

Progress in the Development of PDAC Biomarkers: Haab-Brand-Allen BDL

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Van Andel Institute

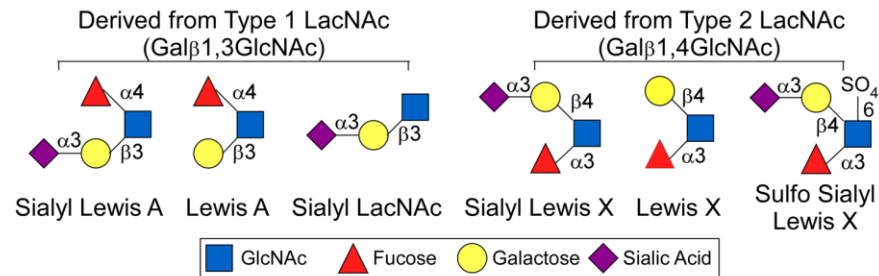
EDRN GI Collaborative Group

June 30, 2020

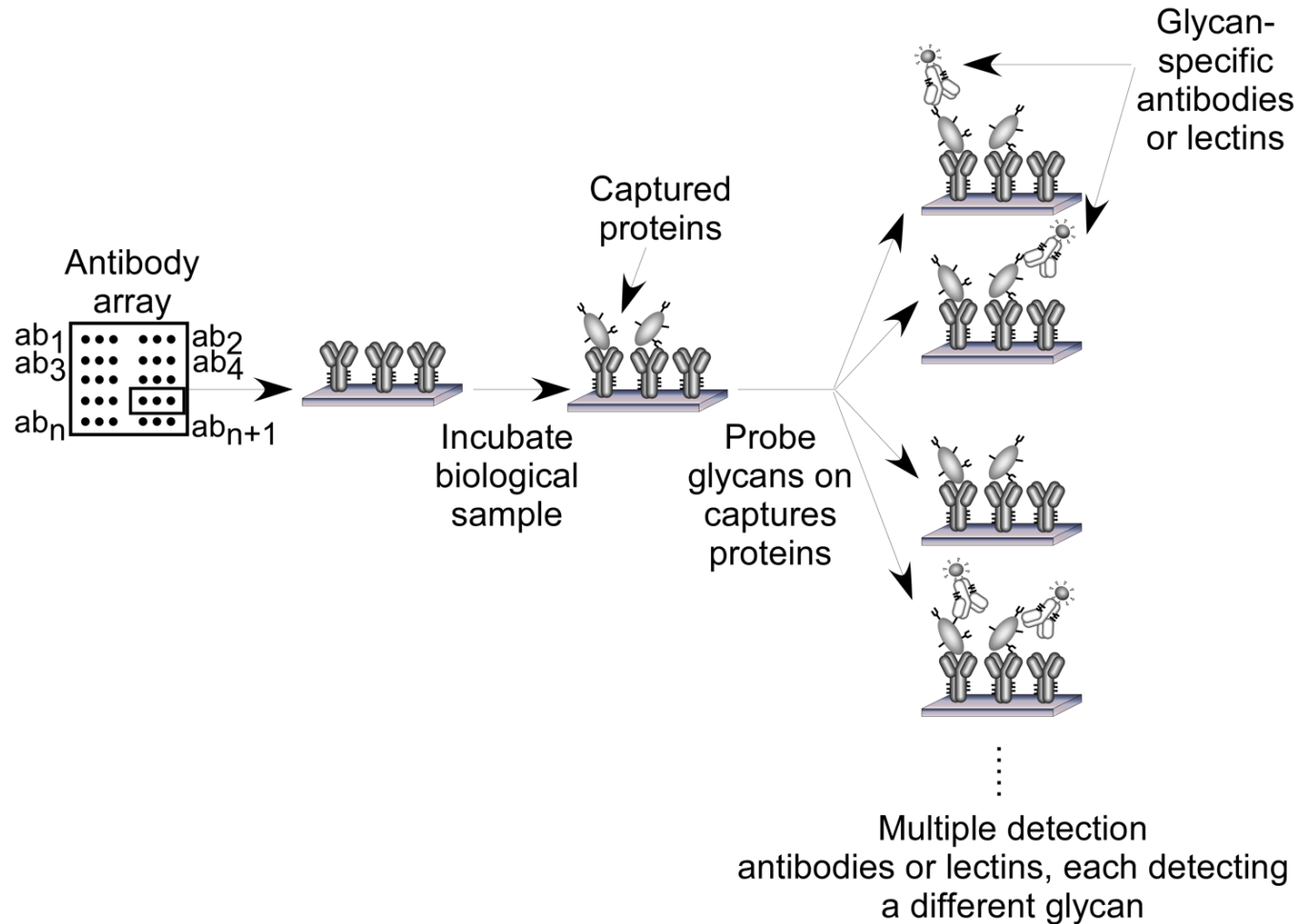
Background – Discovery of sTRA

2016: Glycan profiling around Lewis glycan family members

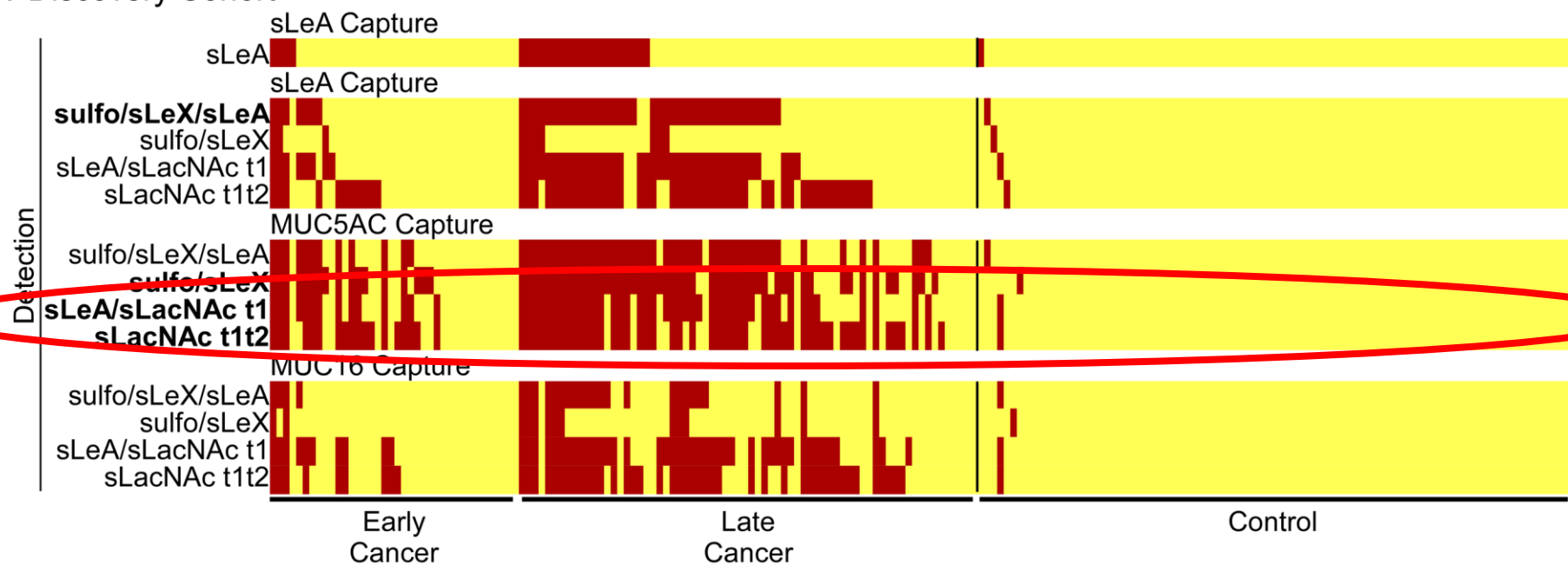
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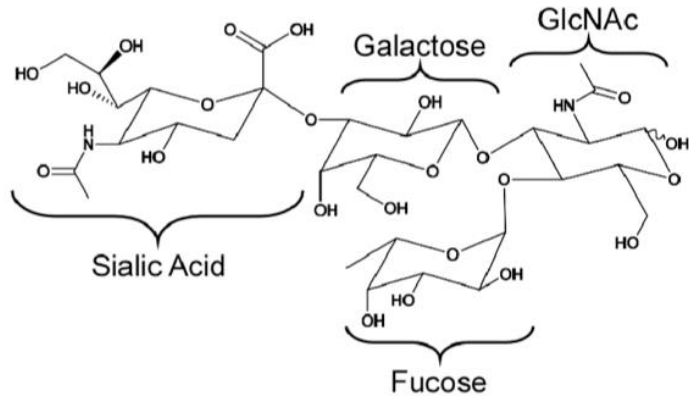
Glycan Profiling On-Chip



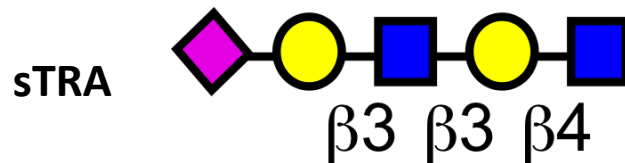
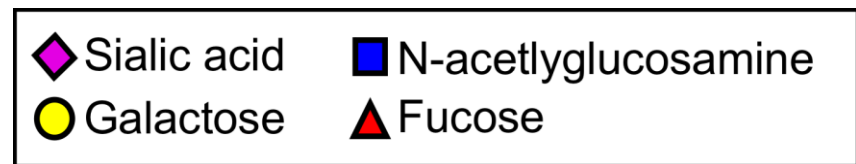
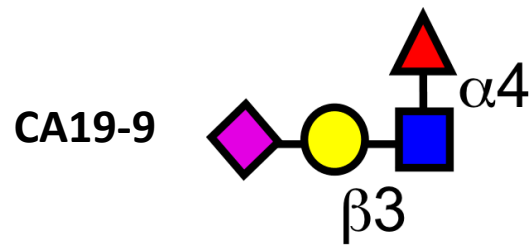
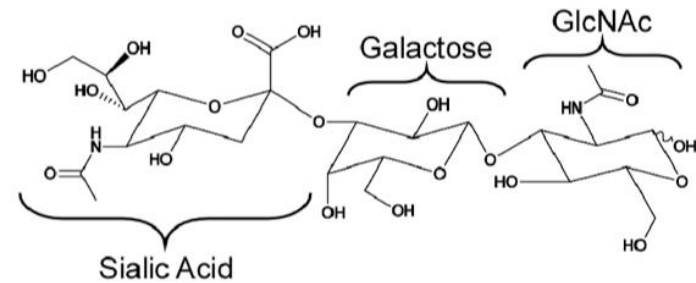
A Discovery Cohort



The CA19-9 antigen

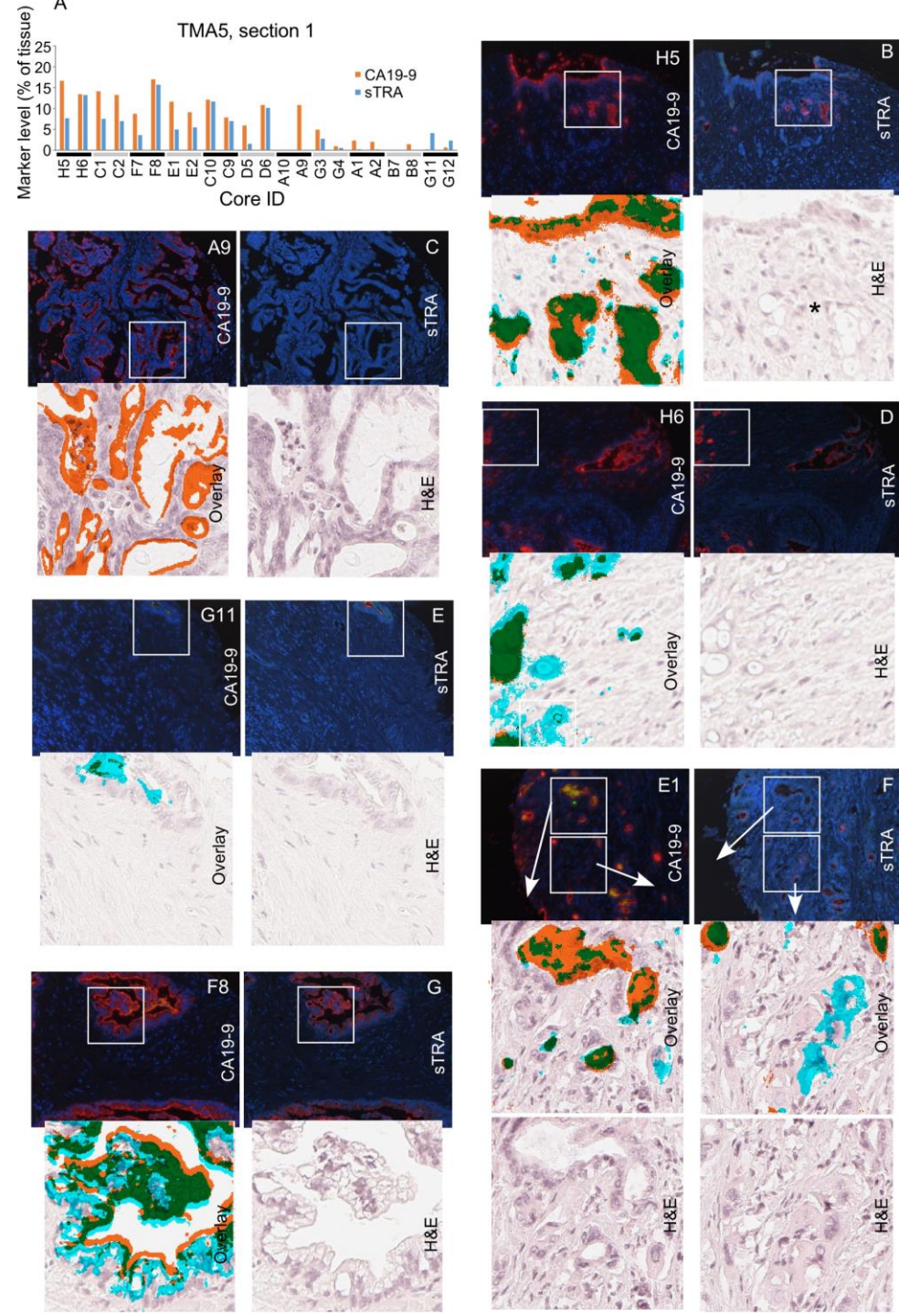


New biomarker: sTRA

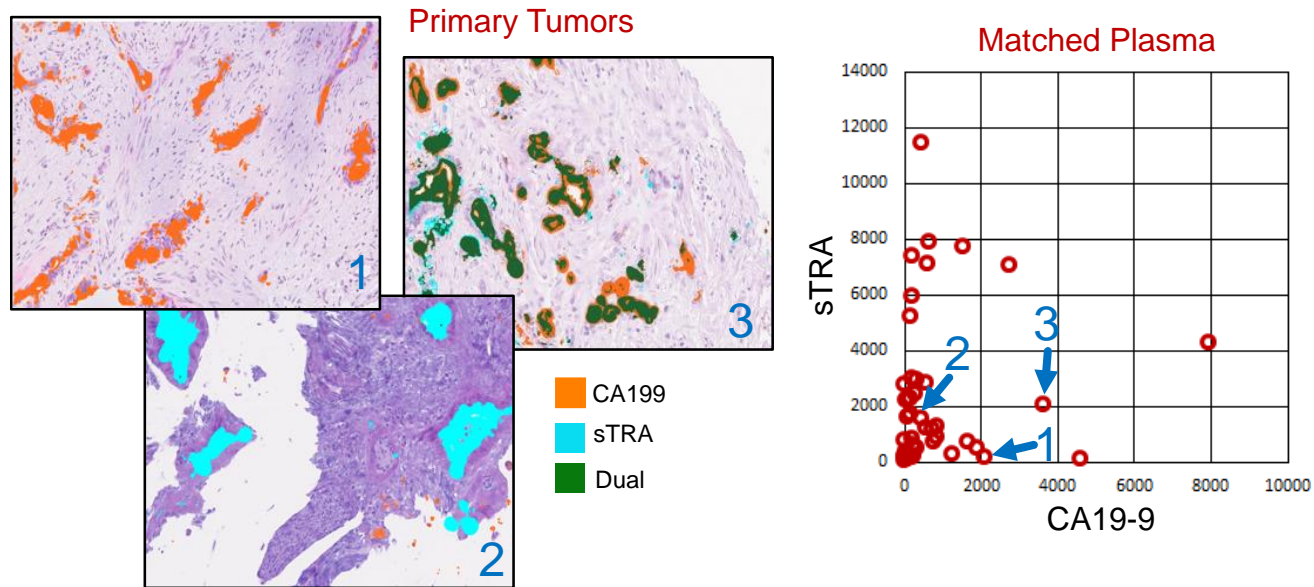


Next – Identification in Separate Subgroups of Tumors

■ CA19-9
■ sTRA
■ Dual

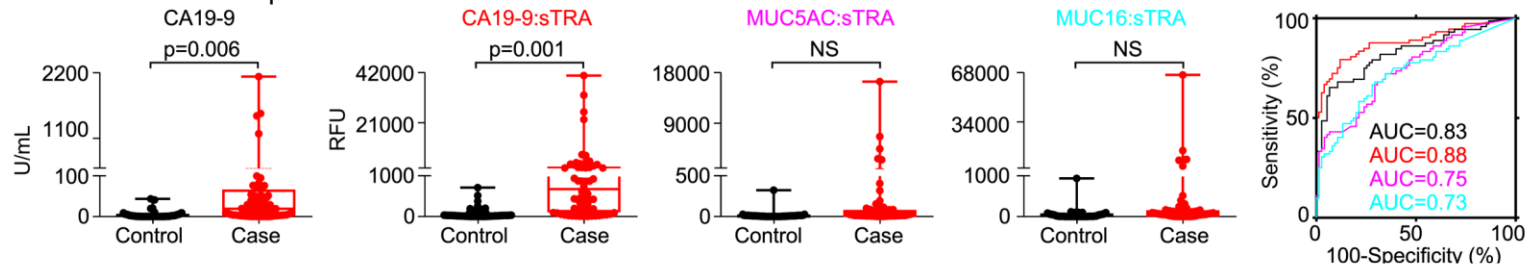


Plasma Correlates with Primary Tumor Levels



Next – Panel Development and Blinded Validation

A. Individual marker performance



Current: Clinical Assay Development and Validation

- ClinicalTrials.gov – NCT04143152 - Pancreatic Cancer Biomarker Study
- Developed a microtiter plate assay to run in a local clinical laboratory.
- Study participants (N = 300) will be recruited from patients being evaluated for a potential pancreatic abnormality or for potential treatment of pancreatic cancer.
- Peripheral blood specimens will be collected at time of enrollment and every 3-6 months for 3 years.
- The specimens will be sent directly to the clinical lab for sTRA biomarker and CA19-9 analysis.
- Participants will be followed for 36 months to track clinical outcomes.
- The performance of the investigation biomarker for the diagnosis, prognosis, or surveillance of pancreatic cancer will be compared to the performance of CA19-9.

➤ The first time a pancreatic cancer biomarker is being tested in this manner.

Bakeoff Results

- Two sets, distributed in 2018 and 2019
- Analysis of first set is complete
- Second set still blinded

Results from blinded calls, Bakeoff 1 and 2 PDAC vs. benign pancreatic conditions, both sets

Panel: Combination of sTRA and CA19-9

Bakeoff 1

Training Set			Bakeoff 1 Set: Blinded case/control calls		
	Spec	Sens		Spec	Sens
CA19-9	97	47	CA19-9	95	30
Panel	97	63	Panel	97	54
97 cases 100 controls			72 cases 75 controls		

Significant Difference, $p < 0.05$

This was a significant result, because it was the first statistically-significant improvement over CA19-9 based on case/control calls made on blinded samples.

Bakeoff 2

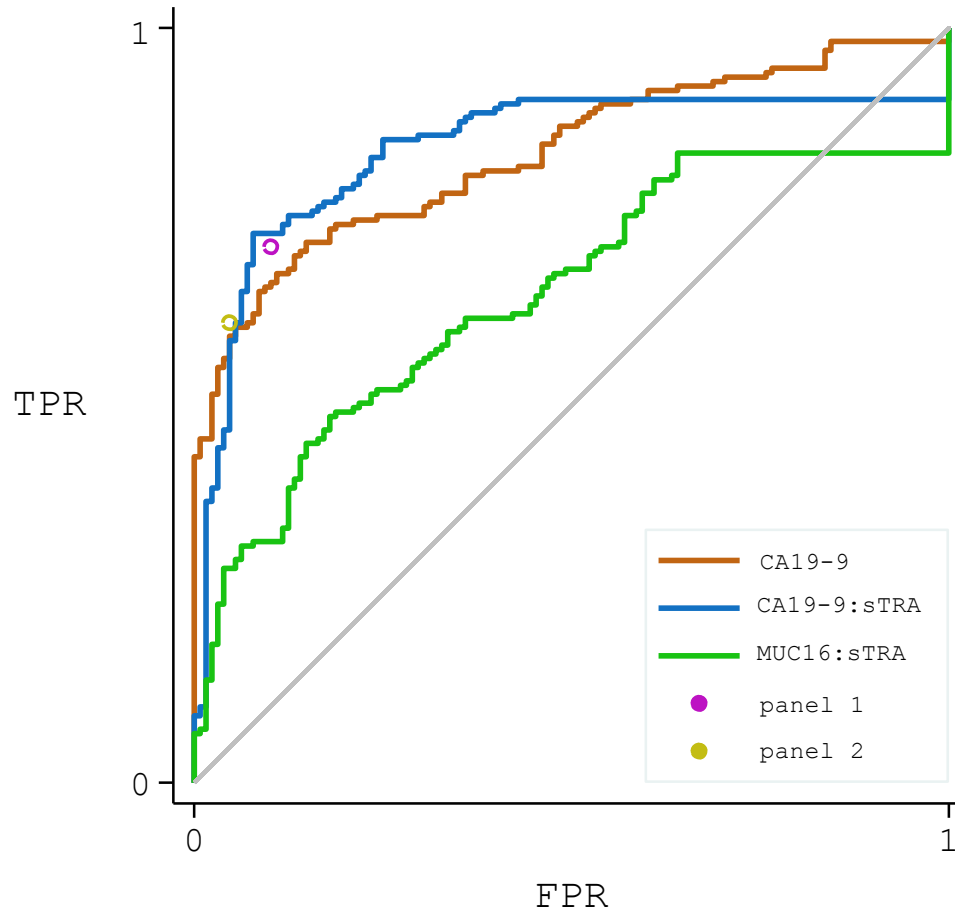
Bakeoff 2 Set: Blinded case/control calls		
	Spec	Sens
Panel	95	61

N = 340

This was a good confirmation of the previous result using a much larger sample set. We are still evaluating comparison with CA19-9. Historical performance of CA19-9 is well below this result. This performance warrants further validation in pre-diagnostic samples.

Panc Ca Bakeoff #2 - VARI results

1) PDAC vs all benign/healthy

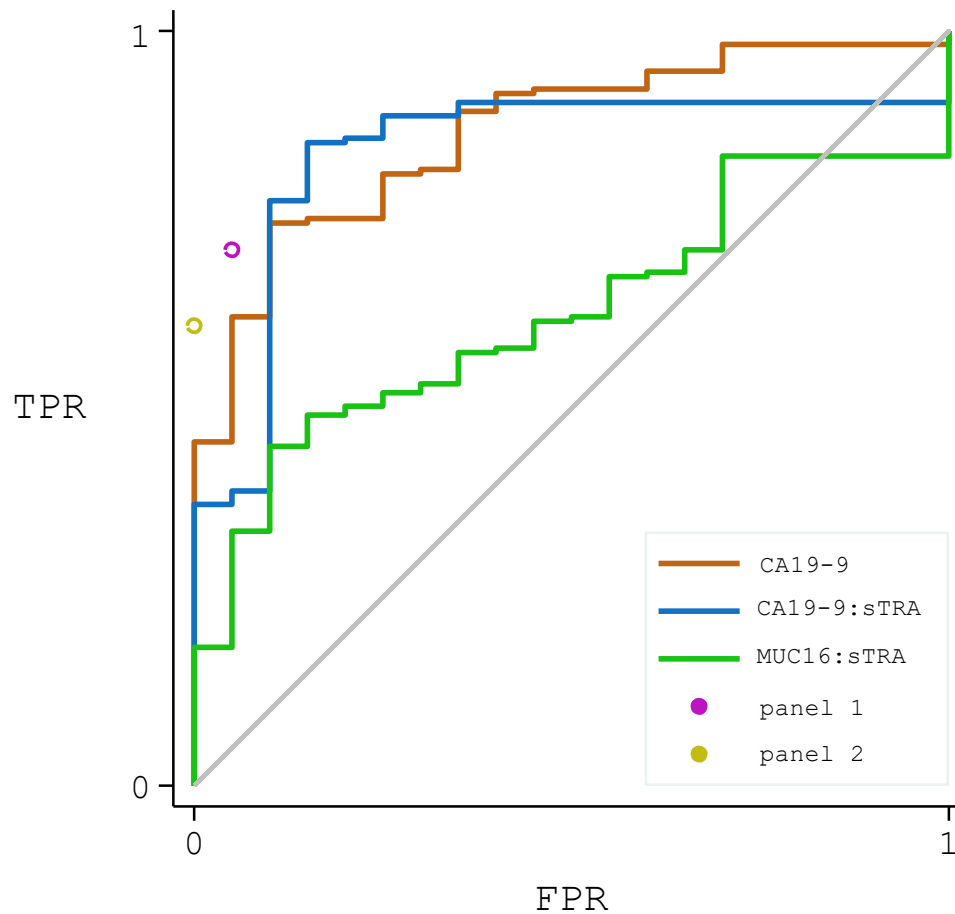


	CA19-9	CA19-9:sTRA	MUC16:sTRA
AUC:	0.83 (0.79,0.88)	0.84 (0.79,0.88)	0.65 (0.58,0.71)
sens(spec=.90):	0.66 (0.55,0.75)	0.73 (0.58,0.80)	0.32 (0.25,0.47)
spec(sens=.90):	0.42 (0.21,0.56)	0.57 (0.00,0.73)	0.00 (0.00,0.00)

95% CI's are bs %tiles based on 3000 bootstrap samples

13 Apr 2020

Panc Ca Bakeoff #2 - VARI results
 5) PDAC vs healthy controls w/fam Hx



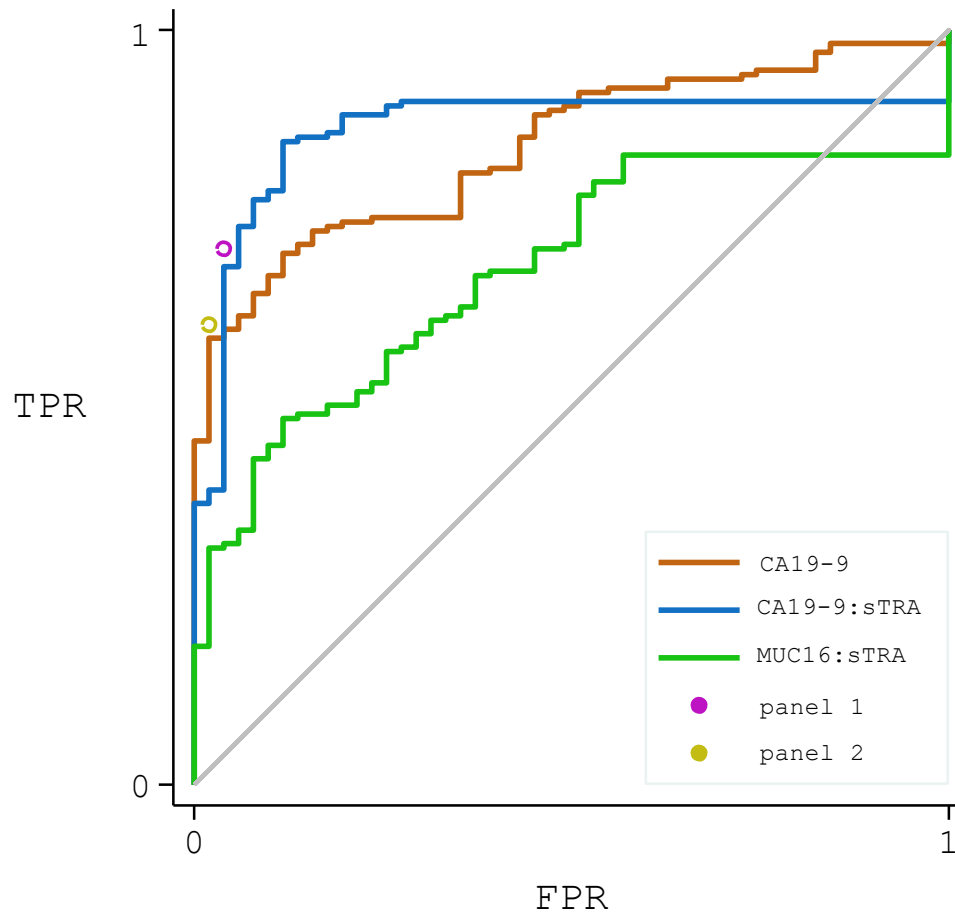
	CA19-9	CA19-9:sTRA	MUC16:sTRA
AUC:	0.87 (0.79,0.93)	0.84 (0.75,0.91)	0.62 (0.52,0.72)
sens(spec=.90):	0.62 (0.41,0.80)	0.39 (0.32,0.89)	0.34 (0.15,0.55)
spec(sens=.90):	0.60 (0.30,0.80)	0.65 (0.00,0.90)	0.00 (0.00,0.00)

95% CI's are bs %tiles based on 3000 bootstrap samples

13 Apr 2020

Panc Ca Bakeoff #2 - VARI results

6) PDAC vs all healthy controls*

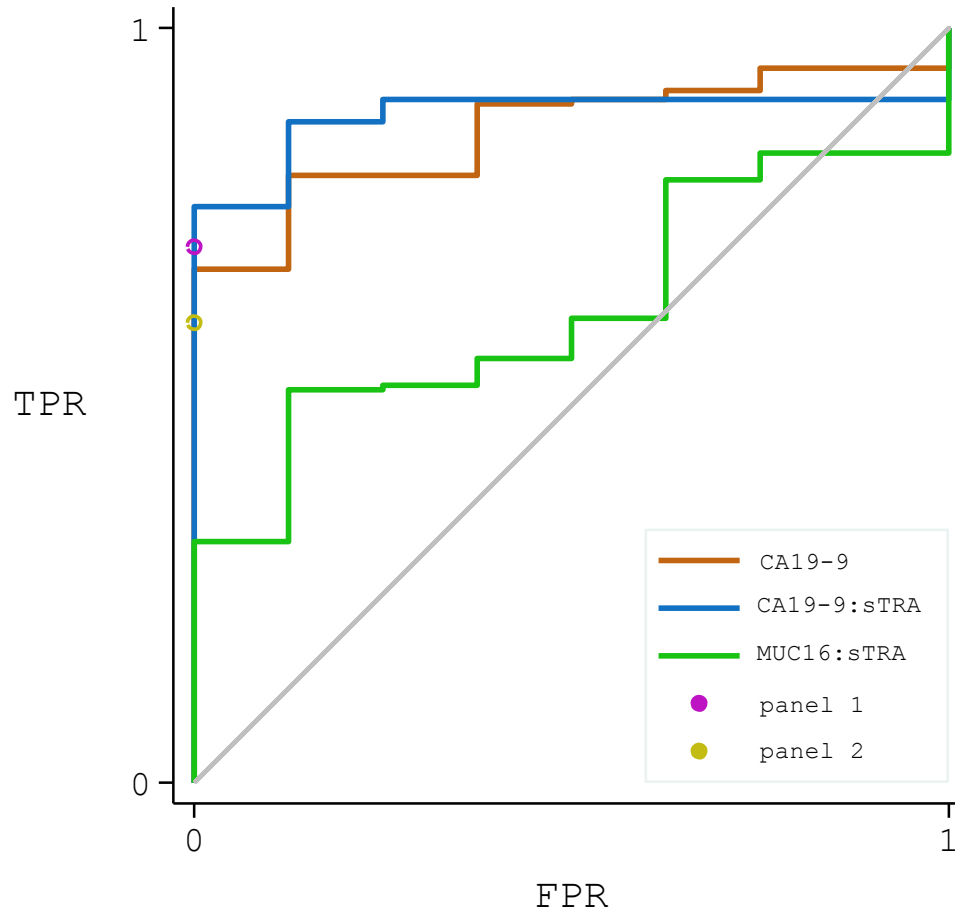


	CA19-9 9:sTRA	CA19- 9	MUC16:sTRA
AUC:	0.84 (0.79,0.89) (0.81,0.92)	0.87	0.68 (0.61,0.75)
sens(spec=.90):	0.67 (0.57,0.78) (0.66,0.91)	0.79	0.45 (0.28,0.56)
spec(sens=.90):	0.49 (0.24,0.67)	0.73	0.00 (0.00,0.00)

95% CI's are bs %tiles (case) on 9000 bootstrap samples
 *all healthy controls = healthy controls with and w/o family history
 13 Apr 2020

Panc Ca Bakeoff #2 - VARI results

8) PDAC vs bgn bil. obstr.



	CA19-9	CA19-9:sTRA	MUC16:sTRA
AUC:	0.86 (0.78,0.93)	0.88 (0.82,0.93)	0.63 (0.49,0.75)
sens(spec=.90):	0.68 (0.62,0.86)	0.76 (0.70,0.92)	0.32 (0.26,0.58)
spec(sens=.90):	0.50 (0.00,0.88)	0.75 (0.00,1.00)	0.00 (0.00,0.00)

95% CI's are bs %tiles based on 3000 bootstrap samples

13 Apr 2020

Thanks To:

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- VAI Optical Imaging Core
- NCI – Early Detection Research Network
- NCI – Alliance of Glycobiologists for Cancer Detection



5 minute Q&A

Chair/Co-Chair/NCI

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and Track Time

NCI and Production Team

answer Chat questions not related to presentations
and use Slack