

Ultrasensitive Molecular Detection for Early and Accurate Diagnostics



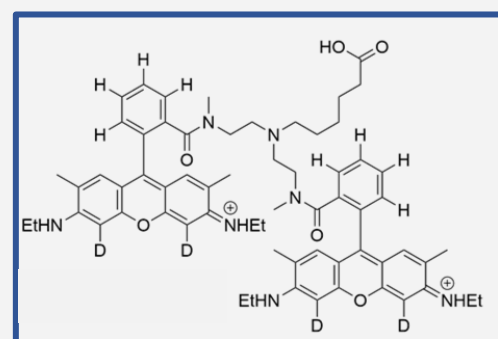
Mike Poderycki, PhD
Director of Research and Technology

*Revolutionizing early
disease detection with
precision cross-modality
optical diagnostics*

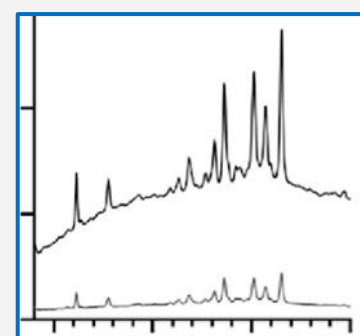
Core technology



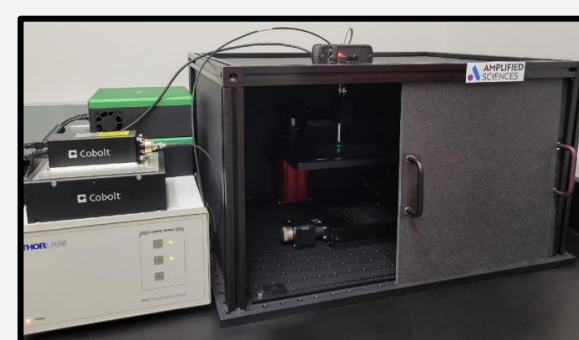
Sensitive optical detection using Raman Spectroscopy



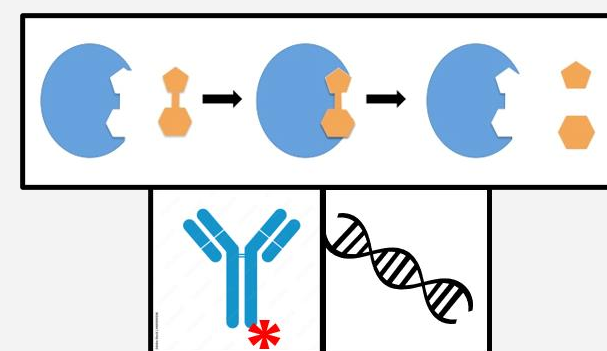
Bright dyes (*V. Jo Davisson; Purdue U*)



Surface-Enhanced Raman Spectroscopy (**SERS**)

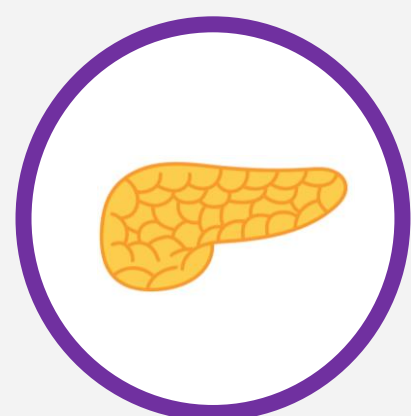


Hardware / software platform (*data acquisition & analysis*)



Assay development (*flexible & multi-modality*)

The clinical problem: Pancreatic cystic lesions (PCL):



Responsible for 10–15% of the 60,000+ annual pancreatic adenocarcinomas



1–3 million detected annually. Most do not lead to cancer.



Testing is often inconclusive:

- Accuracy
- Assay Failure (sample quality)
- Sample Availability (++ volume and multiple tests)

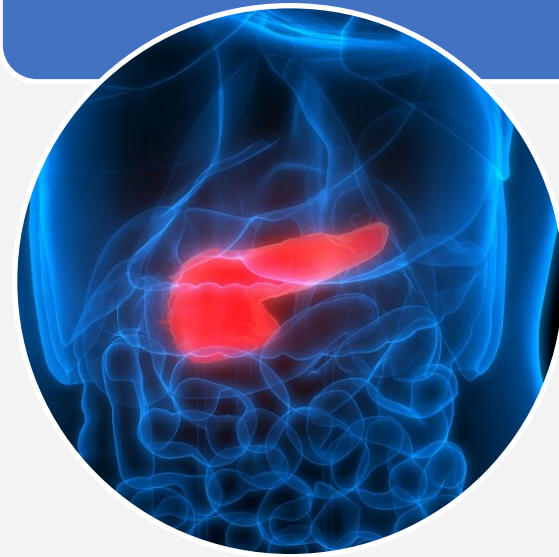


Extended surveillance...Many scared patients...Unnecessary surgeries

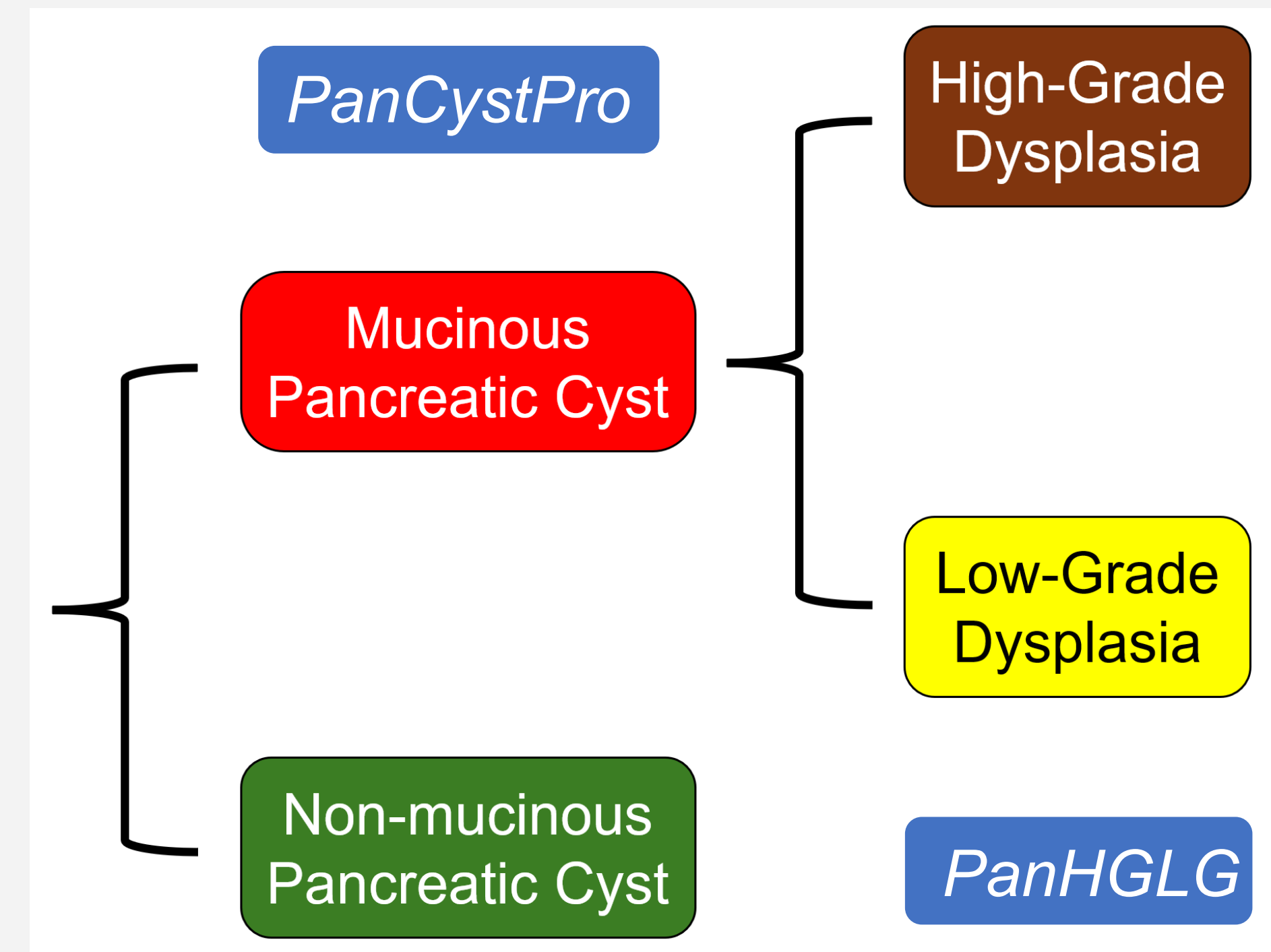
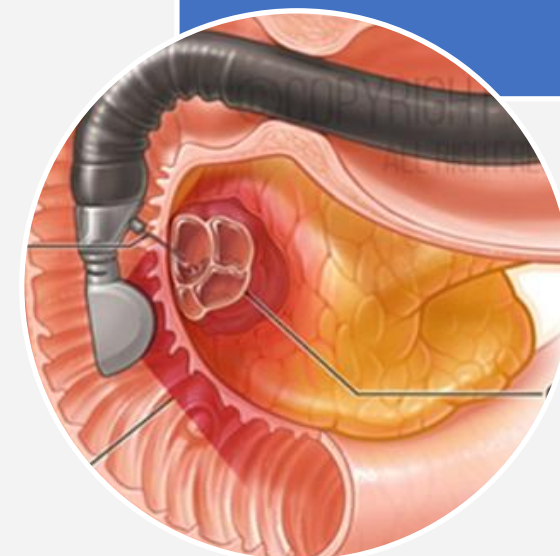
PCL fluid diagnostic pipeline



Imaging reveals cyst



Standard of Care
EUS-FNA



Biology of Human Tumors

Clinical
Cancer
Research

Global Protease Activity Profiling Provides Differential Diagnosis of Pancreatic Cysts

Sam L. Ivry^{1,2}, Jeremy M. Sharib³, Dana A. Dominguez³, Nilotpal Roy⁴, Stacy E. Hatcher³, Michele T. Yip-Schneider⁵, C. Max Schmidt⁵, Randall E. Walter G. Park⁷, Matthias Hebrok⁴, Grace E. Kim⁸, Anthony J. O'Donoghue⁹, Kimberly S. Kirkwood³, and Charles S. Craik¹

UCSF School of
Medicine

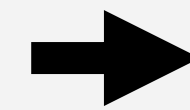


Ectopic activity of gastricsin protease in cyst fluid is associated with mucinous cysts

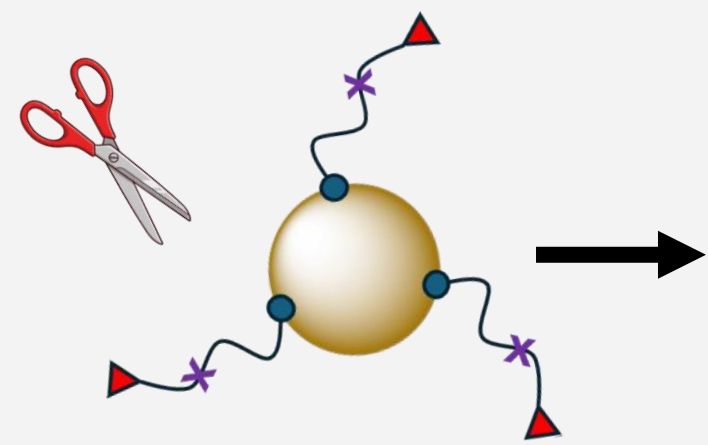
Building a SERS biomarker assay - gastricsin

Alignment with the SERS technology

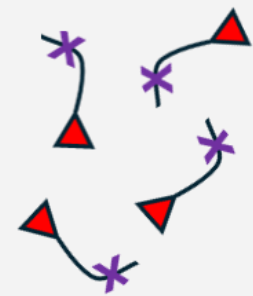
- Ultra-low volume protease activity assay
- Avoid matrix effects with 2000x dilution



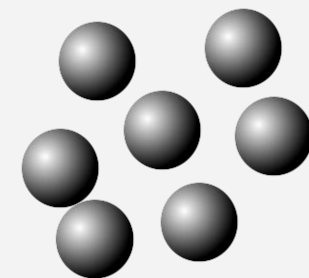
Maintain high sensitivity & conserve sample



Magnetic bead-based assay



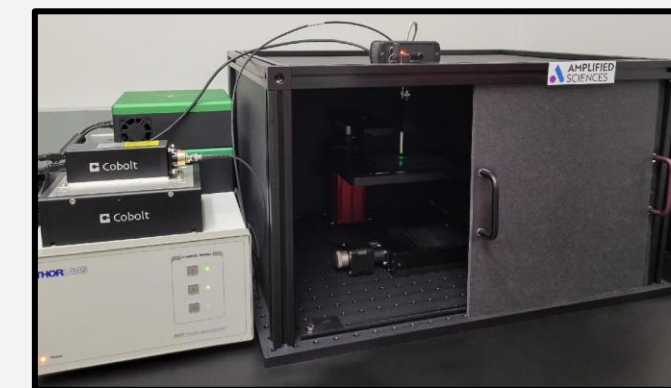
Dye release



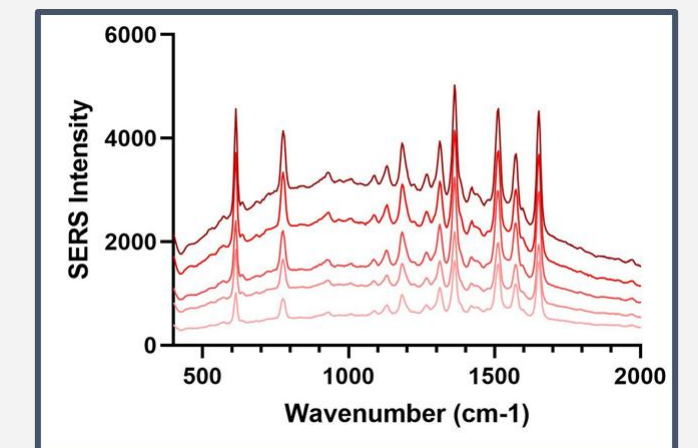
Silver nanoparticles amplify Raman signal



Transfer to 384-well plate



Automated SERS

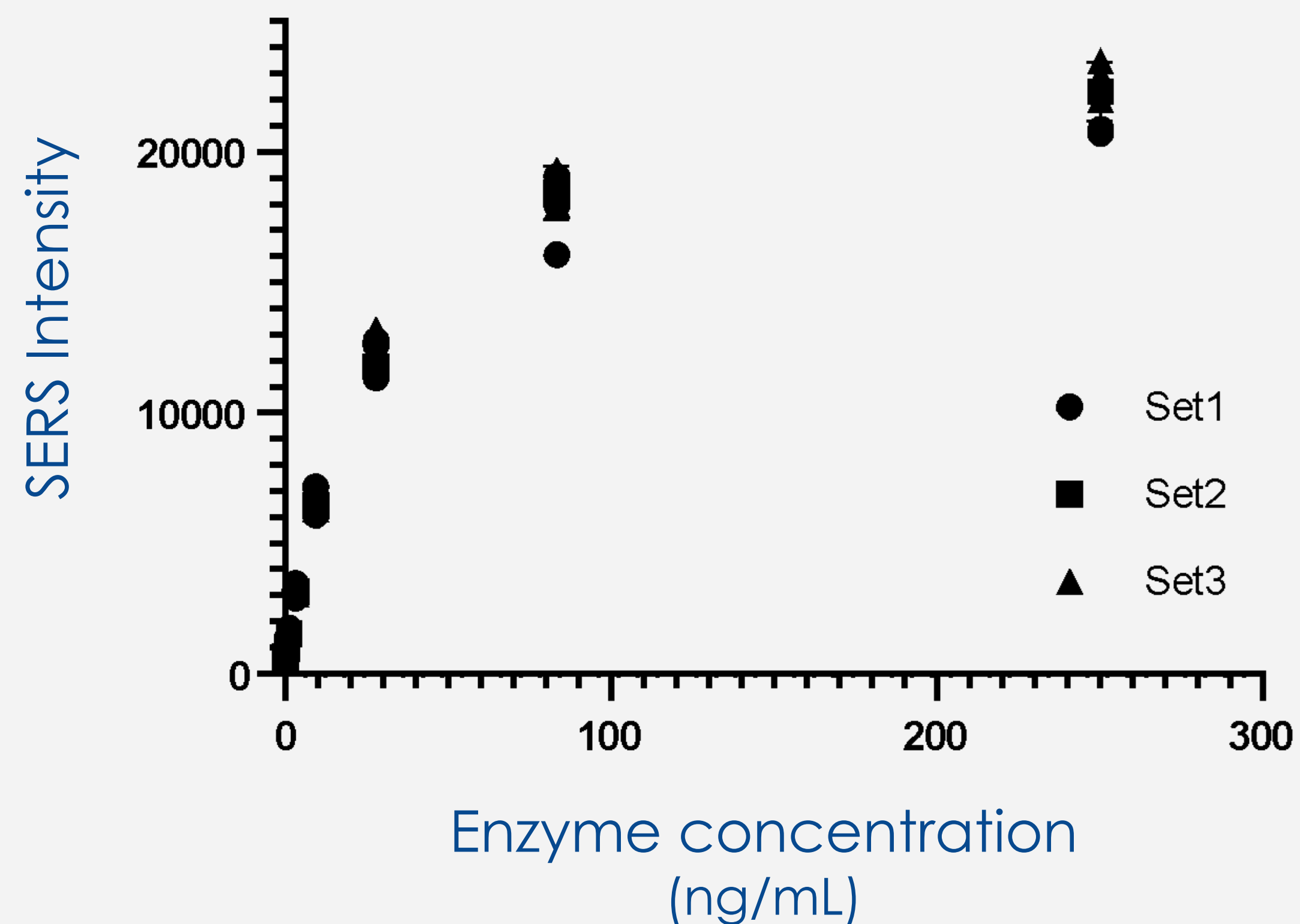


Automated spectral deconvolution

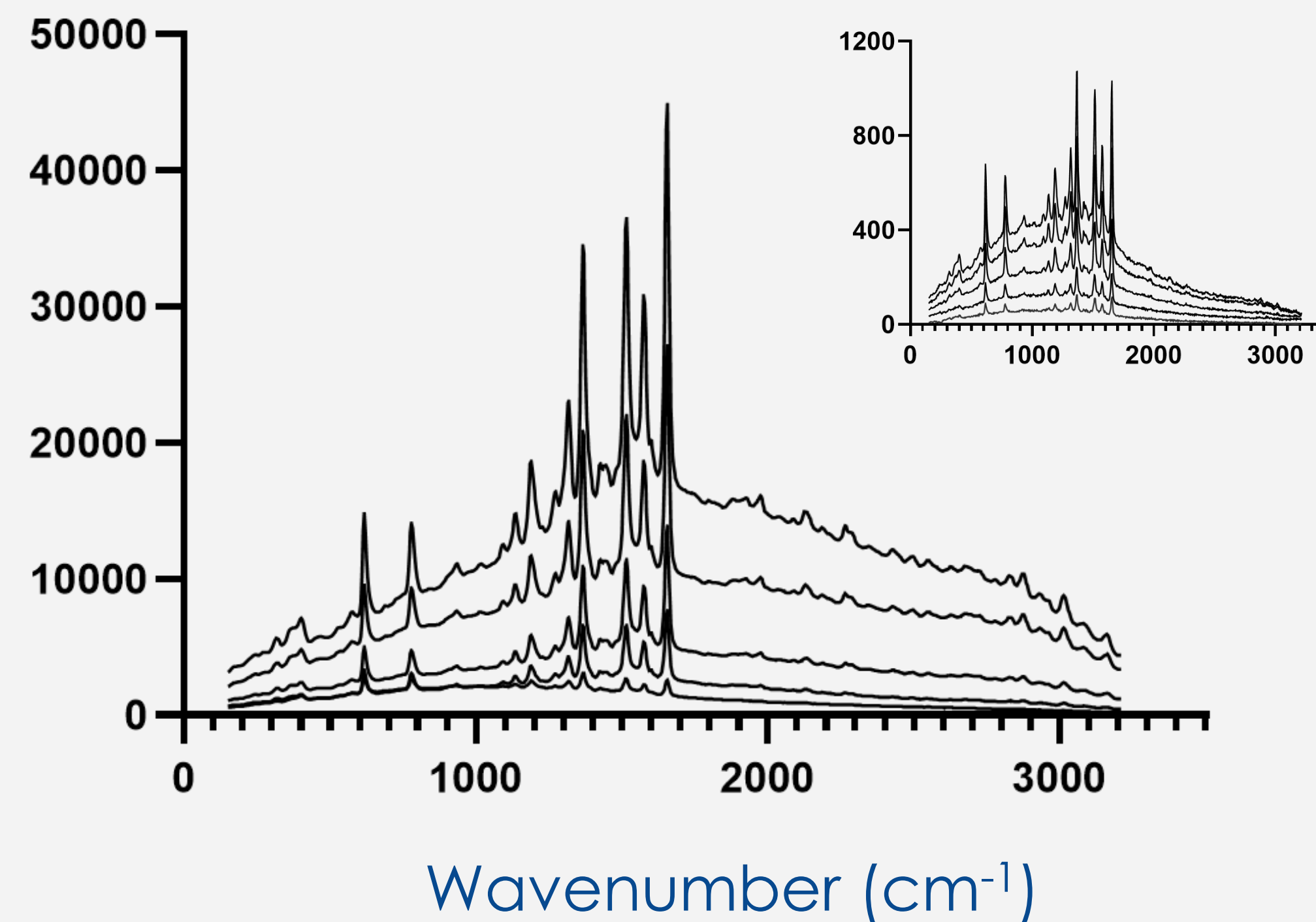
- 0.005 to 0.5 μ L requirement per reaction
- 0.5 to 5 μ L volume per reaction in practice

Gastricsin activity assay

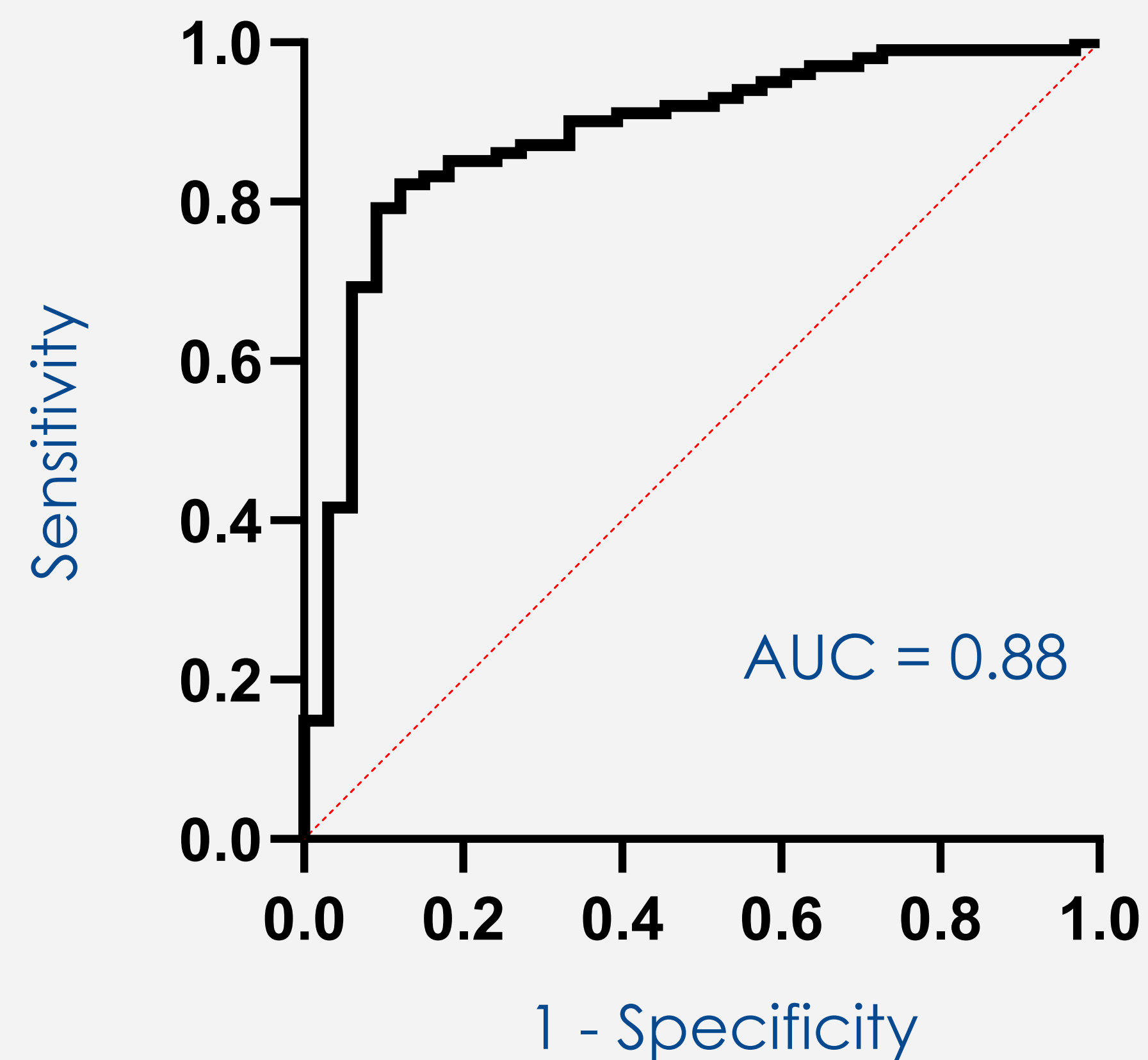
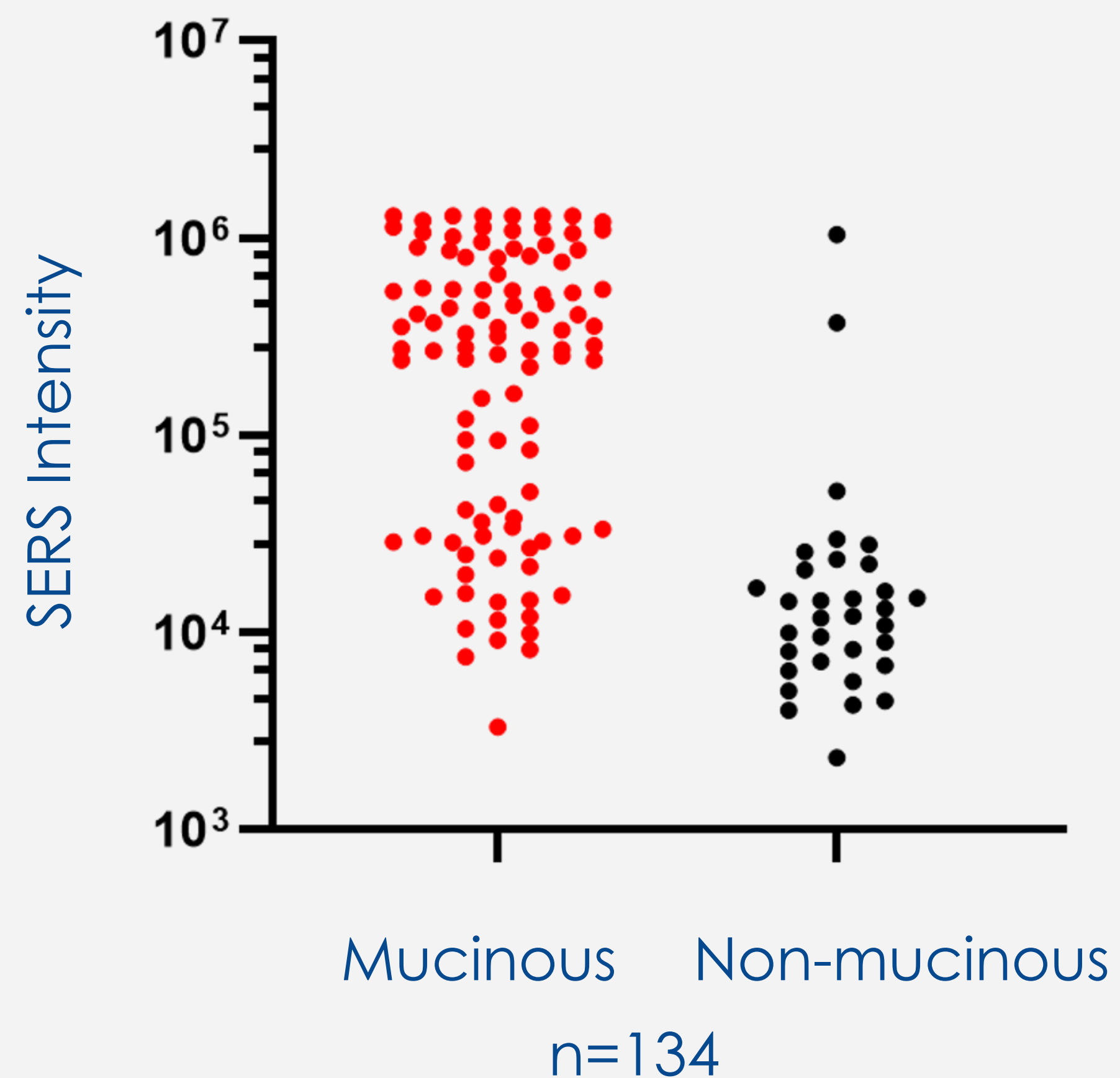
Model System



Cyst Fluid – Raw spectral data

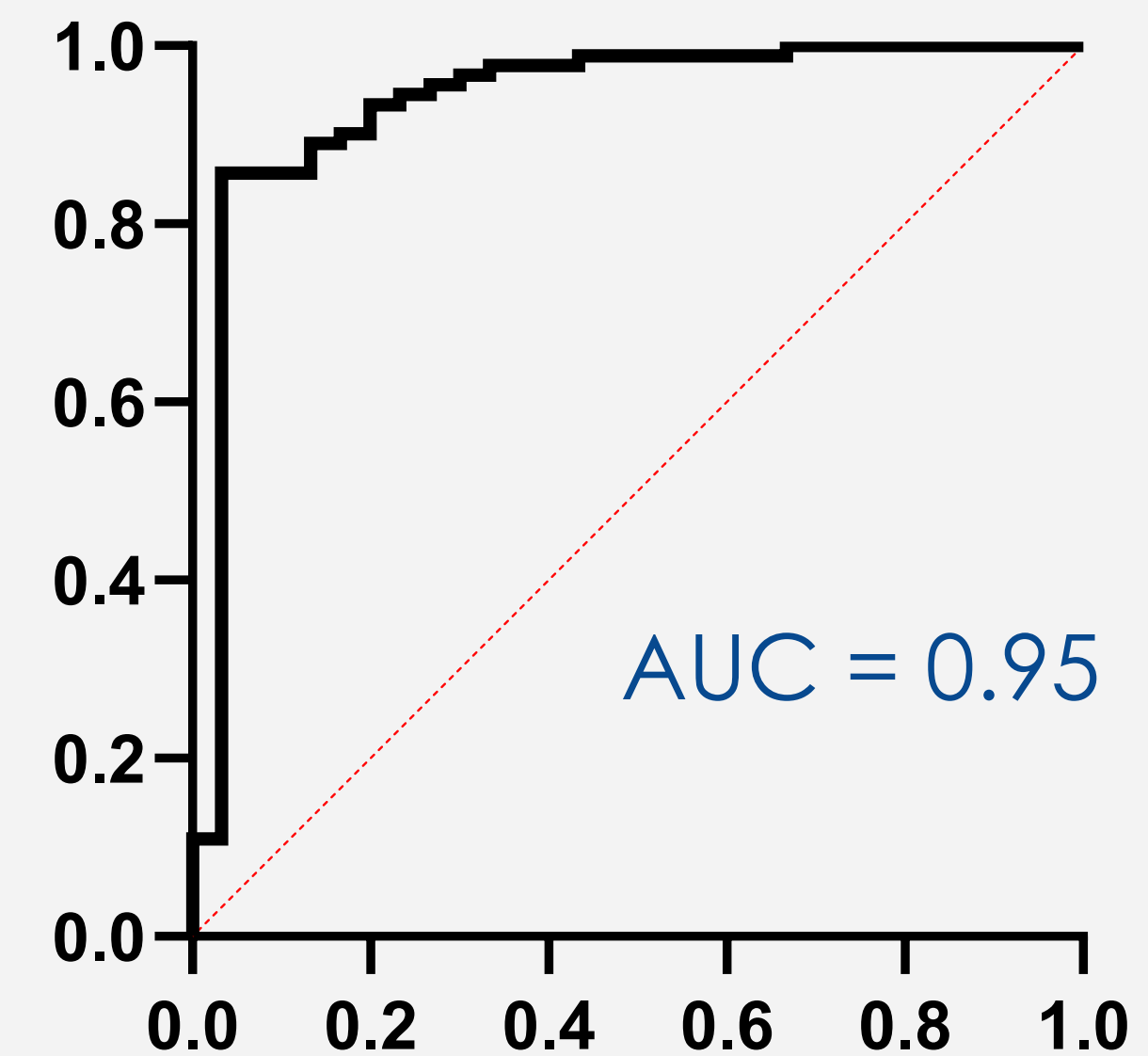
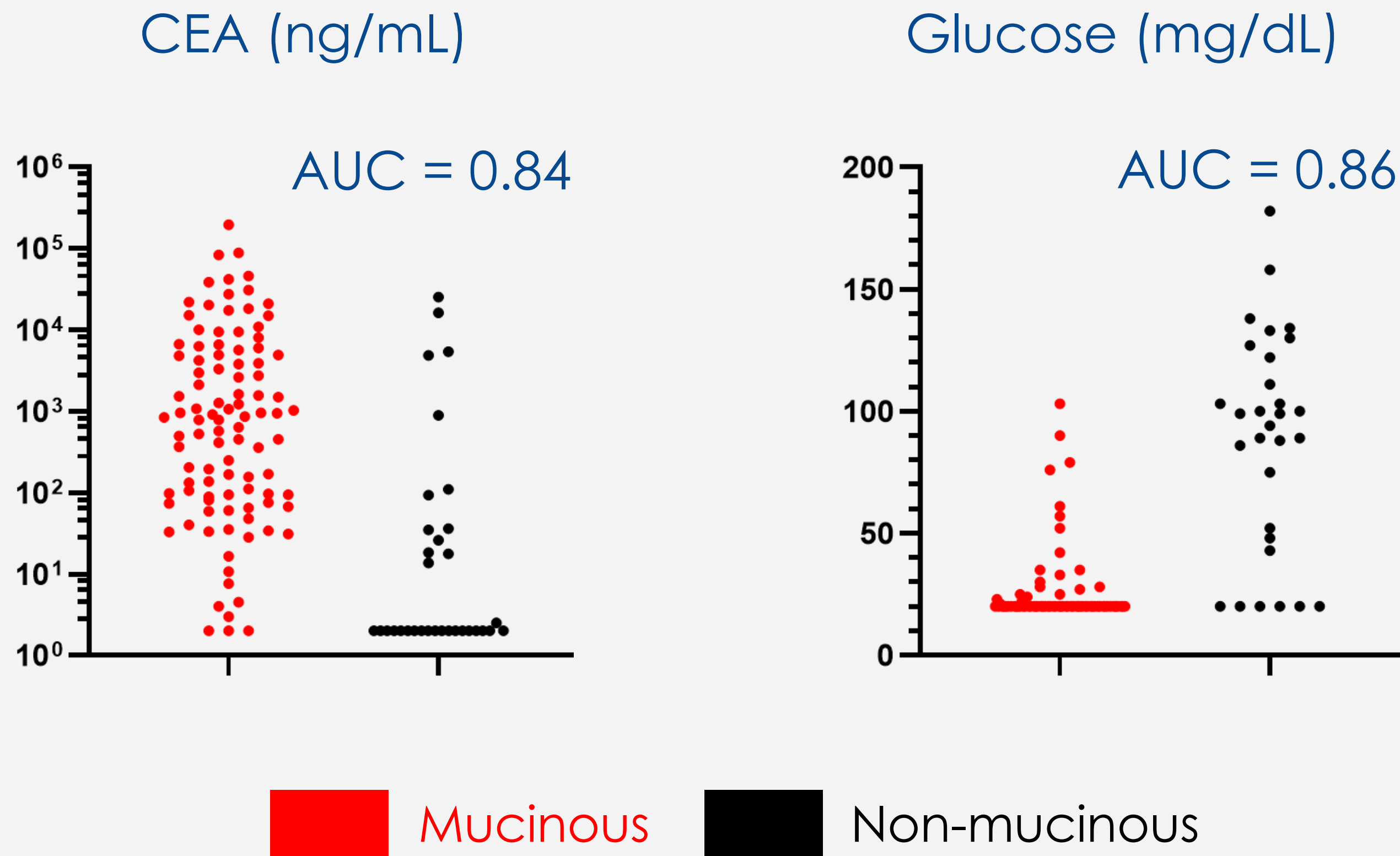


Gastricsin activity in a training cohort



Addition of “traditional” markers

3-marker performance

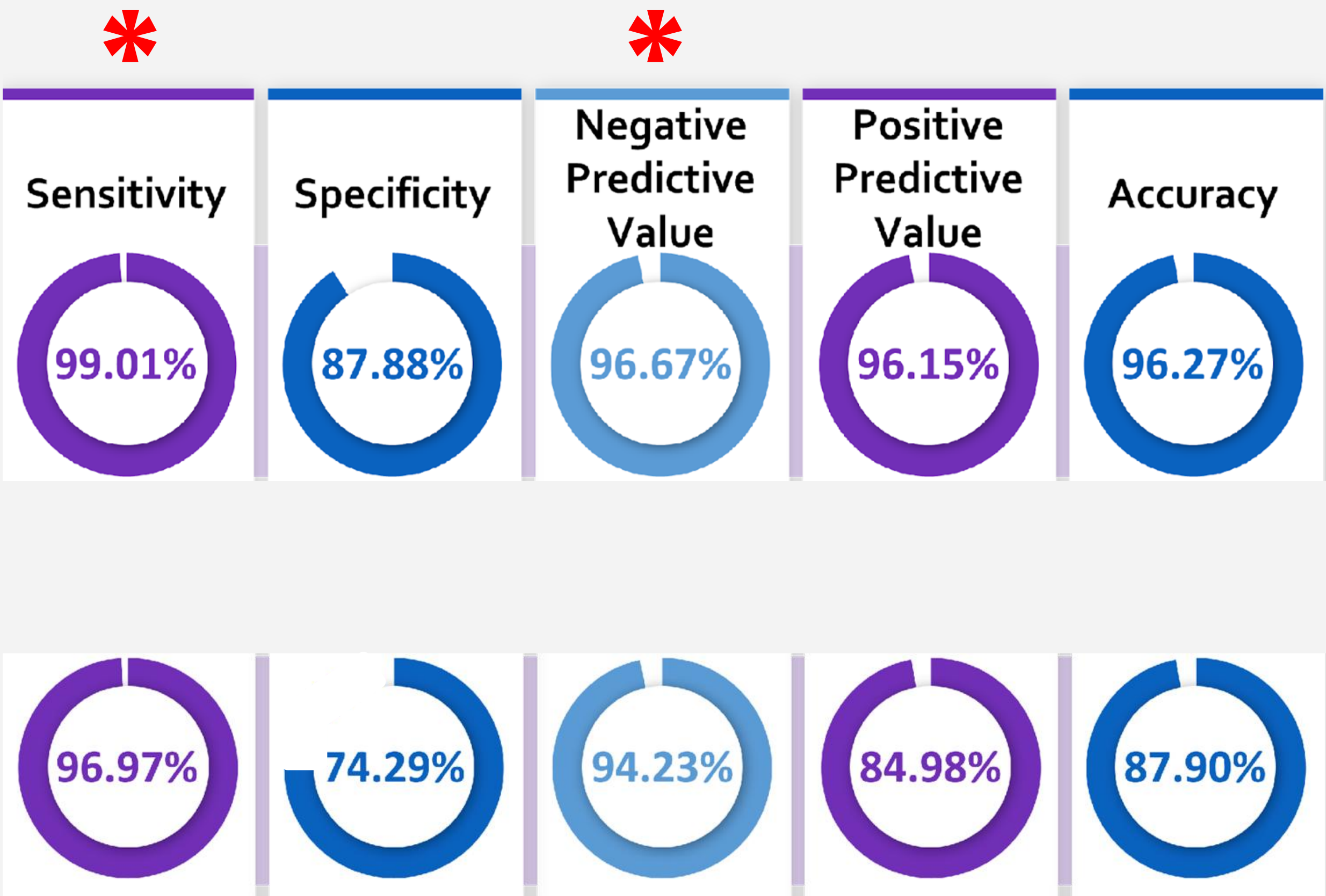


- CEA and Glucose are low-volume but not SERS (yet)
- Glucose can fail – default to 2-marker ruleset with thresholds SKEWED conservatively toward mucinous

PanCystPro performance

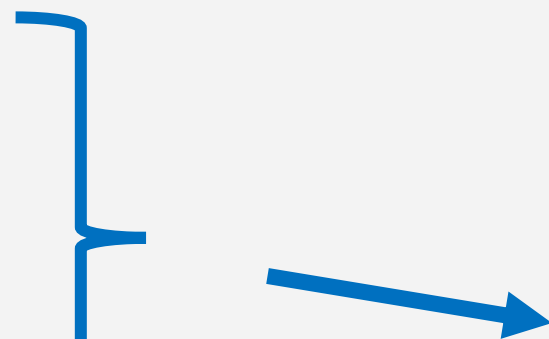


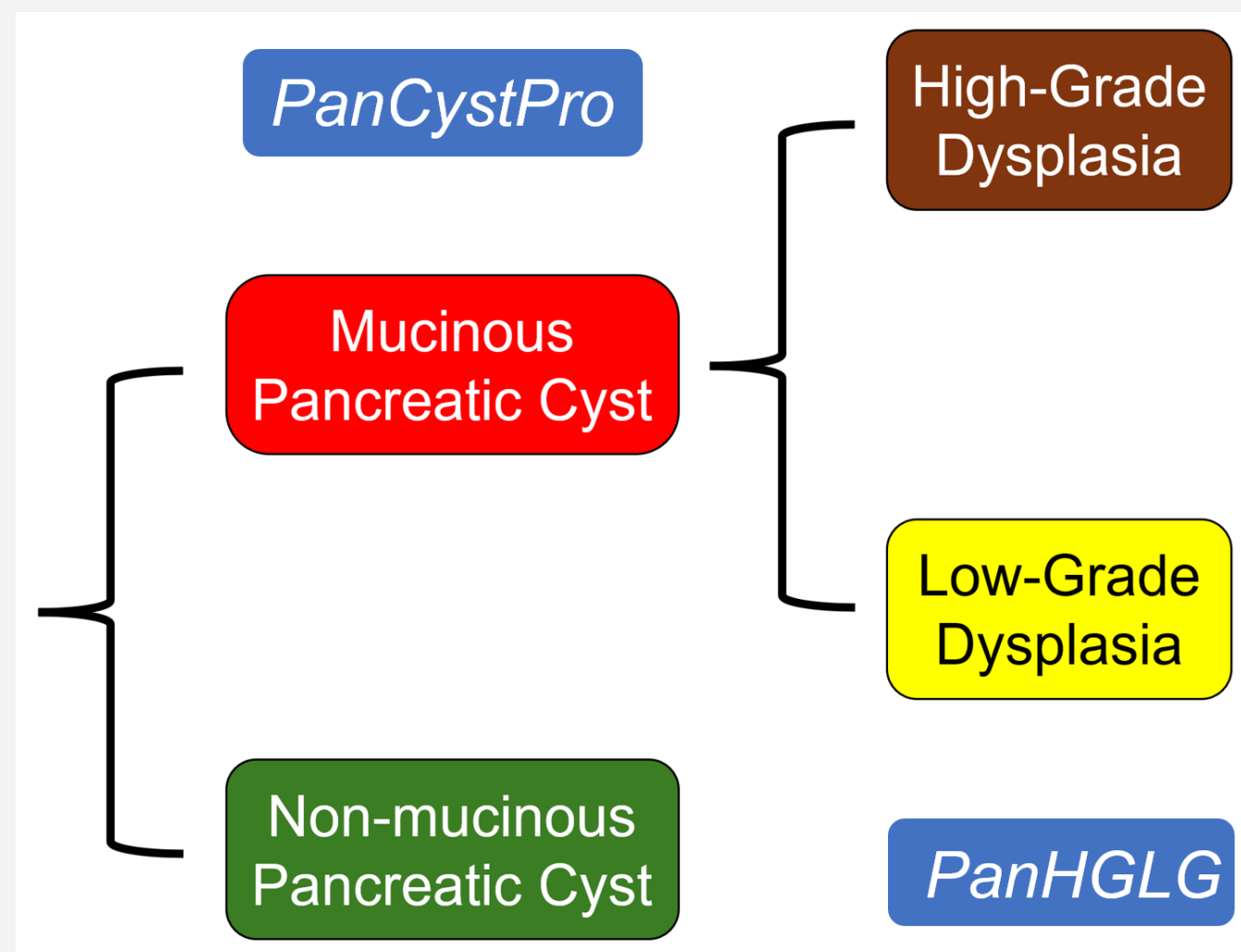
- Retrospective patient samples
- 4 clinical sites
- Rule-out test



Algorithm Training
n=134

Testing
(CLIA / CAP)
n=68

- *Publication (revised manuscript in process)*
 - *Clinical Utility study*
 - *Early Access*
 - *Prospectively collected samples*
- 
- *Process improvements*
 - *High level of R&D oversight*
 - *Long term outcome studies*
-
- *After PanCystPro – transition future tests to 100% Raman (SERS)*



Rule out test – Identify patients that we are very confident do NOT have risky cysts with High-Grade dysplasia

Primary – Intraductal Papillary Mucinous Neoplasm (IPMN)

Secondary – Mucinous Cystic Neoplasm (MCN) if possible

Which patients will this be intended for?

Mucinous call made by PanCystPro (reflex test)

Mucinous call without PanCystPro

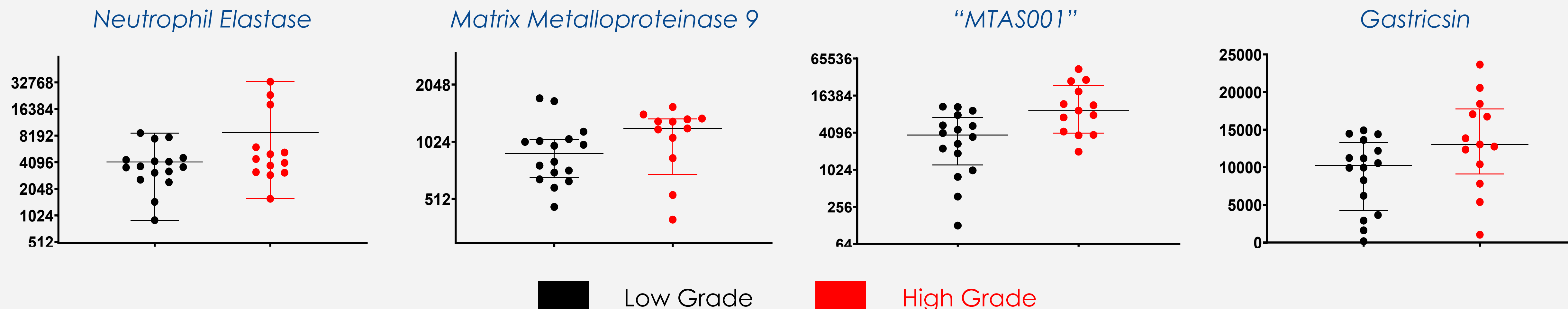


Biomarker panel must ALSO identify non-mucinous cysts that “sneak through” as possessing Low-Grade dysplasia

PanHGLG development (1)

More than 1 possible approach to assemble a Biomarker Panel

Approach 1. Repeat the Gastricsin protease activity journey

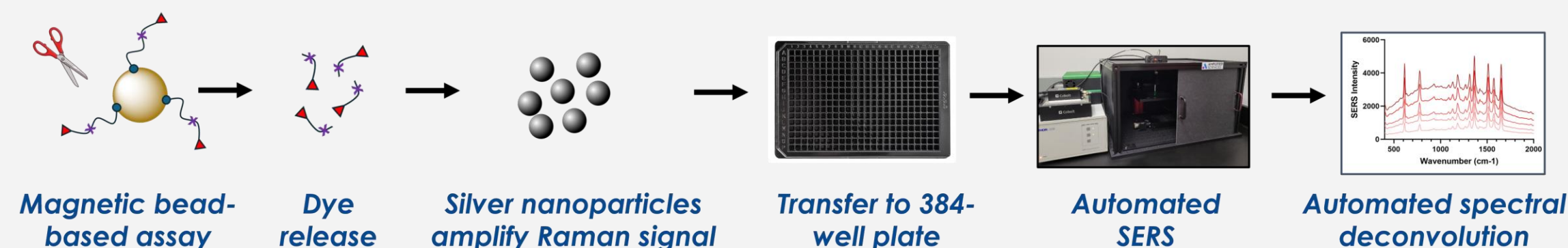


- 4-marker assay panel targets multiple protease activities
- Very small cohort (n=29)
- Sensitivity = 100% Specificity = 94%

- Turnover assays can be cumbersome
- Not always necessary

PanHGLG development (2)

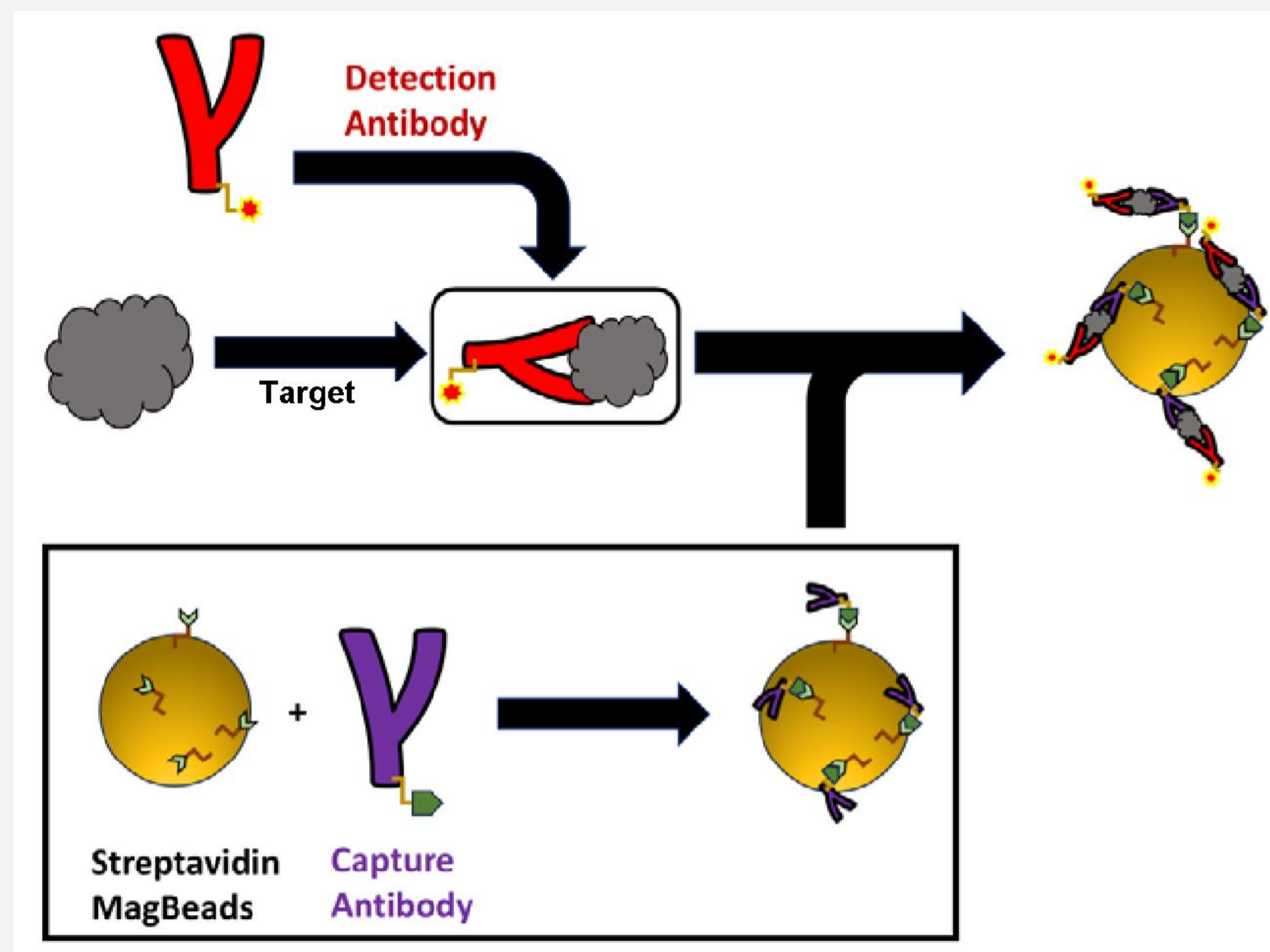
Approach 2. Leverage flexibility of the SERS platform



Only strict requirement is the ability to create an assay utilizing a SERS-active dye

- Protease activities
- Other enzymatic activities
- Metabolites
- Protein Quantification
- Nucleic acids

ImmunoSERS (iSERS)

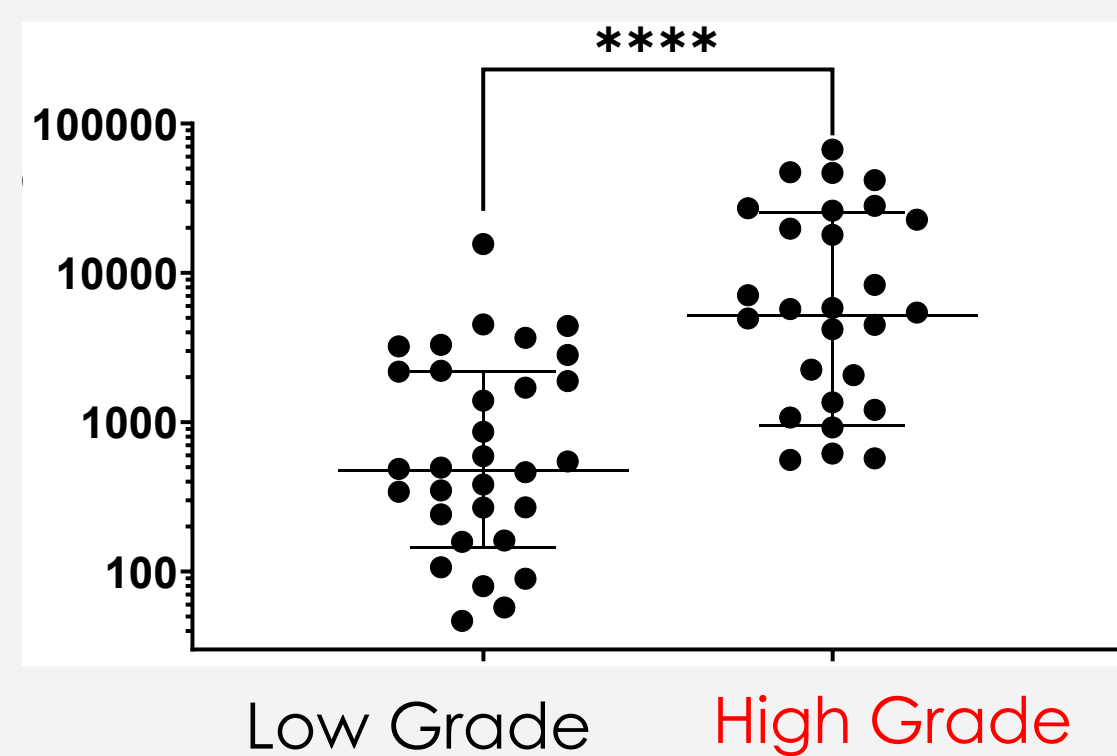


Combination panels

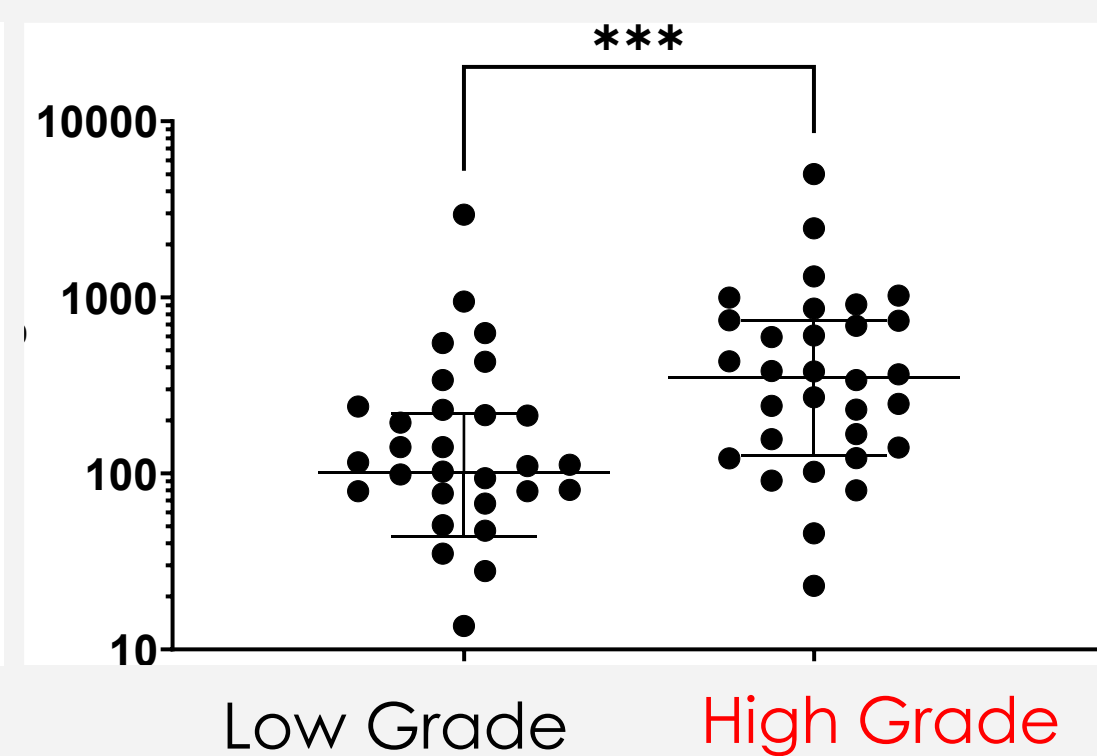
ImmunoSERS

Protease Activity

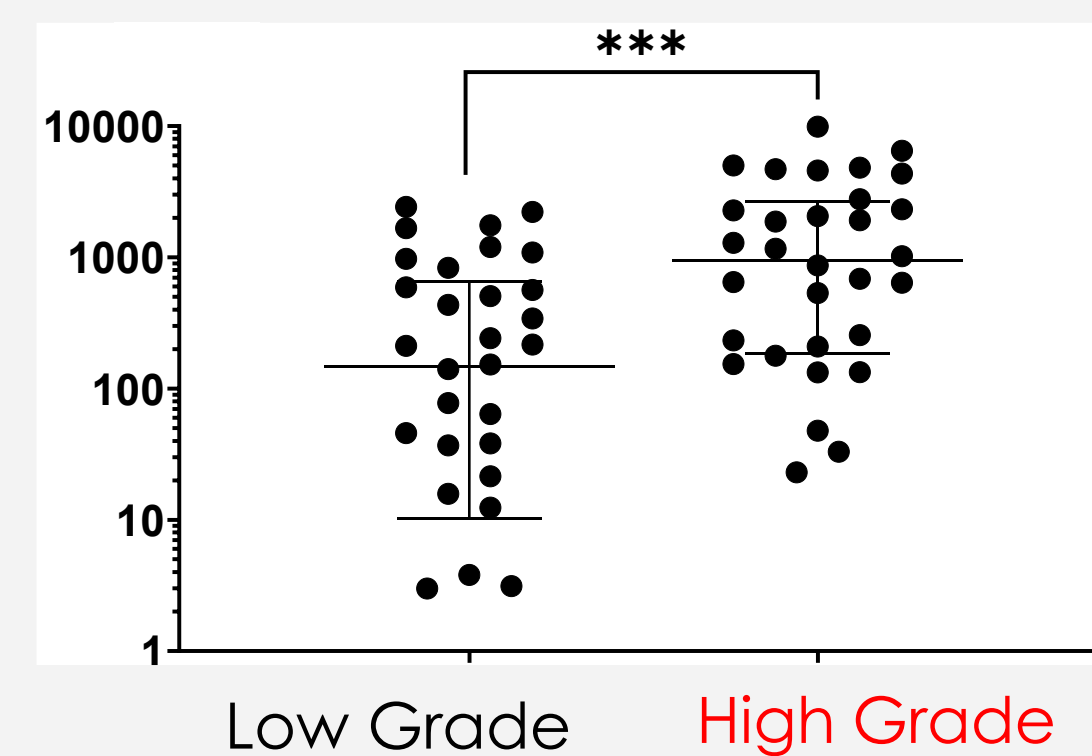
Neutrophil Elastase



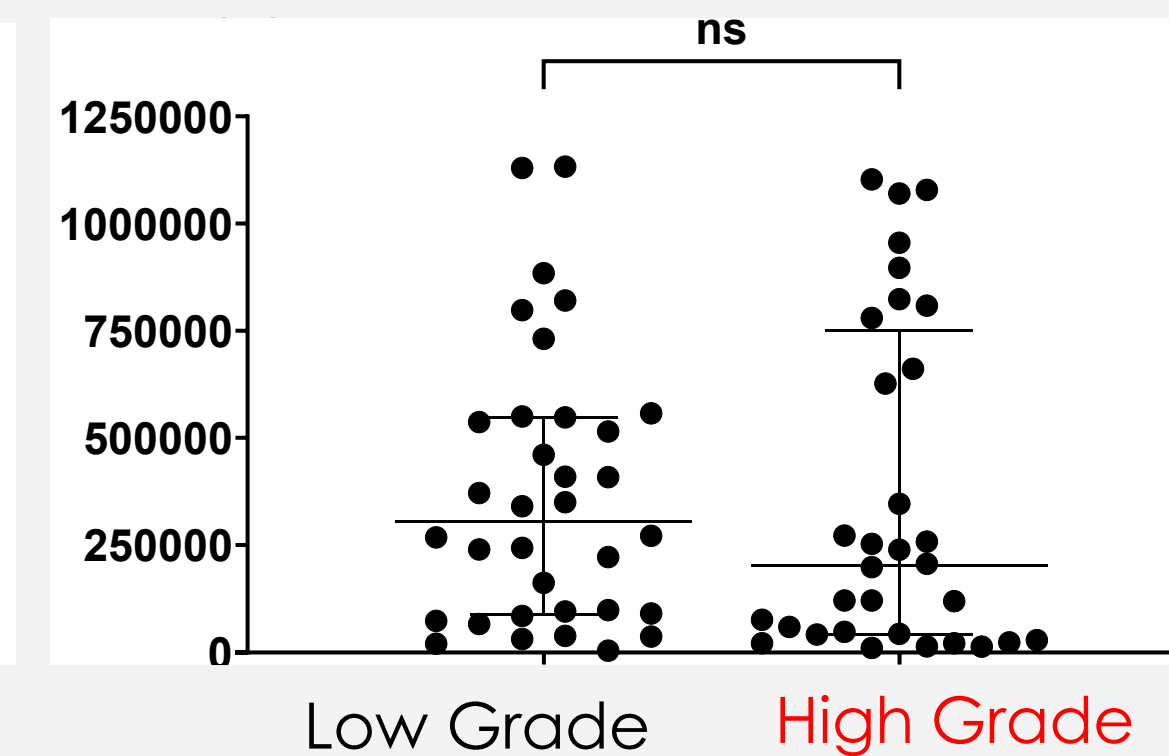
Myeloperoxidase



MTAS001 Activity



Gastricsin Activity



- Combination of iSERS and Protease Activities
- Cohort size of $n=66$
- Sensitivity = 97% Specificity = 88%

Technology roadmap

Assay Panel Development

- Panel Refinement
- Analytical Validation
- Addition of clinical features (e.g., imaging)
- Bigger Cohorts (clinical validation)

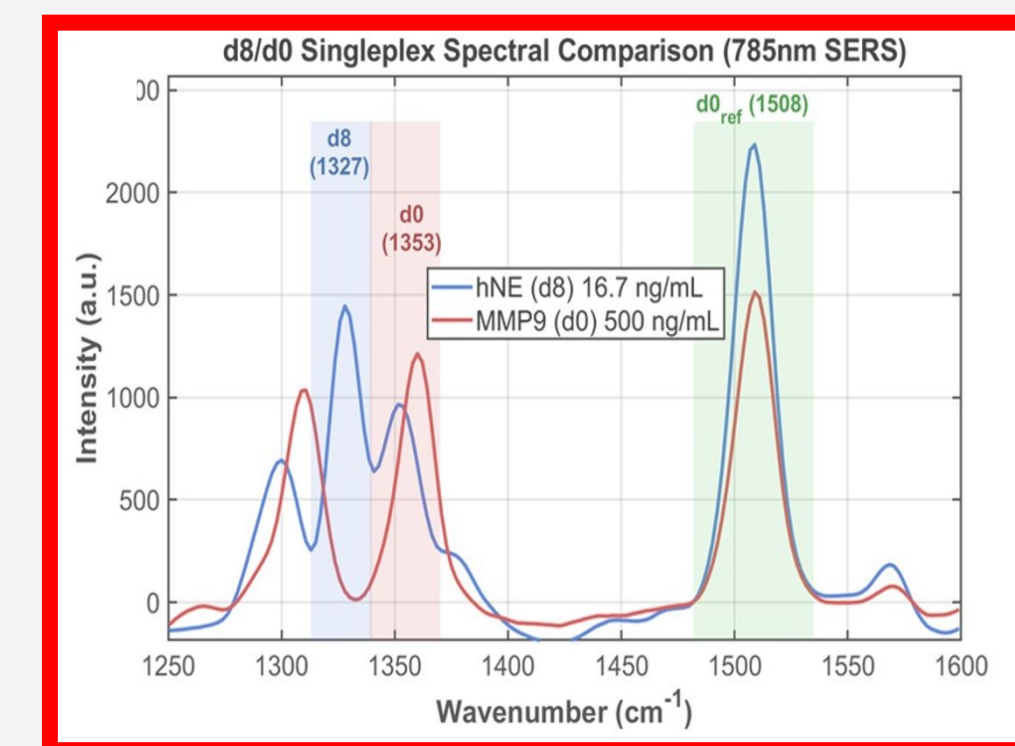
New tests

- Analyte Class Expansion
- Related Indications

Platform Development



Automated liquid handling



Dye variants for multiplexed assays

Collaborators

