Pancreatic Cancer Screening
Pancreatic cancer: One of America’s most lethal cancers

48,960 new cases per year

40,560 deaths per year

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
Pancreatic Cancer Screening

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Gastroenterologist, Gatton Professor of Digestive Diseases Research, Mayo Clinic
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

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
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

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

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<tbody>
<tr>
<td>Mass/nodule</td>
<td>50-75%</td>
</tr>
<tr>
<td>Cyst</td>
<td>30%</td>
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Fine Needle Aspirate (FNA)

Image courtesy of The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins
Translating diagnostic challenges into opportunities

<table>
<thead>
<tr>
<th>Issues</th>
<th>Current Approach</th>
<th>Future Test</th>
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<tr>
<td><strong>Accuracy</strong></td>
<td>Suboptimal (results in under/over Rx)</td>
<td>Potentially High</td>
</tr>
<tr>
<td><strong>Morbidity</strong></td>
<td>&lt;5%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td><strong>Endoscopic ultrasound facility needed</strong></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>Special training</strong></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>Requires anesthesiologist</strong></td>
<td>Yes</td>
<td>No</td>
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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)
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

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

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*

**Action:**
- **+** Surgery, treatment, palliative care, observation
- **-** Monitor

- Cysts
- Small solid nodules
- Large masses
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
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

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
### US market opportunity to detect pancreatic cancer

<table>
<thead>
<tr>
<th># of Patients with Cysts that need Monitoring</th>
<th>US Market Opportunity</th>
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<tr>
<td>Diagnosing pancreatic cysts for high-grade</td>
<td>550-650K</td>
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<td>$500M+</td>
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