Exoscope

Taking the bite out of heart transplant monitoring

Yale PitchFest 2023
The last breakthrough in heart transplant rejection monitoring was in 1963.

60 years later, Exoscope is developing the next breakthrough

**Academic inventor, co-founder, PI**

Dr. Prashanth Vallabhajosyula
- Assoc. Prof. Cardiac Surgery
- Assoc. Program Director, Cardiothoracic Surgery
- Director, Aortic Institute

**Academic inventor, co-founder**

Laxminarayana Korutla, PhD
- Senior Research Scientist, Yale School of Medicine
- 11+ years of exosome-based diagnostic research

**Co-founder, CEO**

Joseph Gennaro, PhD
- Full-time commitment
- Yale spin-out / tech transfer experience
- 4 patents in microfluidics / assay dev

**Clinical Advisor**

Dr. Sounok Sen
- Assistant Professor
- Medical Director, Cardiac Transplantation
9,000 heart transplants / year
65,000 living patients

$530M TAM*

50% die by year 10

*65,000 patients, 4 tests/year, $2,000/test.
Walking the immunosuppression tightrope

Contribution to mortality in heart transplant recipients

- Infection
- Acute rejection
- Malignancy

Hsich 2022, Giuliano 2020
Goal: enable precision care without surgical biopsy

Surgical biopsy
- Up to 20x in 2 years
- $10k-$60k cost
- Discordant reads in severe rejection

Circulating DNA/RNA
- n/a for first 1-2 months
- Can only rule out rejection
- Poor correlation with rejection severity

Breakthrough diagnostic
- Works from first week on
- No surgical follow-up
- Enables precision treatment
Exosomes are nanoscale vesicles that mediate intercellular communication

Contreras-Naranjo JC, Wu HJ, Ugaz VM 2017
Exosomes provide molecular window into rejection pathophysiology

*Protected by 5 patent applications co-assigned to Yale*
12-patient / 70-sample pilot validates high performance of 8 biomarkers

- Detected all rejection episodes
- Highly time-specific
- Started working in first week

Detailed data available on request with CDA
Our biomarkers correlate with rejection severity

**Exoscope biomarkers***

*Detailed data available on request with CDA
p-values for Grades 0/1R vs 2R/3R rejection

p=3.9x10^-5

p=5.6x10^-6

p=6.0x10^-5

p=6.9x10^-7

p=9.1x10^-5

p=9.9x10^-6

p=1.6x10^-5

**Commercially available assay**

p=0.002

Kim 2022
Use of development award: enabling clinical trial

Study outcomes:
- Determine predictive power for acute rejection in larger, true-prevalence cohort
- Demonstrate reduced mortality, increased QOL, and/or reduced cost in simulated surgery-free care

<table>
<thead>
<tr>
<th>Category</th>
<th>Consumables</th>
<th>Labor</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exosome enrichment / quality control</td>
<td>$16,000</td>
<td>$36,000</td>
<td>$52,000</td>
</tr>
<tr>
<td>Protein biomarker analysis (Keck Proteomics Core)</td>
<td>25,000</td>
<td>120,000</td>
<td>145,000</td>
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<tr>
<td>RNA biomarker analysis</td>
<td>45,000</td>
<td>20,000</td>
<td>65,000</td>
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<tr>
<td>Regulatory / Process / Bioinformatics</td>
<td>--</td>
<td>38,000</td>
<td>38,000</td>
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<tr>
<td><strong>Cost to analyze 400 samples (out of 900 available)</strong></td>
<td><strong>$86,000</strong></td>
<td><strong>$214,000</strong></td>
<td><strong>$300,000</strong></td>
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</table>
Thank you!

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Surgical biopsy: standard of care in heart transplant surveillance

Biopsy shows rejection?

More treatment

Baseline treatment

More infection, cancer

Increased risk of rejection

Surgical biopsy
- Expensive
- Invasive
- Imprecise

50% of heart transplant patients die in 10 years
Existing liquid biopsies have not replaced surgical biopsy

- o n/a for first 1-2 months
- o Can only rule out rejection
- o Poor correlation with rejection severity
Opportunity to improve patient outcomes and reduce cost of care

Molecular window into rejection

Precisely guide treatment

- Improve quality of life
- Reduce mortality
- Reduce burden of care

Exoscope goal
- Works from first week on
- No surgical follow-up
- Enables precision treatment
Comparable Liquid Biopsy Validation Studies

<table>
<thead>
<tr>
<th>Company</th>
<th>CareDx</th>
<th>Natera</th>
<th>HEARTBiT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biomarkers</td>
<td>GEP (11 mRNA)</td>
<td>GEP (11 mRNA)</td>
<td>GEP (20 mRNA)</td>
</tr>
<tr>
<td>Time post-bx</td>
<td>≥6 months</td>
<td>≥6 months</td>
<td>≥2 months</td>
</tr>
<tr>
<td># Patients (% ≥2R, # sites)</td>
<td>133 (38%, 8)</td>
<td>598 (32%, 8)</td>
<td>602 (11%, 13)</td>
</tr>
<tr>
<td># EMB/sample pairs (% ≥2R)</td>
<td>528 (23%)</td>
<td>958 (21%)</td>
<td>1190 (5%)</td>
</tr>
<tr>
<td>Est. cost*</td>
<td>$396k</td>
<td>$719k</td>
<td>$1,184k</td>
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<tr>
<td>Performance profile**</td>
<td>[Graph]</td>
<td>[Graph]</td>
<td>[Graph]</td>
</tr>
</tbody>
</table>

*Assumes liquid biopsy costs $500. For clinical studies, assume clinic bears cost of standard care.

**Vertical bars depict sensitivity, specificity, positive predictive value, negative predictive value, and area under the curve on 0-100% scale. All statistics for discriminating ≥2R vs 0/1R. Detailed data with sources available upon request.
Comparable Liquid Biopsy Validation Timeline

Deng 2016