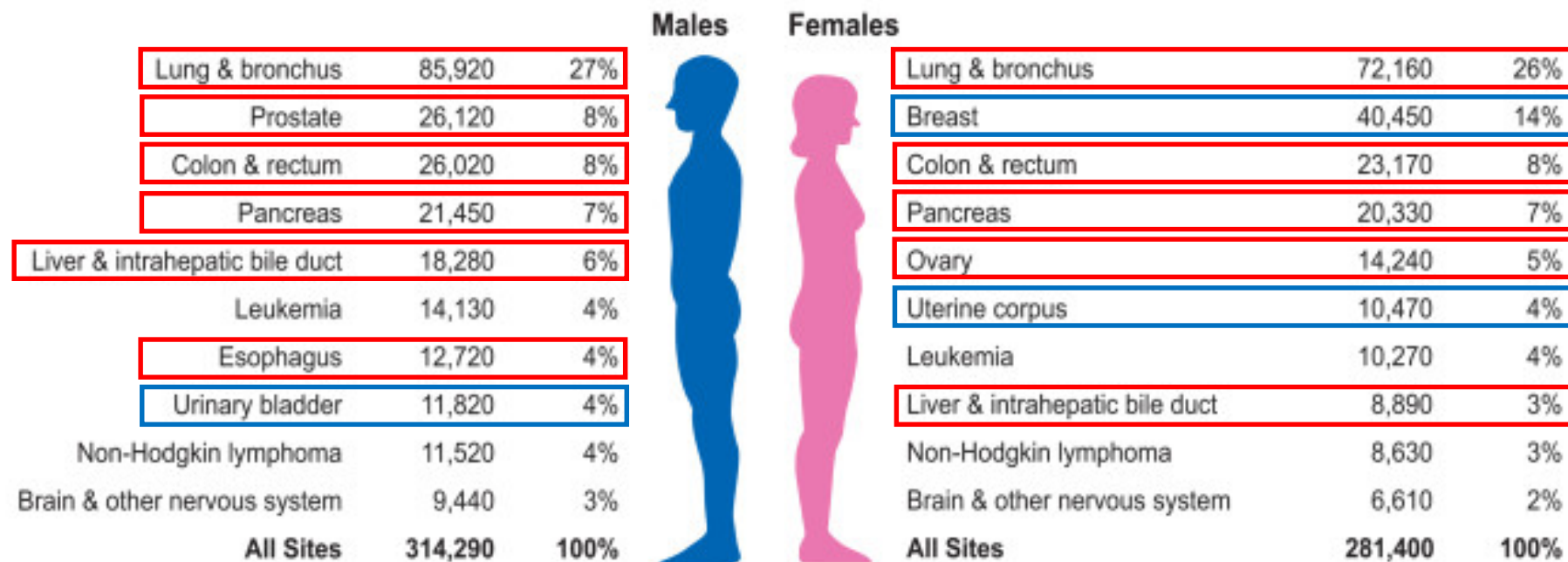
International Journal of Cancer, **133**(5), 1143-1152 (2013)



6-Step Process



Estimated Deaths



 Clinical data

56% of all cancer deaths

 Planned

17% of all cancer deaths

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