Pancreatic Cancer Screening

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Pancreatic cancer:
One of America's most lethal cancers

48,960
new cases per year

40,560
deaths per year

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Source: Am Cancer Soc. *Cancer Facts & Figures* 2015. Atlanta: American Cancer Society; 2015.

Collaborating to detect pancreatic cancer early

- Leveraging long-standing relationship and building on success of Cologuard®
- Significant intellectual property portfolio
- Proprietary know-how and biospecimens
- World leadership in cancer care through early detection

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Pancreatic Cancer Screening

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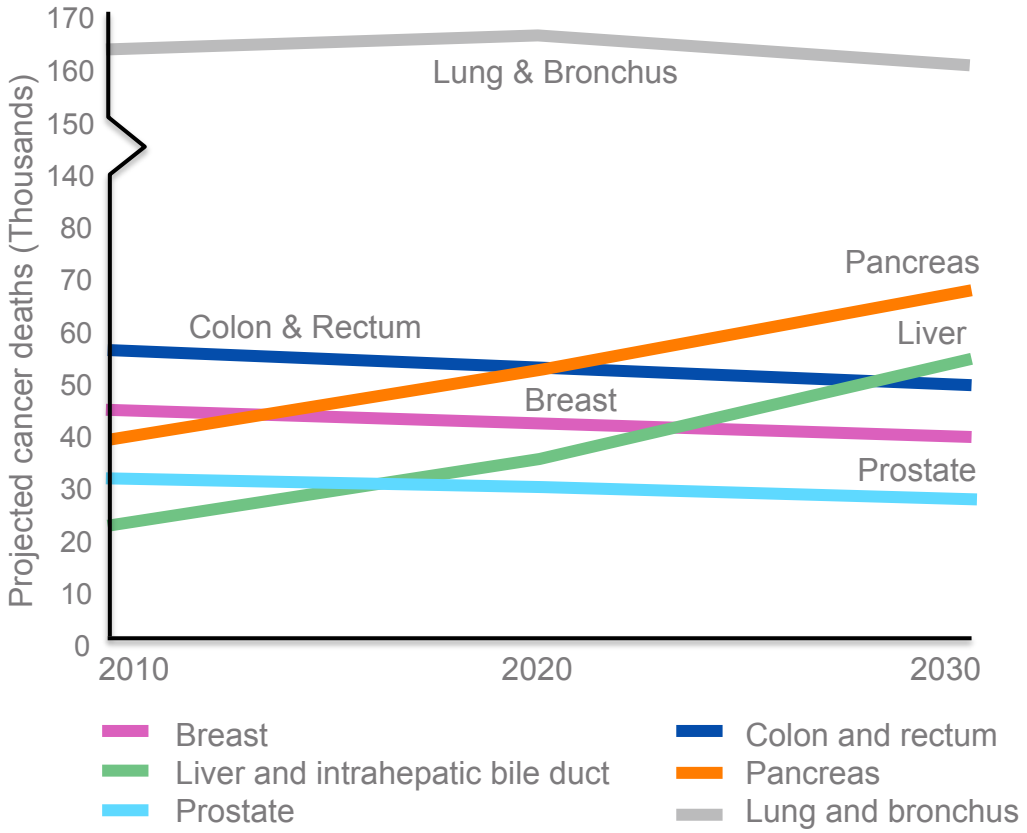
US mortality from pancreatic cancer rapidly increasing

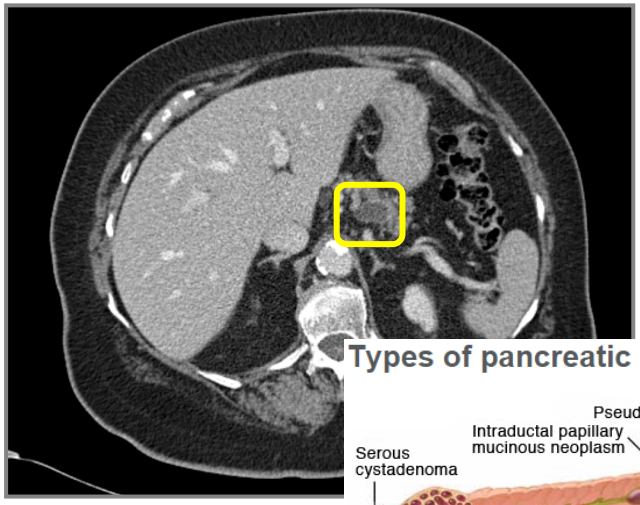
- Current: 4th leading cause of cancer deaths
- 2020: Increases by 70% (from 2010 levels) to become 2nd leading cause of cancer deaths

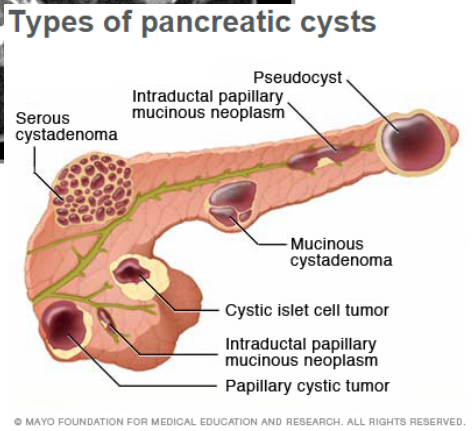


Source: *Rahib et al. Cancer Res 2014;74:2913

Two target lesions for early detection

- Earliest stage pancreatic cancer
  - Pre-symptomatic, Stage I
  - Challenges
    - No effective population screening tool
    - May appear as small nodules or cysts on imaging
    - Current tests inaccurate and potentially dangerous
- Pancreatic precancers
  - Cystic lesions
  - Challenges
    - Most incidentally found
    - Most do not progress
    - Unclear diagnosis and treatment management





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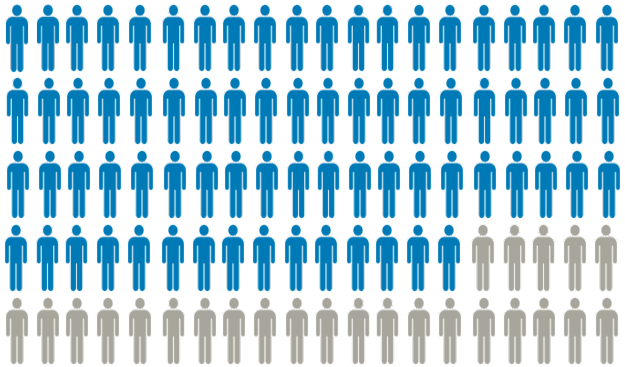
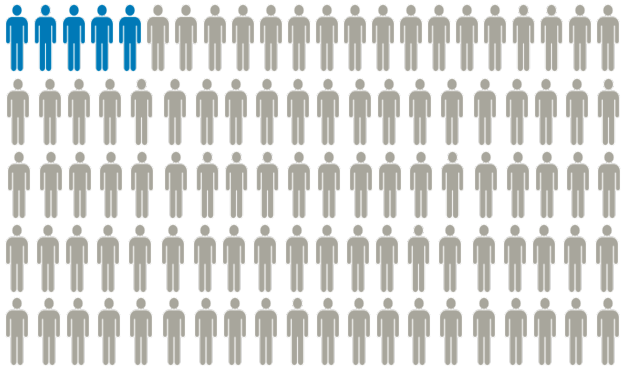
Urgency to detect pancreatic cancer in earliest stage



3 out of 4
survive 5 years if
asymptomatic with
Stage I



<5 out of 100
survive 5 years if
diagnosed with
Stages II, III or IV

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Source: SEER 18 2004-2010

Challenges with current diagnostic approach

- >600,000 incidental pancreatic lesions in US per year
  - 5-15% of all abdominal CT or MRI scans
- Limited accuracy of endoscopy and FNA

Mass/nodule	50-75%
Cyst	30%

Fine Needle Aspirate (FNA)

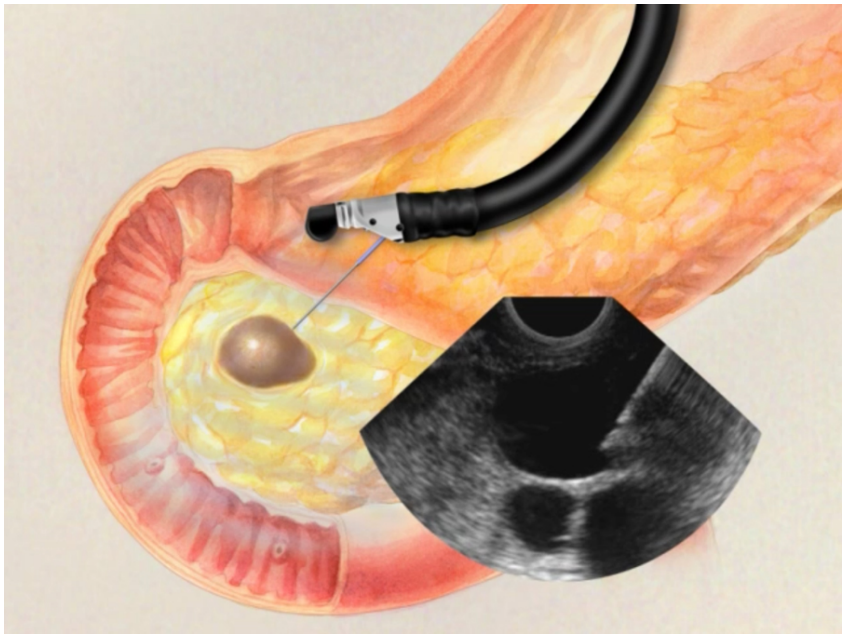

Image courtesy of The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

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Translating diagnostic challenges into opportunities

	Current Approach	Future Test
Issues	**Fine Needle Aspirate**	**Pancreatic Juice**
Accuracy	Suboptimal (results in under/over Rx)	Potentially High
Morbidity	<5%	<1%
Endoscopic ultrasound facility needed	Yes	No
Special training	Yes	No
Requires anesthesiologist	Yes	No

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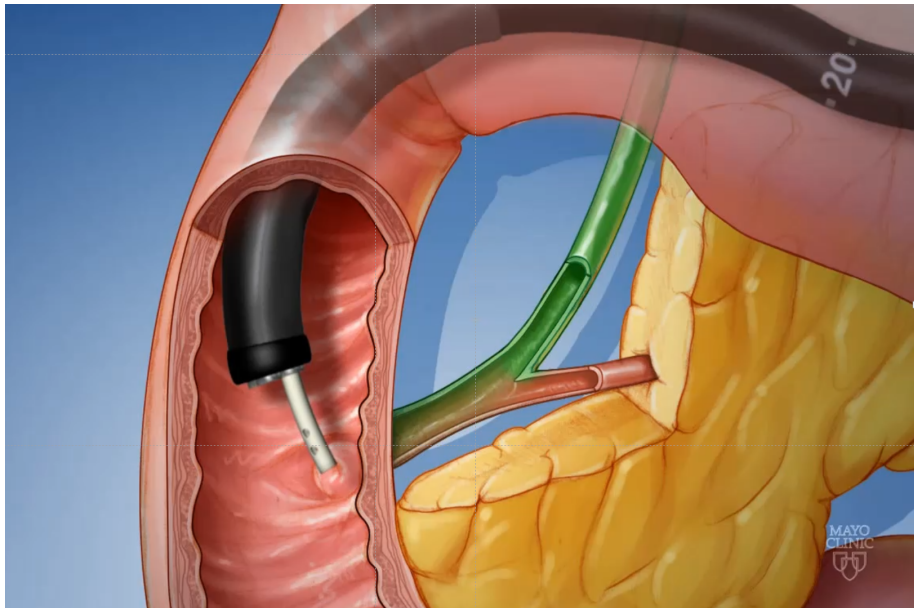
Collecting pancreatic juice during endoscopy

- Pancreatic juice easily collected as part of a routine endoscopy
  - Secretin I.V. stimulates immediate pancreatic juice outflow
  - Juice collected from duodenum through endoscope
- Avoids
  - Risks with biopsy/FNA
  - Anesthetist coverage
  - Complex endoscopy (endoscopic ultrasound)



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Our approach to detection with pancreatic juice

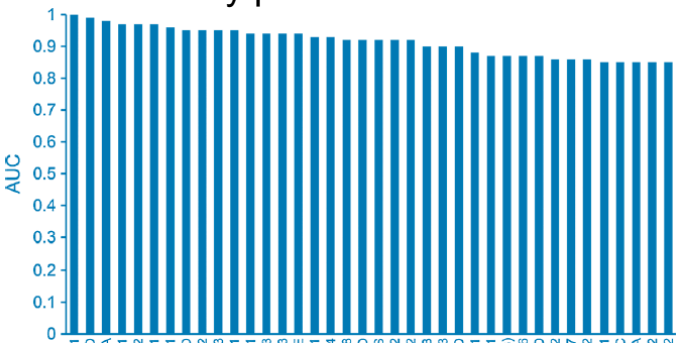
- ✓ Identified and secured best-in-class markers*
  - Whole methylome discovery
  - Comprehensive tissue validation
- ✓ Established feasibility*
  - Best individual meth DNA markers highly discriminant in pancreatic juice (e.g., CD1D)
- ✓ Optimized marker combinations and methods
  - Best 4-marker combination

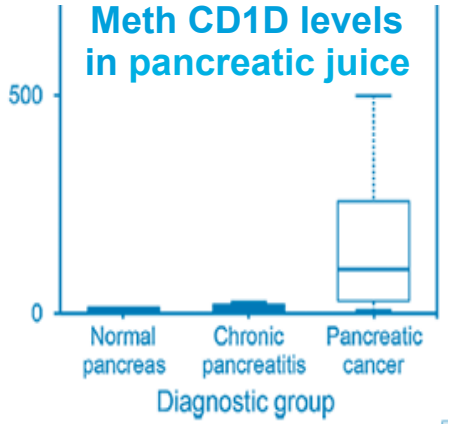
Sensitivity	96%
Specificity	97%

- Validate performance in well-designed clinical case-control study

Cancer vs. Normal Tissue

Best candidate markers show nearly perfect discrimination





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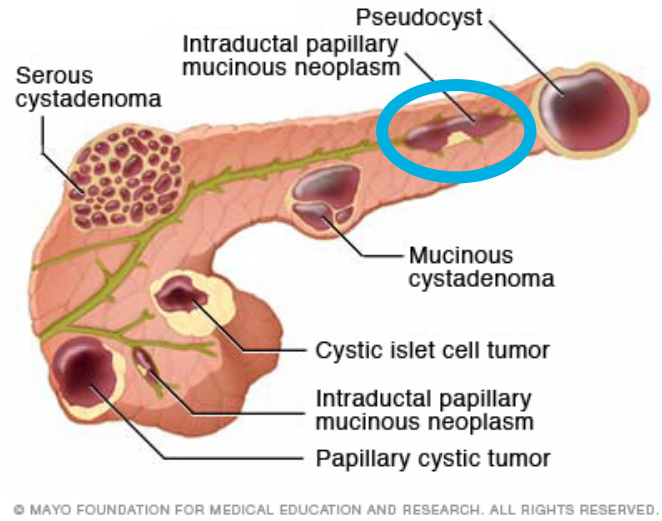
Sources: *Kisiel et al. Clin Cancer Res 2015
PMID:26023084.DOI:10.1158/1078-0432.CCR-14-2469

Molecular pancreatic juice testing

Indication: Diagnostic evaluation and monitoring of *pancreatic lesions*



- **Cysts**
- Small solid nodules
- Large masses

Action:

+	Surgery, treatment, palliative care, observation
−	Monitor

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Mayo Clinic 3-site prospective study underway

- Primary aim
  - Assess accuracy of methylated DNA markers in pancreatic juice to detect cancer and high-grade dysplasia

N=300
Pancreatic cancer cases (100)
Pancreatic cysts (100)
Normal controls (100)

- Biospecimens collected: pancreatic juice, cyst fluid, stool and blood

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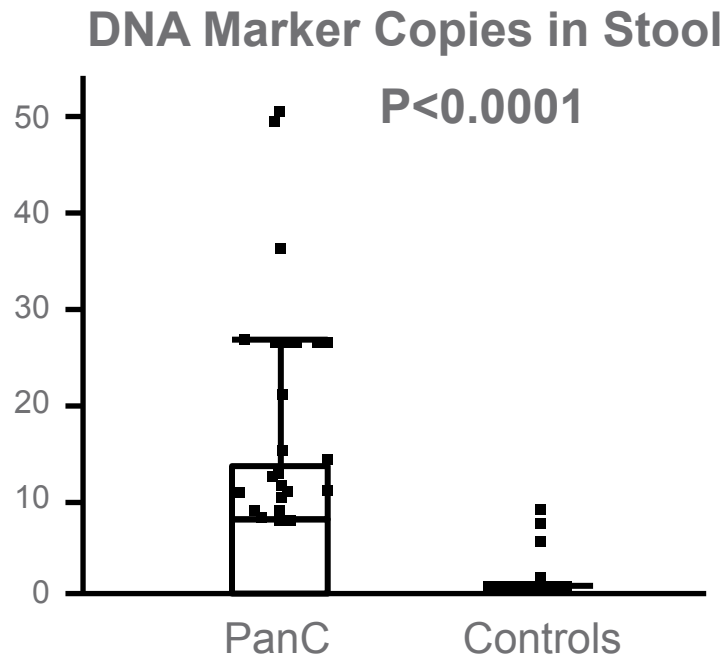
Expanding opportunities for new molecular tools

- Evaluation of nodules/cysts (near-term)
  - Pancreatic juice
- Population cancer screening (longer-term)
  - Stool
    - Early studies suggest feasibility[1]
    - Optimal markers & methods needed
  - Blood
    - 83% detection accuracy (combined stages) in pilot study using plasma assay of meth DNA markers, reported[2]
    - Optimal markers and methods needed



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Sources: *Kisiel et al. Cancer 2012;118:2623
** Kisiel et al. AACR 2015

Goals of molecular testing in pancreatic juice

Improved Accuracy

Early Detection

Reduced Procedures

LDT Opportunity

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US market opportunity to detect pancreatic cancer

	# of Patients with Cysts that need Monitoring	US Market Opportunity
Diagnosing pancreatic cysts for high-grade	550-650K	$500M+

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