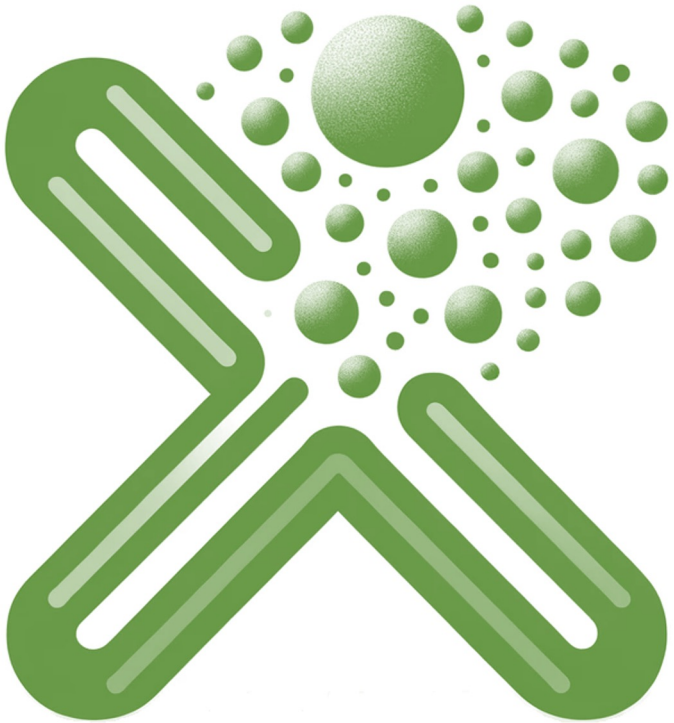
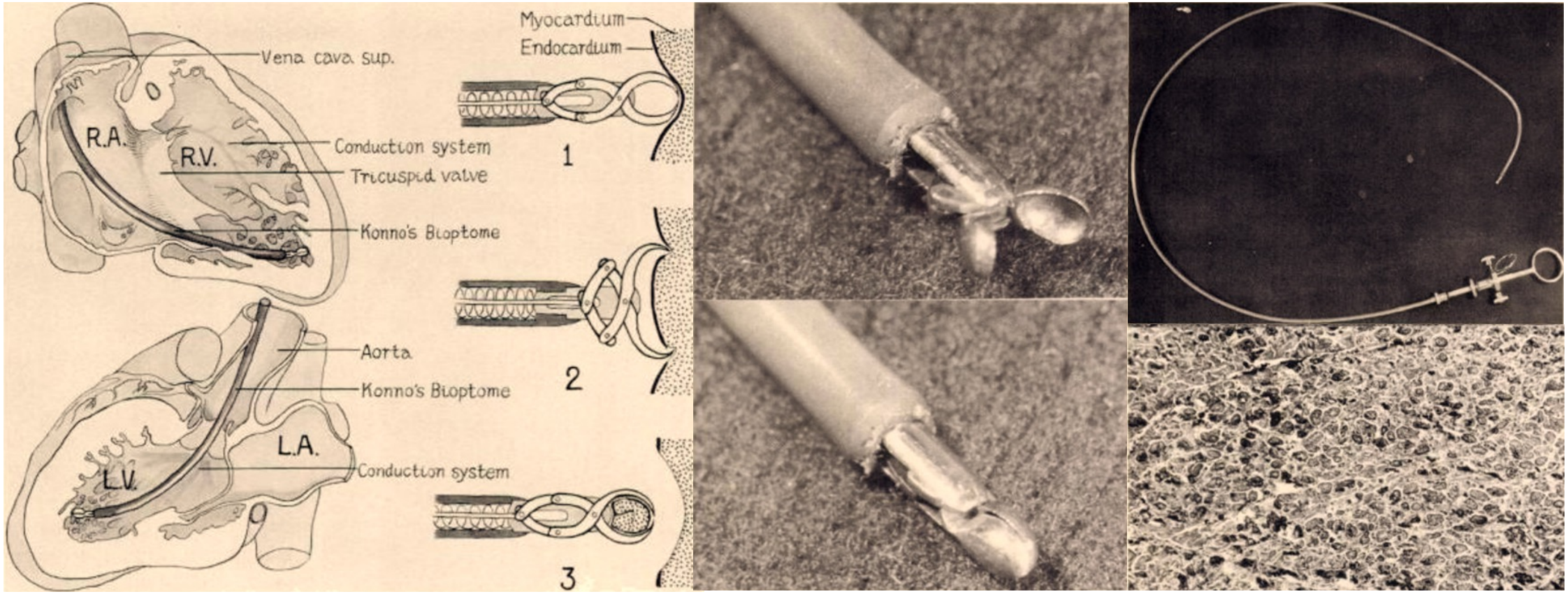


Exoscope

Taking the bite out of heart transplant monitoring

Yale PitchFest 2023

The last breakthrough in heart transplant rejection monitoring was in 1963



Konno & Sakakibara. (**1963**). Endo-myocardial biopsy. Diseases of the chest, 44, 345–350.

60 years later, Exoscope is developing the next breakthrough

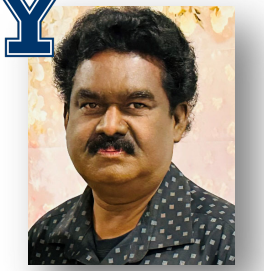
Academic inventor, co-founder, PI

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

Co-founder, CEO

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

Academic inventor, co-founder

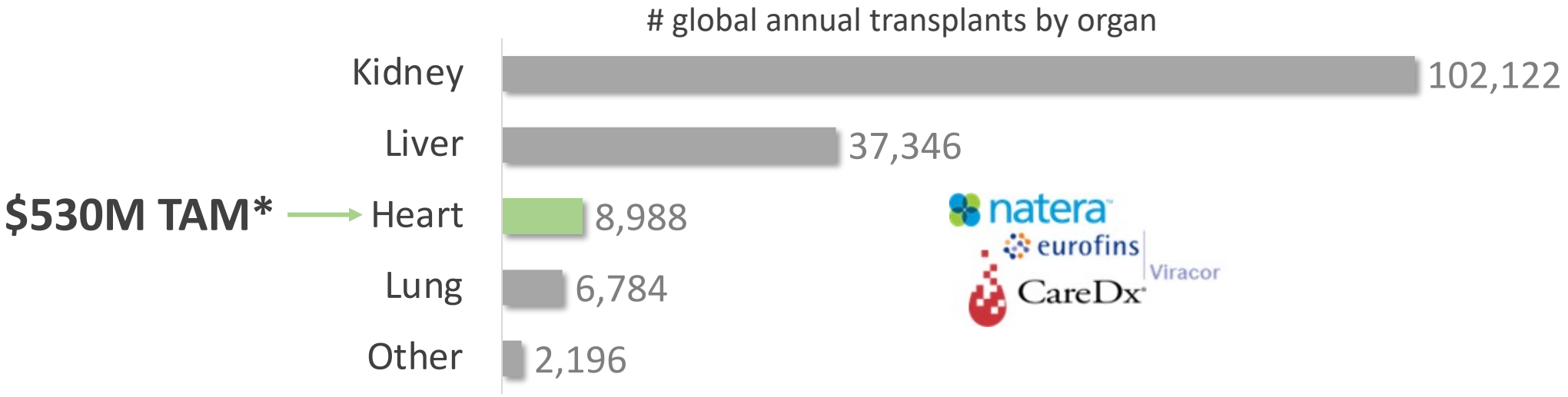


Laxminarayana Korutla, PhD
- Senior Research Scientist, Yale School of Medicine
- 11+ years of exosome-based diagnostic research

Clinical Advisor

Dr. Sounok Sen
- Assistant Professor
- Medical Director, Cardiac Transplantation

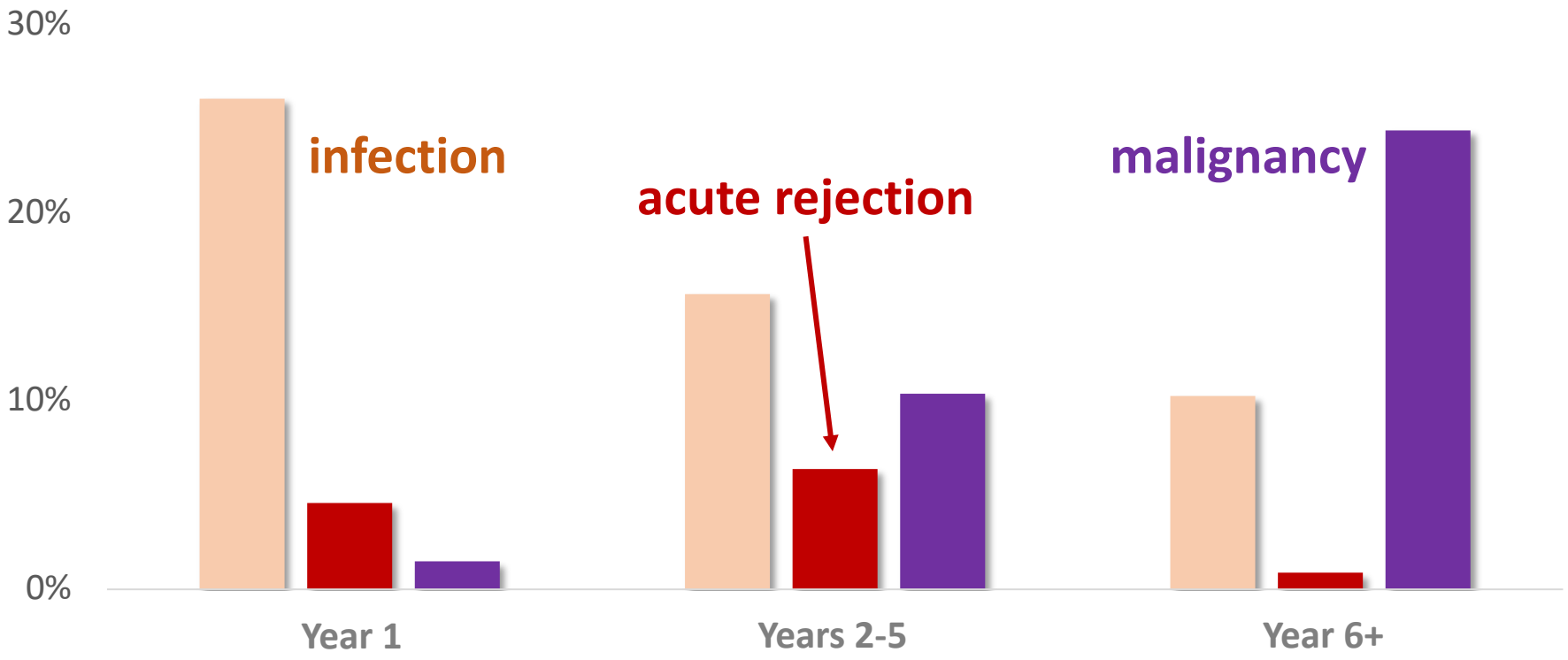
9,000 heart transplants / year
65,000 living patients



50% die by year 10

*65,000 patients, 4 tests/year, $2,000/test.

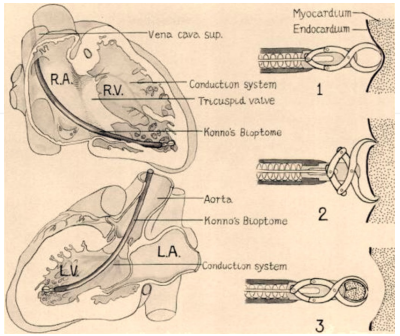
Walking the immunosuppression tightrope



Contribution to mortality in heart transplant recipients

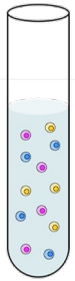
Hsich 2022, Giuliano 2020

Goal: enable precision care without surgical biopsy



Surgical biopsy

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



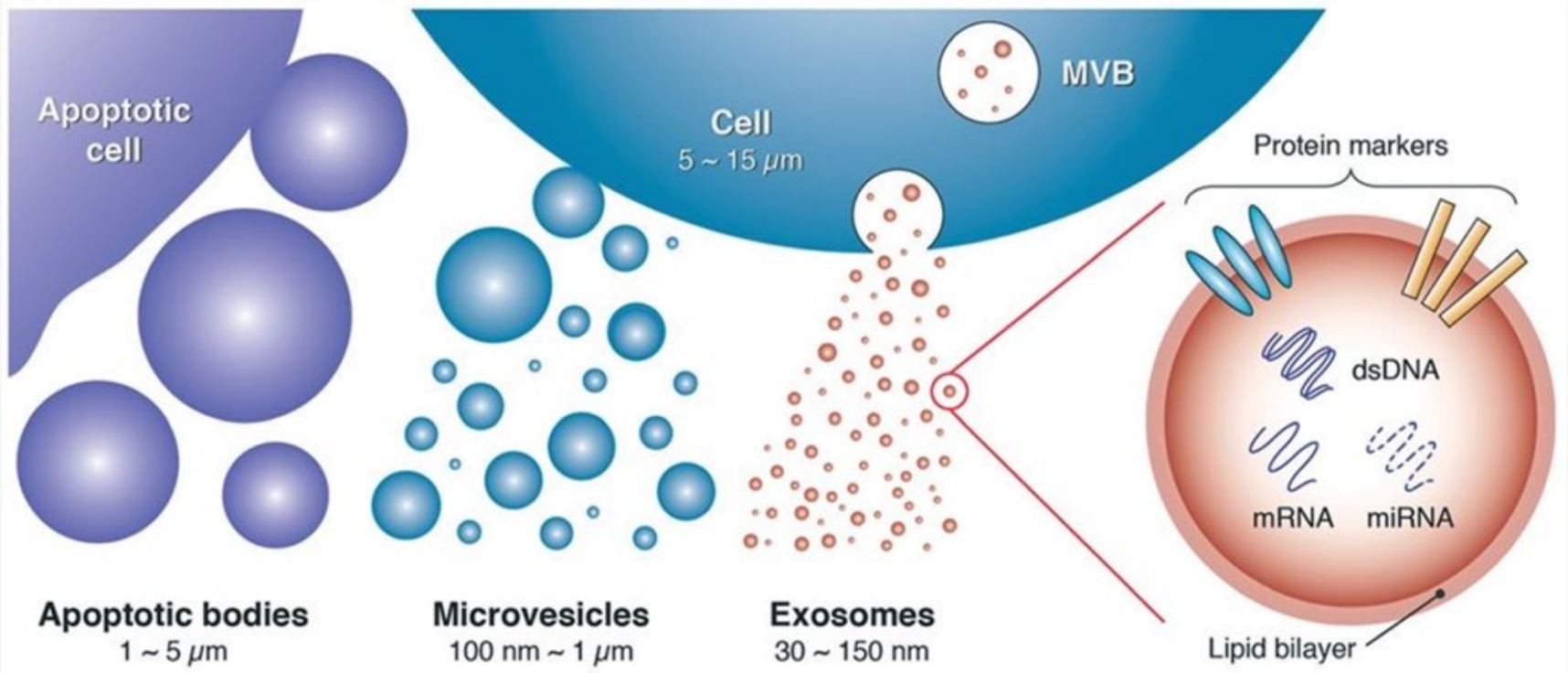
Circulating DNA/RNA

- n/a for first 1-2 months
- Can only rule <u>out</u> rejection
- Poor correlation with rejection severity

Breakthrough diagnostic

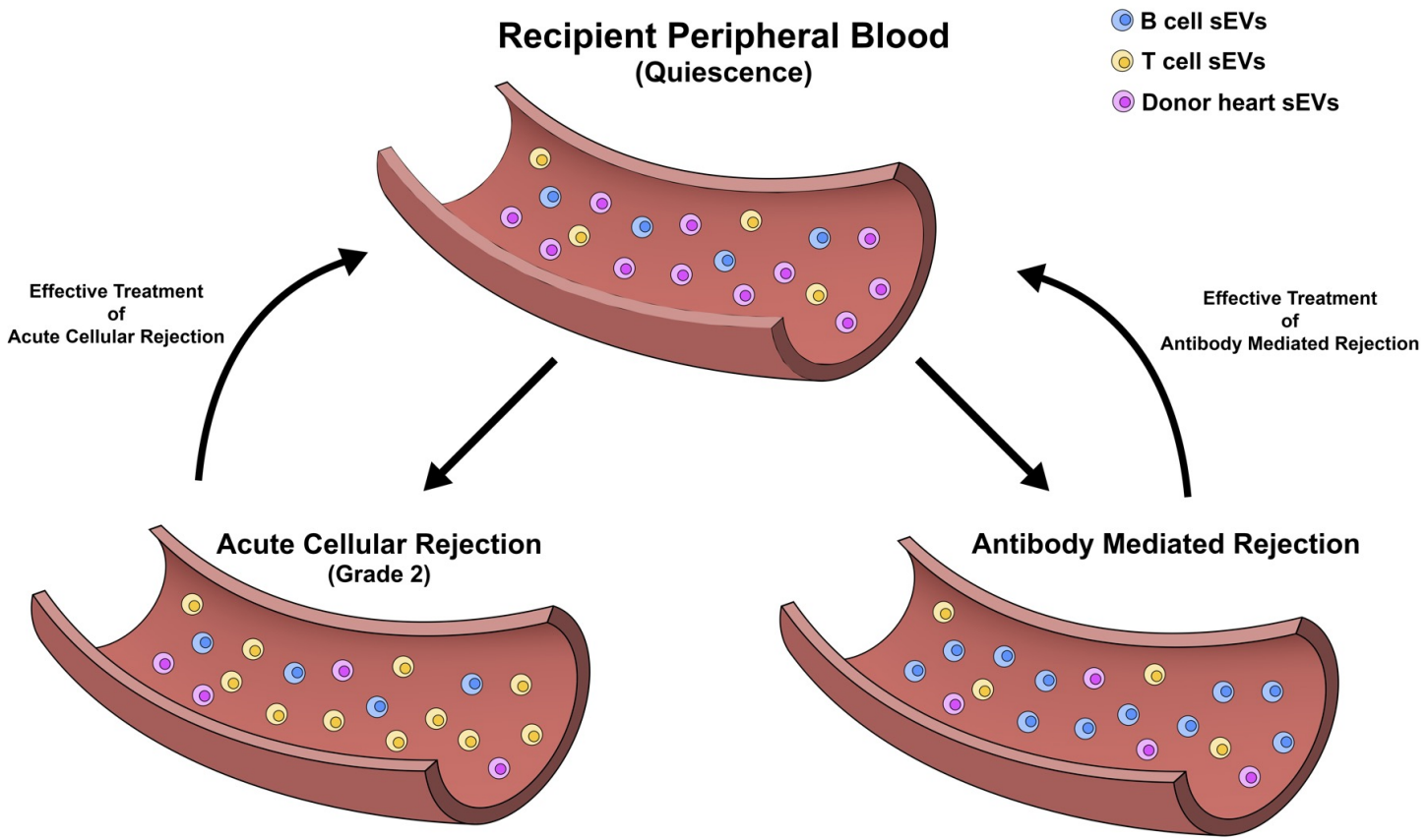
- ✓ Works from first week on
- ✓ No surgical follow-up
- ✓ Enables precision treatment

Exosomes are nanoscale vesicles that mediate intercellular communication



Contreras-Naranjo JC, Wu HJ, Ugaz VM 2017

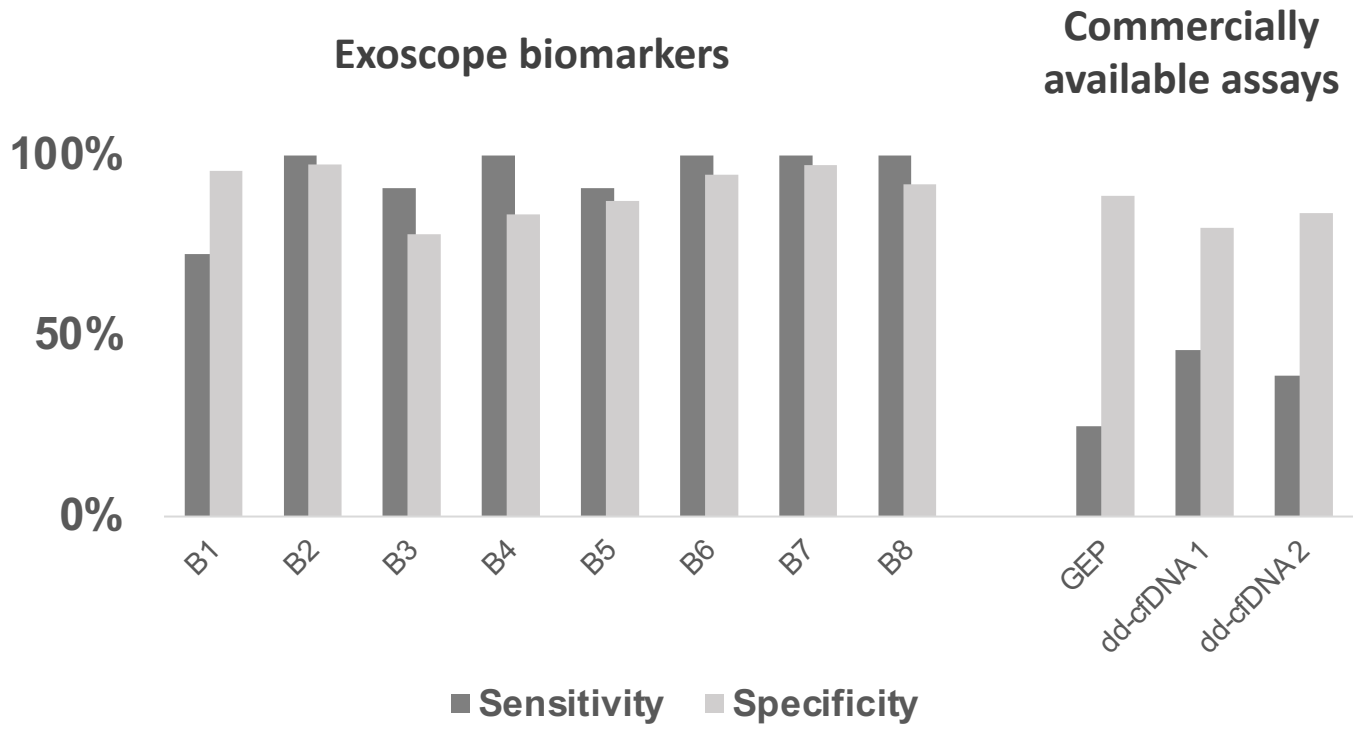
Exosomes provide molecular window into rejection pathophysiology



*Protected by 5 patent applications co-assigned to Yale

12-patient / 70-sample pilot validates high performance of 8 biomarkers

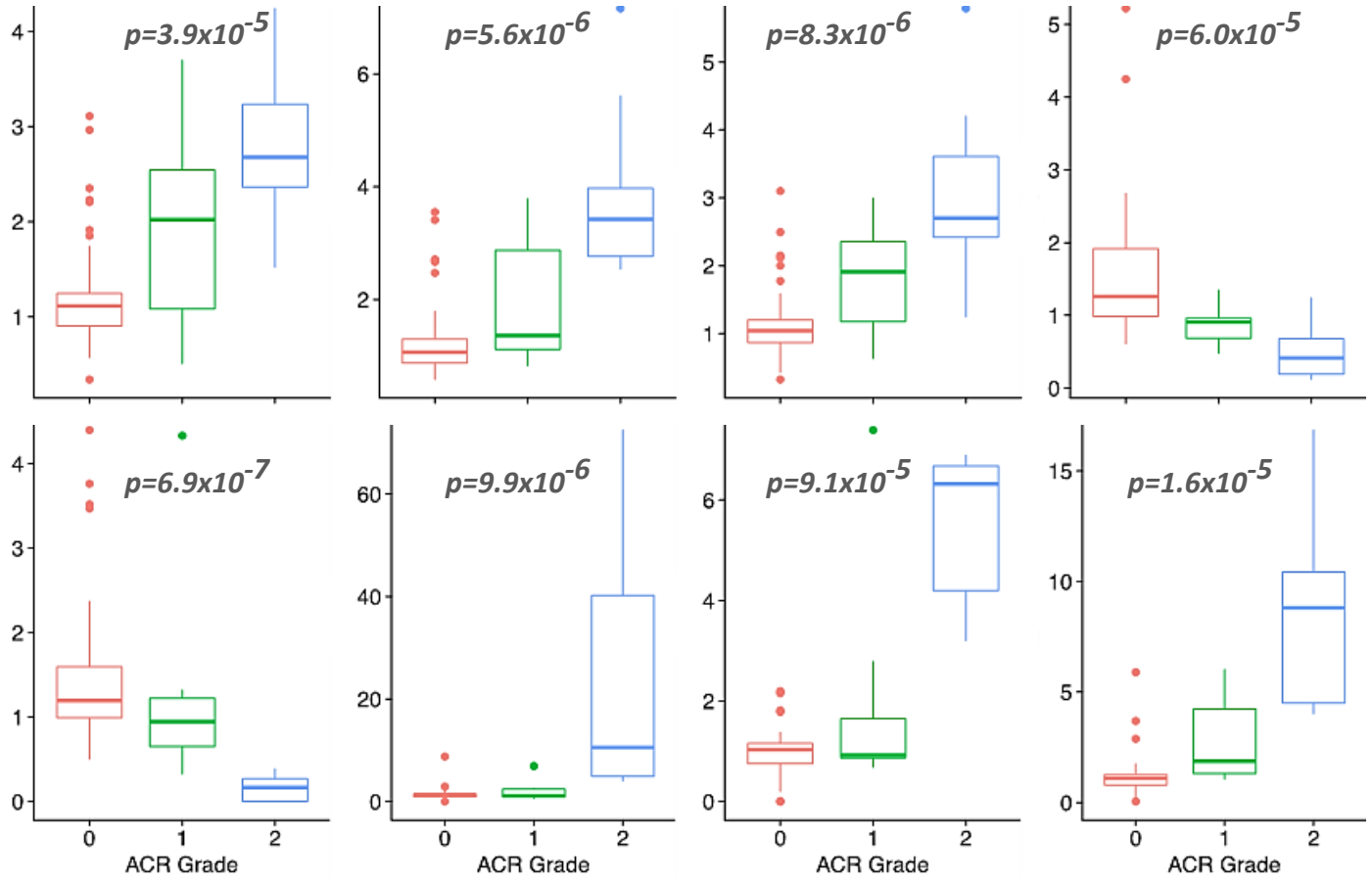
- ✓Detected all rejection episodes
- ✓Highly time-specific
- ✓Started working in first week



Detailed data available on request with CDA

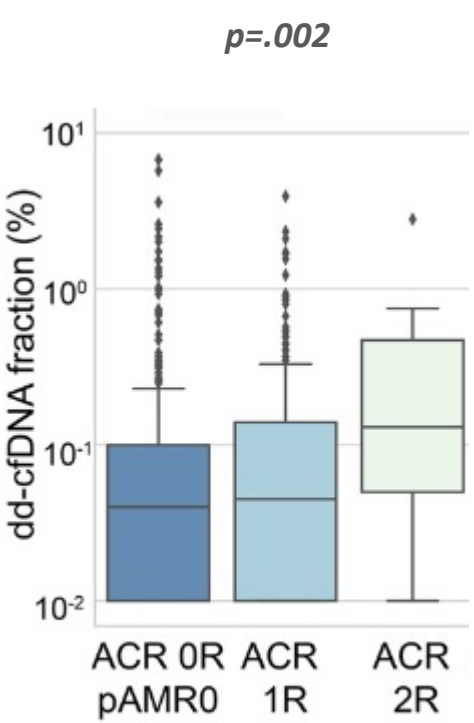
Our biomarkers correlate with rejection severity

Exoscope biomarkers*



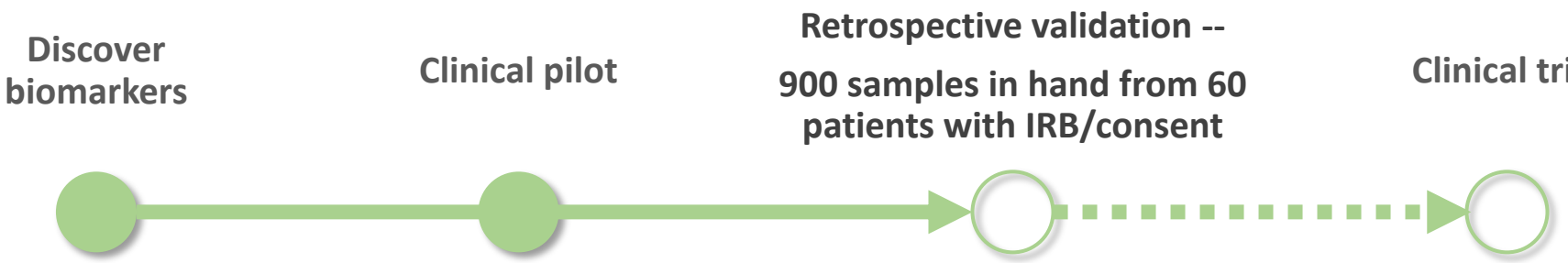
*Detailed data available on request with CDA
p-values for Grades 0/1R vs 2R/3R rejection

Commercially available assay



Kim 2022

Use of development award: enabling clinical trial

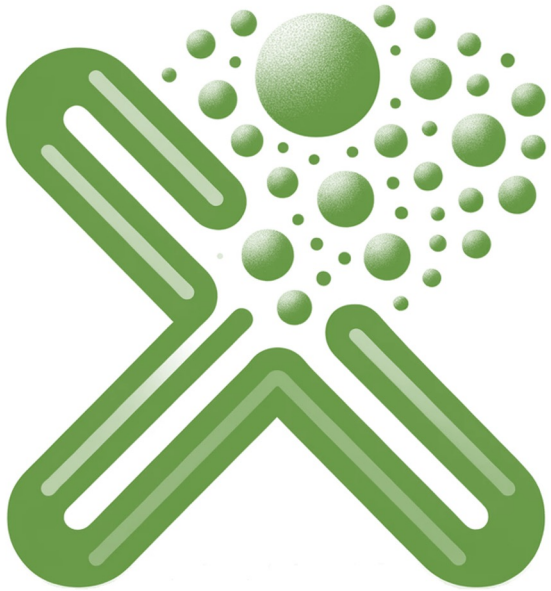


Study outcomes:

- ❑ 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

Category	Consumables	Labor	Total
Exosome enrichment / quality control	$16,000	$36,000	$52,000
Protein biomarker analysis (**Keck Proteomics Core**)	25,000	120,000	145,000
RNA biomarker analysis	45,000	20,000	65,000
Regulatory / Process / Bioinformatics	--	38,000	38,000
Cost to analyze 400 samples (out of 900 available)	**$86,000**	**$214,000**	**$300,000**

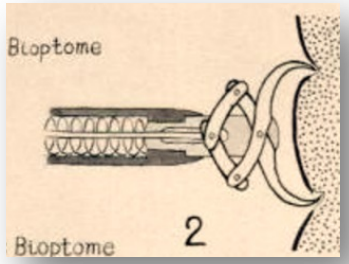
Thank you!



prashanth.vallabhajosyula@yale.edu

joe@exoscope.bio

Surgical biopsy: standard of care in heart transplant surveillance



Surgical biopsy

- Expensive
- Invasive
- Imprecise

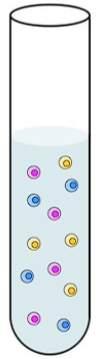
Biopsy shows rejection?

More treatment → More infection, cancer

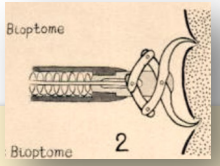
Baseline treatment → Increased risk of rejection

50% of heart transplant patients die in 10 years

Existing liquid biopsies have not replaced surgical biopsy

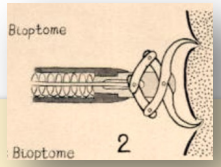


Month 1-2?



Surgical biopsy

Liquid biopsy positive?



Surgical biopsy

Baseline treatment

Existing liquid biopsies

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

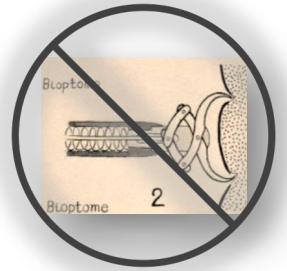
Opportunity to improve patient outcomes and reduce cost of care

Exoscope goal

- ✓ Works from first week on
- ✓ No surgical follow-up
- ✓ Enables precision treatment

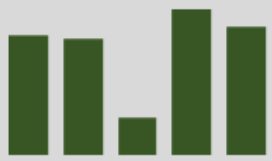
Molecular window into rejection

Precisely guide treatment



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

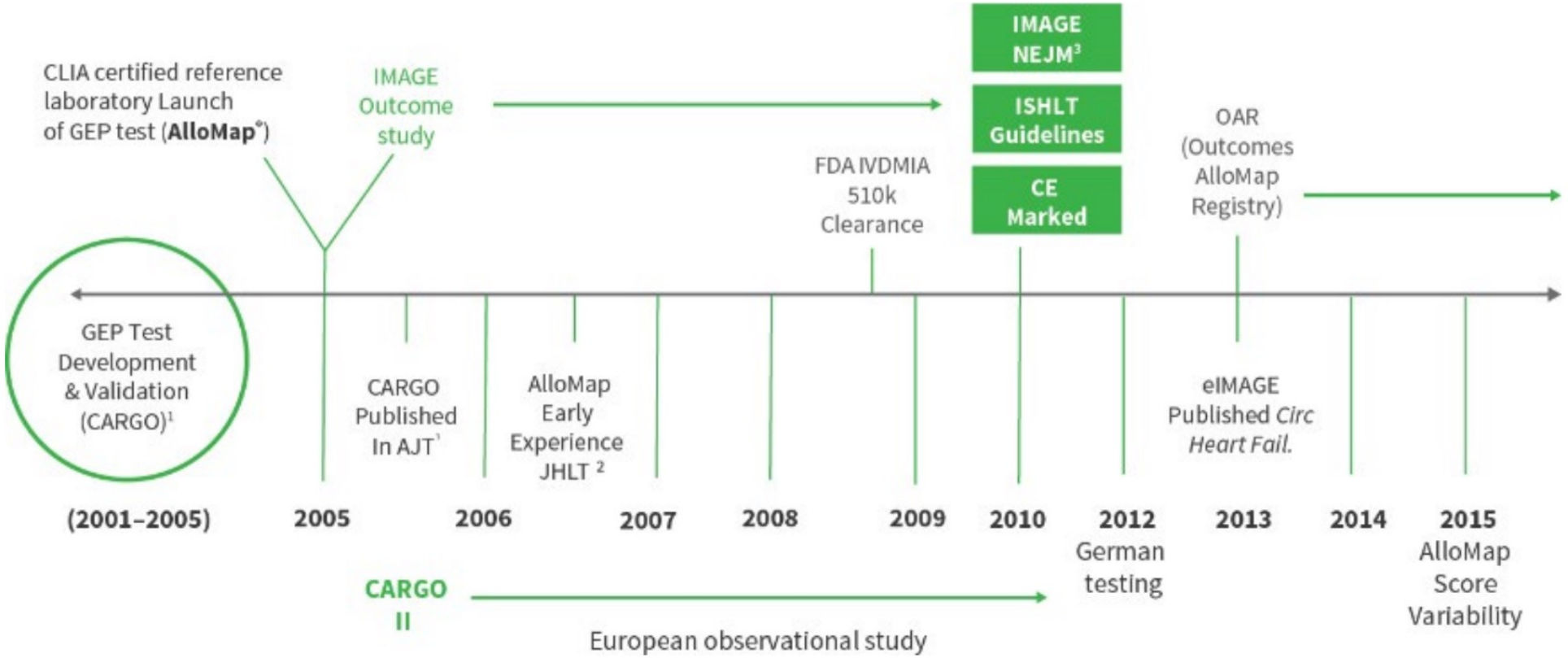
Comparable Liquid Biopsy Validation Studies

Company	CareDx					Natera	HEARTBiT
Study, year	CARGO pre-clinical, 2006	CARGO, 2006	IMAGE, 2010	CARGO II, 2016	D-OAR, 2019	Kim 2022	Shannon 2020
Biomarkers	GEP (11 mRNA)	GEP (11 mRNA)	GEP (11 mRNA)	GEP (20 mRNA)	dd-cfDNA (266 SNPs)	dd-cfDNA (>13k SNPs)	Circulating mRNA (x9)
Time post-tx	≥6 months	≥6 months	≥6 months	≥2 months	≥2 months	≥1 month	Promptly
# Patients (% ≥2R, # sites)	133 (38%, 8)	598 (32%, 8)	602 (11%, 13)	468 (10%, 17)	1187 (3%, 26)	245 (14%, 2)	177 (20,3%, 8)
# EMB/sample pairs (% ≥2R)	528 (23%)	958 (21%)	1190 (5%)	1579 (3.2%)	841 (4%)	811 (6%)	1582 (3.2%)
Est. cost*	$396k	$719k	$893k	$1,184k	$631k	$608k	$1,187k
Performance profile**							

**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