

Peter Pinto MRI

- When MRI target present, fusion biopsy detected significant cancer 12% more often than standard template biopsy
 - Not everyone received biopsy
 - Biomarkers not evaluated
- Combined targeted and standard template better for detection of higher grade disease

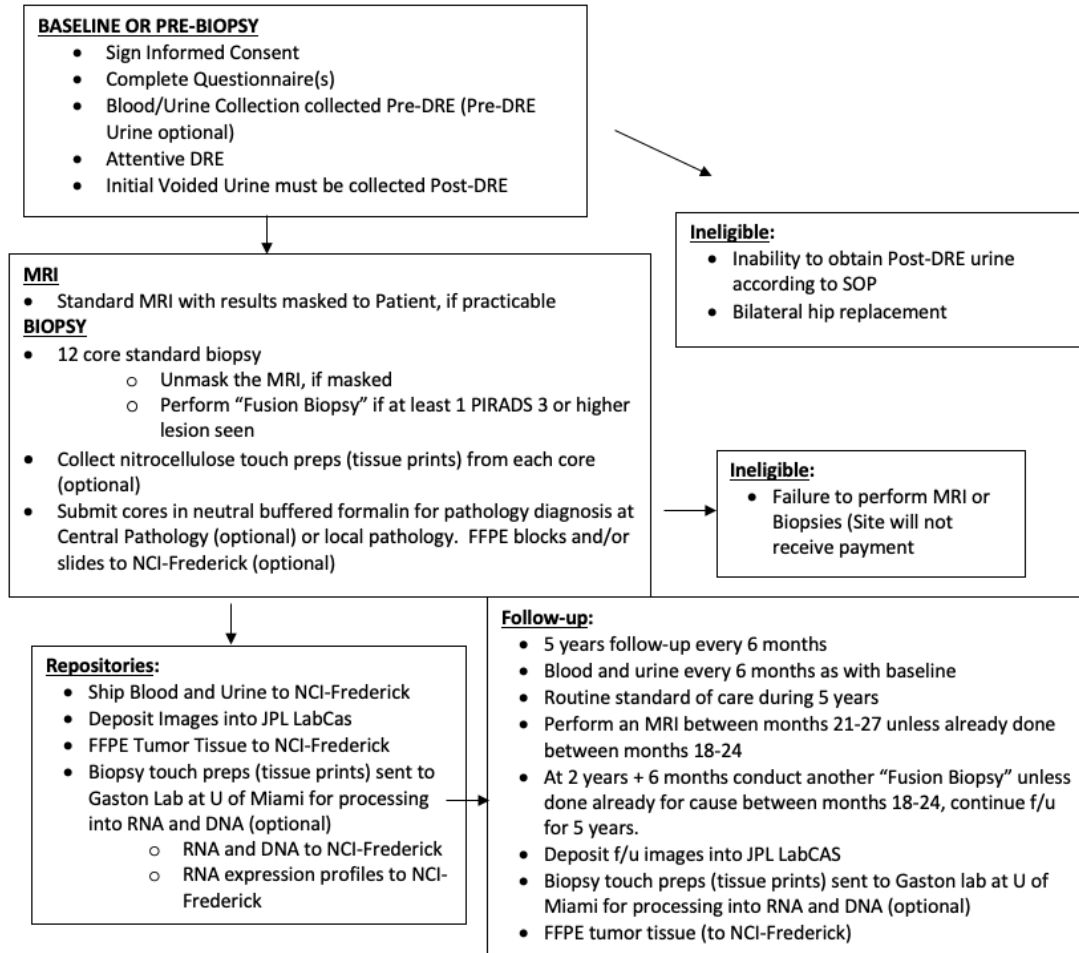
EDRN PROSTATE MRI BIOMARKER STUDY AND REFERENCE SET: BACKGROUND

- Current state:
 - Our EDRN validation studies support role for laboratory biomarkers (PSA, PCA3, TMPRSS2:erg) in biopsy naïve men presenting for early detection
 - Costly MRI often ordered in clinical setting
 - Benefit of MRI in this setting is uncertain
- Knowledge gap:
 - How best to use prostate MRI for cancer early detection in the biopsy naïve setting, given available laboratory biomarkers (eg PSA, PCA3, TMPRSS2:erg)
 - Lack data driven algorithm for use of laboratory biomarkers + prostate MRI

EDRN PROSTATE MRI BIOMARKER STUDY AND REFERENCE SET: DESIGN

- Unique longitudinal MRI / biomarker study to determine the role of MRI and how to optimize detection of high grade cancer in the setting of men presenting for an initial biopsy
- Multi site study with unique biorepository that includes MRI+biomarkers
 - 14 Study Sites: University of Michigan (John Wei Lead Investigator), UT Southwestern, UT San Antonio, University of Alabama, Harvard (Brigham and Beth Israel), Cornell, Vanderbilt, Emory, Moffitt, Stanford, Montefiore, CPDR, University of Miami
 - Analytic sites/DMCC: JHU, UMICH, UMIAMI/FHCRC and JPL (MRI repository)
- Primary Aim: To examine the incremental specificity for high grade prostate cancer (ie Gleason 6+) of prostate MRI above and beyond PSA, PCA3 and TMPRSS2:ERG with the sensitivity held constant at 90% in the initial biopsy setting.
- Primary endpoint: High-grade prostate cancer (ie Gleason 6+) on needle biopsy; specificity for high-grade prostate cancer (ie Gleason 6+) with sensitivity held constant
 - Proposed enrollment: 1500 men undergoing initial prostate biopsy *followed longitudinally for 2-5 years* (Currently in Phase 1 – enroll first 500 cases)

EDRN PROSTATE MRI BIOMARKER STUDY AND REFERENCE SET: Schema/Status



• Status

– 9 sites open for enrollment

- 78 cases enrolled to date

- 54 confirmed

- 1 withdrawal

– 5 sites pending approval

- Interim analysis after first 340 cases

Administrative change

- Rationale
 - Accrual hampered by
 - Uncovered MRI costs – only \$500, and 50% rule inadequate for some sites
 - Regulatory conflict with Medicare secondary payer rule - precludes billing CMS a different rate than another sponsor, eg NIH study
 - MRI coverage by study
 - Will now cover both MRI
 - \$750/MRI
 - reduces phase 1 enrollment from 500 to 340
 - Does not affect plans to perform interim analyses
 - Should address barriers to enrollment above

Changes in RNA extraction to high throughput

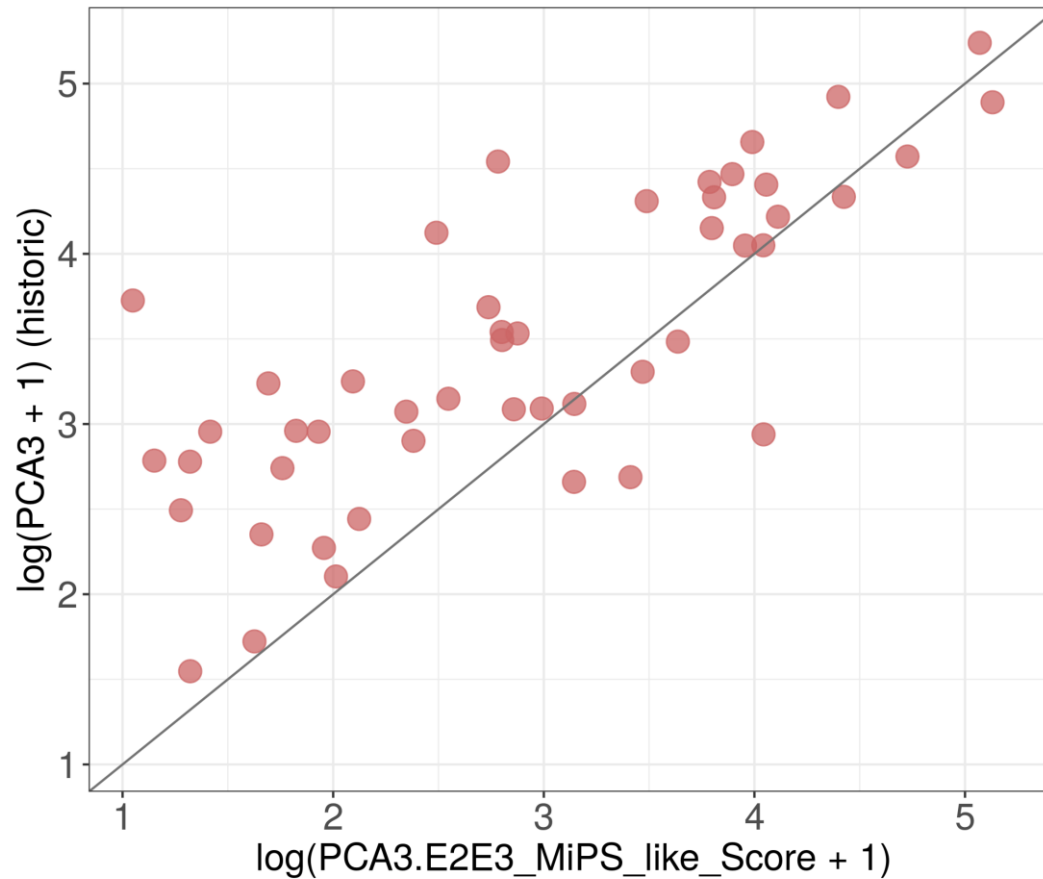
- Cani/Tomlins lab
 - Post DRE urine in Genprobe media
 - using the ZR Viral RNA Kit (Zymo Research, Irvine, CA).
 - Used 5 ml urine:media mix
- Lanbo lab
 - Post DRE urine in Genprobe media
 - ThermoFisher's Kingfisher automatic nuclear isolation system.
 - Uses 0.5 ml urine:media mix

NGS (Tomlins Assay)

Batch 1, n=48, RNA isolation: Andi method,

Batch 1, n=48, RNA isolation: Andi method, 5ml urine:media mix

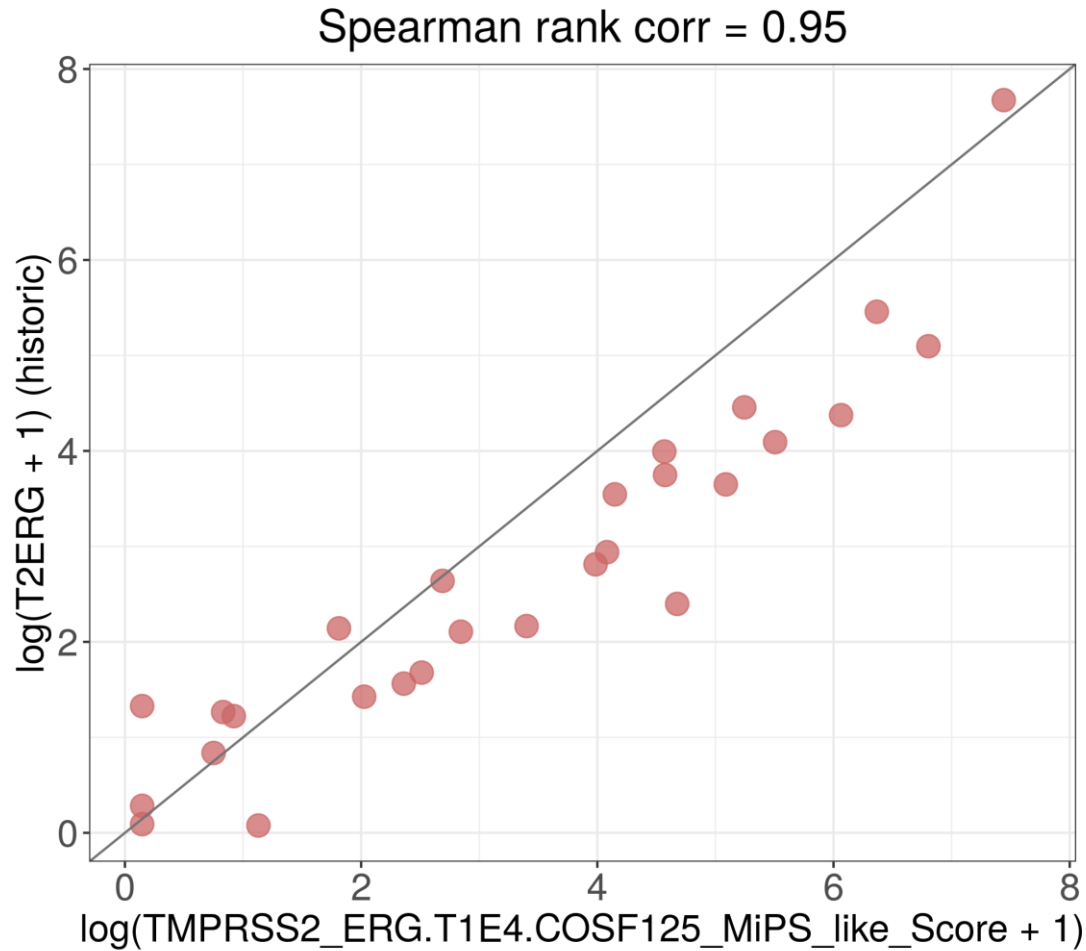
Spearman rank corr = 0.74



x-axis - NGS-MiPS

y-axis - Traditional MiPS

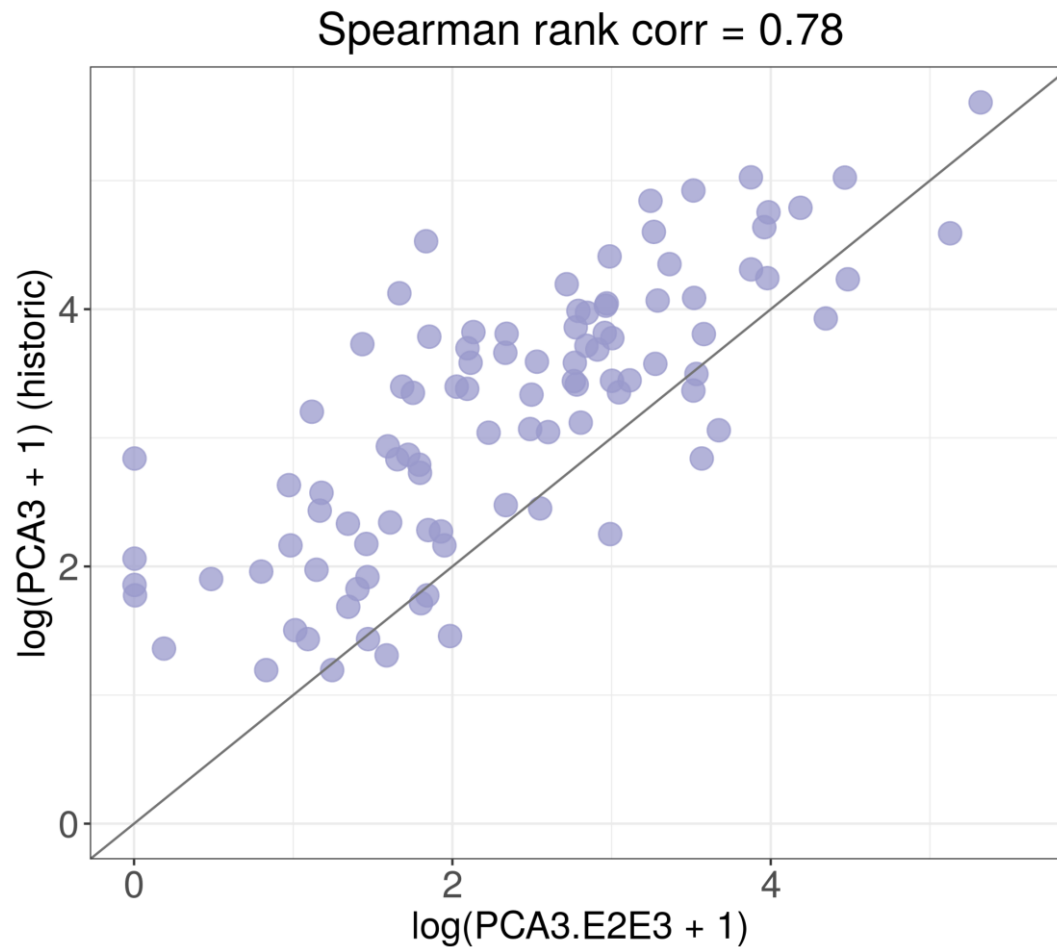
**Batch 1, n=48, RNA isolation: Andi method, 5ml urine:media mix
T2ERG (log scale)**



x-axis - NGS-MiPS

y-axis - Traditional MiPS

**Batch 2, n=98, RNA isolation: Lanbo method, 0.5 ml urine:media mix
PCA3 (log scale)**

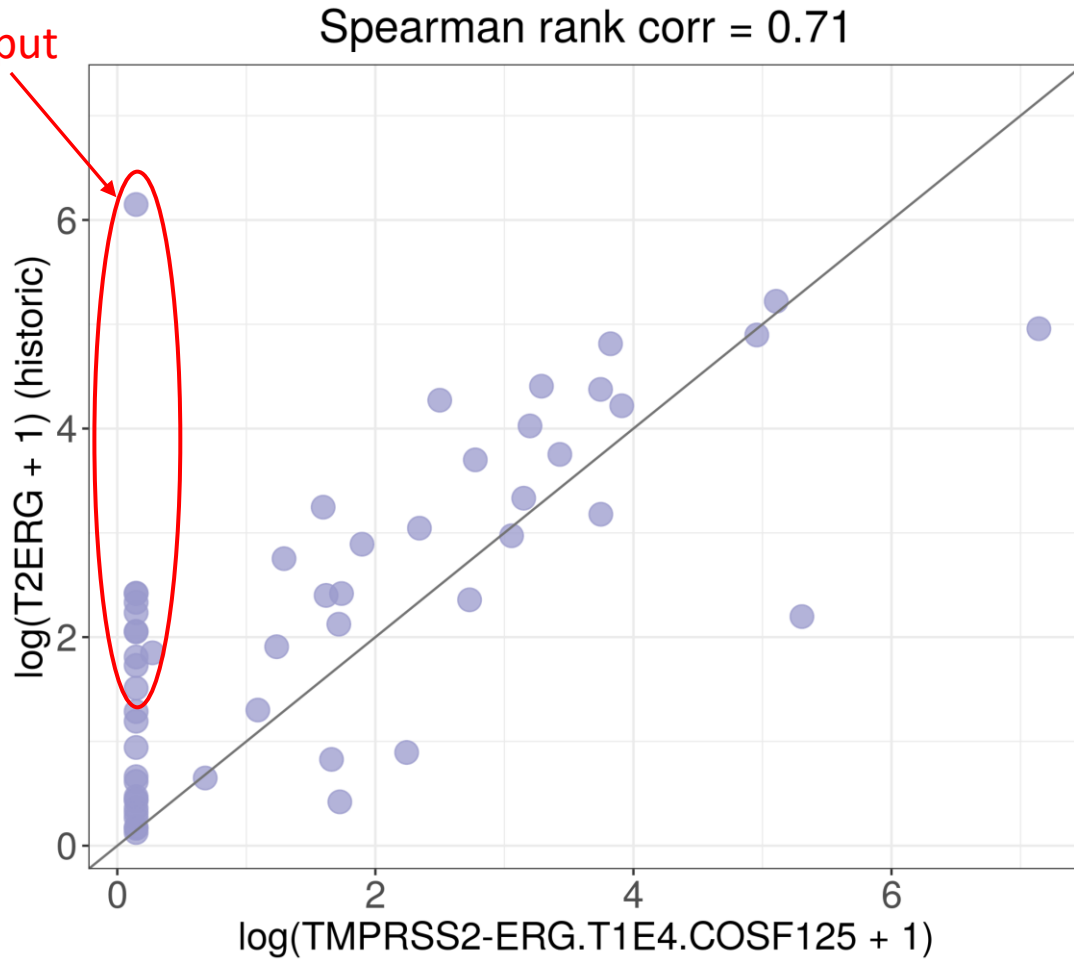


x-axis - NGS-MiPS

y-axis - Traditional MiPS

Batch 2, n=98, RNA isolation: Lanbo method, 0.5 ml urine:media mix
T2ERG (log scale)

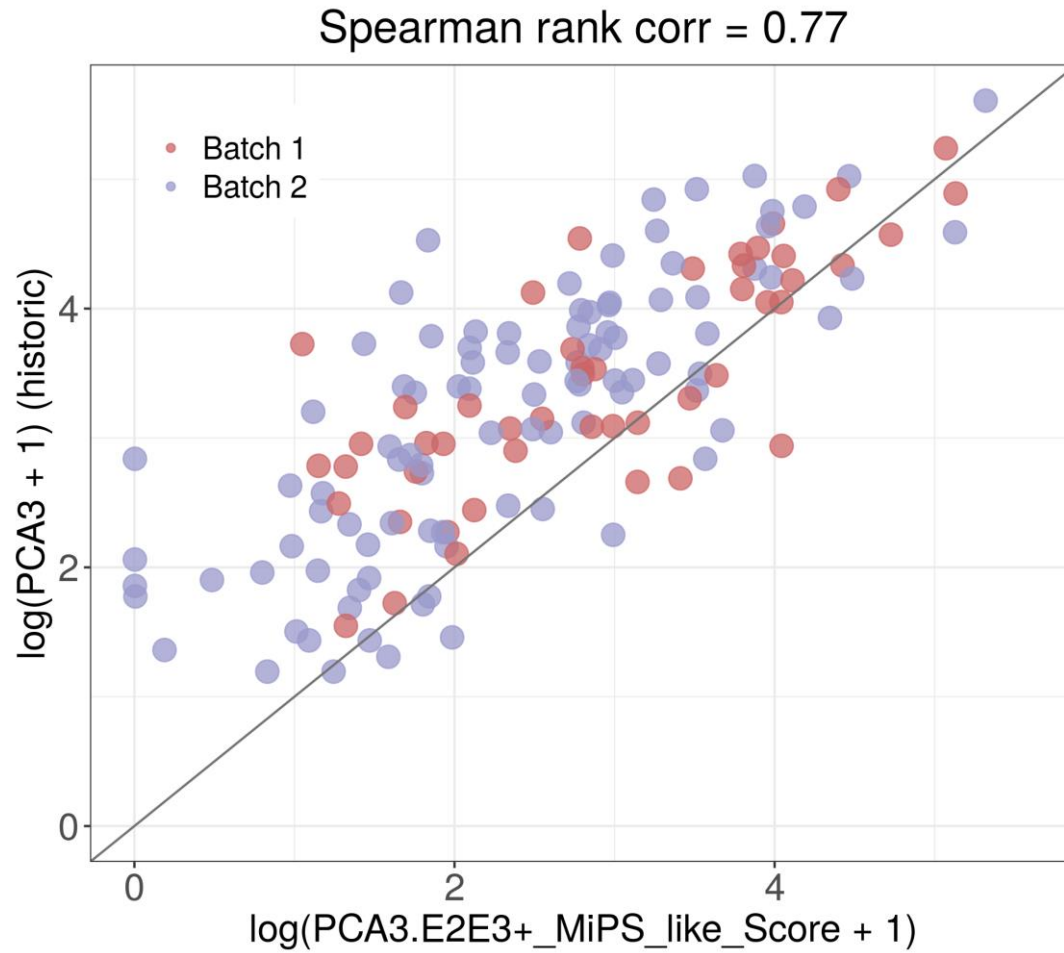
Likely due to low input



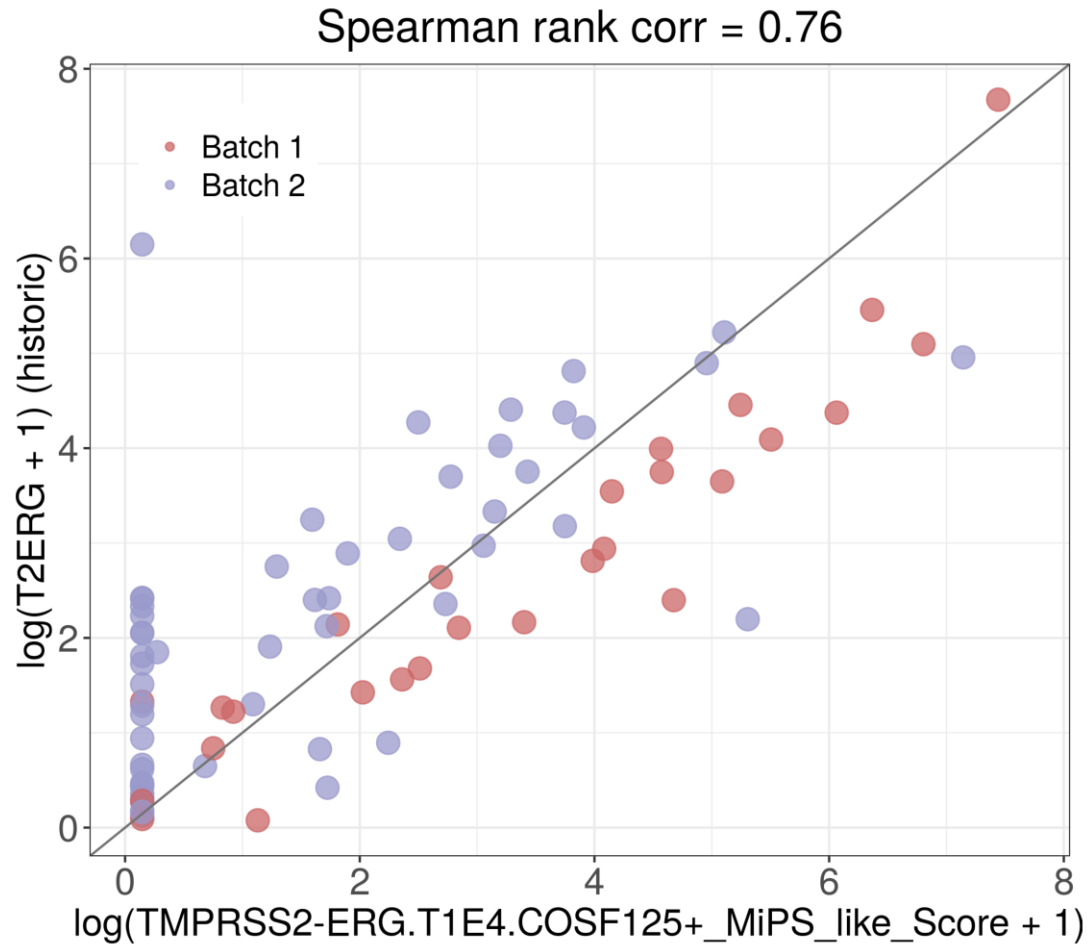
x-axis - NGS-MiPS

y-axis - Traditional MiPS

**Batch 1+2 above combined, n=146,
PCA3 (log scale)**



**Batch 1+2 above combined, n=146,
T2ERG (log scale)**



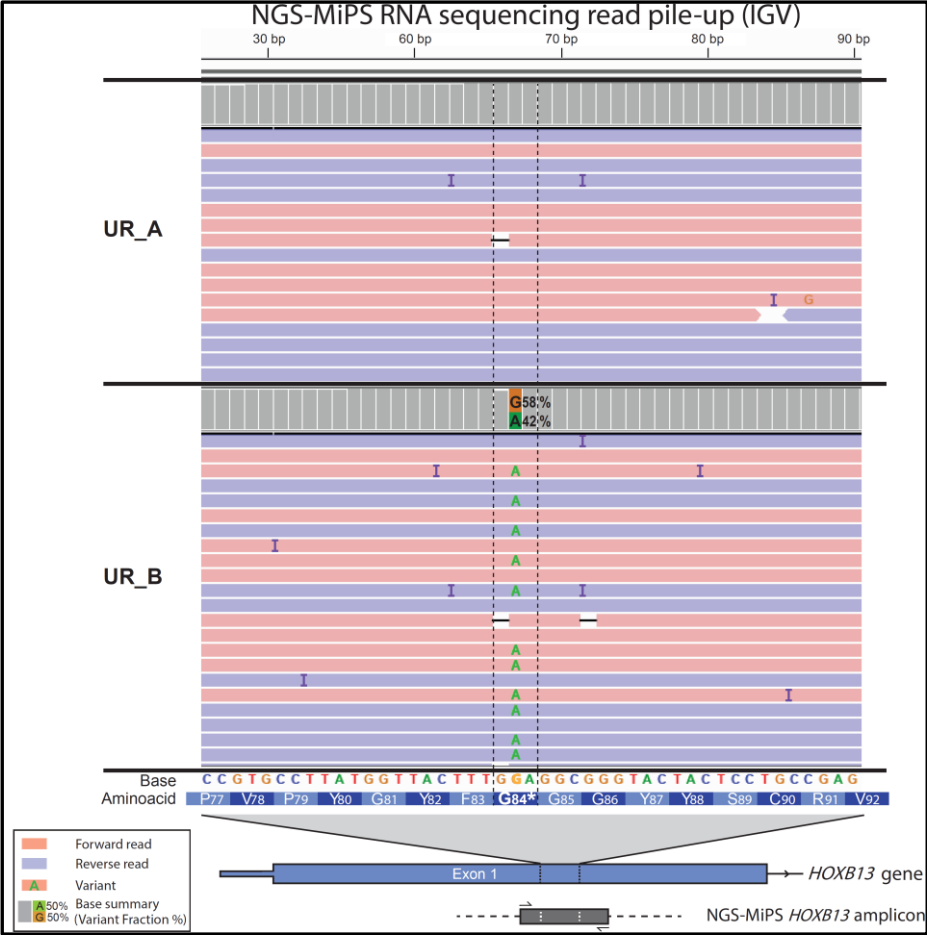
Submission NGS paper

Development of a Whole-Urine, Multiplexed, Next Generation RNA-Sequencing Assay for Aggressive Prostate Cancer Early Detection

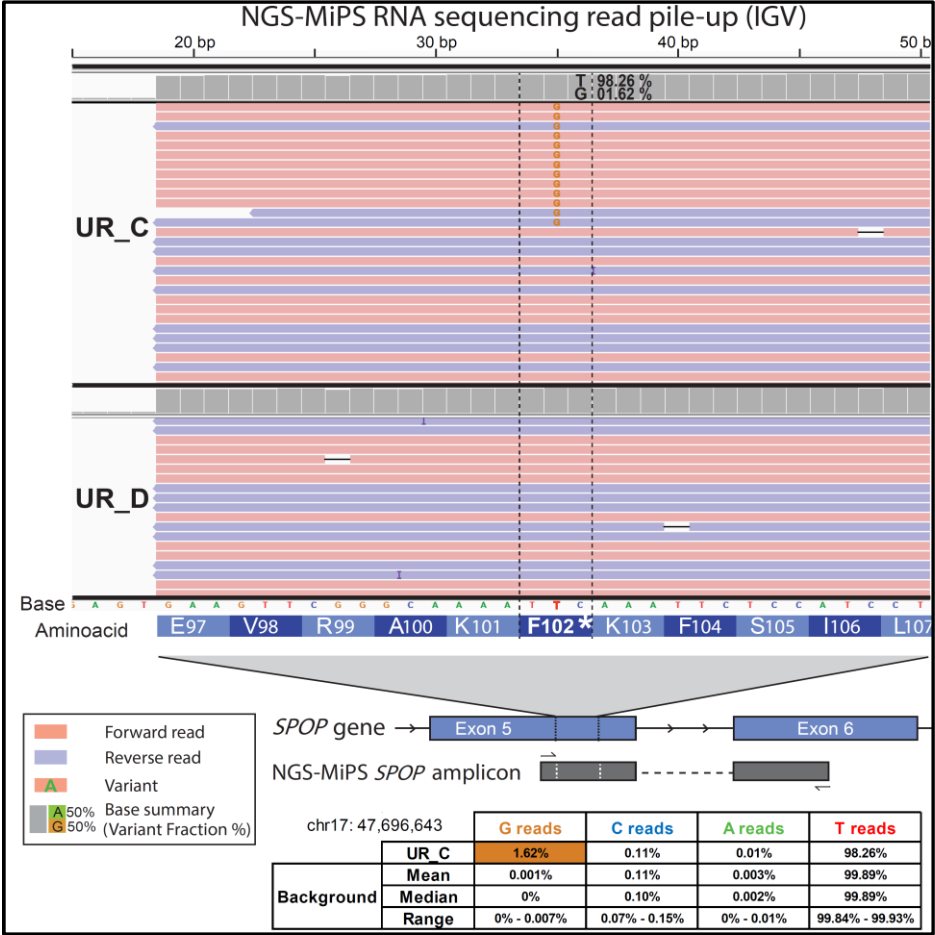
Andi K. Cani, PhD^{a,b,c,d}, Kevin Hu, BS^{a,e}, Chia-Jen Liu, MS^{a,c,d}, Javed Siddiqui, MS^{a,c}, Yingye Zheng, PhD^f, Sumin Han, PhD^{a,c}, Srinivas Nallandhighal, MS^g, Daniel H. Hovelson, PhD^{a,c,e}, Lanbo Xiao, PhD^{a,c,d}, Trinh Pham, BS^g, Heng Zheng, MD^{a,c,d}, Randy Vince, Jr, MD^g, Jeffrey J. Tosoian, MD,MPH^g, Ganesh S. Palapattu, MD^{d,g}, Todd M. Morgan, MD^{d,g}, John T. Wei, MD^{a,g}, Aaron M. Udager, MD-PhD^{a,c,d}, Arul M. Chinnaiyan, MD-PhD^{a,b,c,d,g}, Scott A. Tomlins, MD-PhD^{a,b,c,c,g,g,§}, Simpa S. Salami, MD,MPH^{a,d,g,§}.

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Detection of germline predisposing SNP and somatic hotspot mutations



Sample:UR_B
 HOXB13
 p.G84E
 VF=42%



Sample:UR_C
 SPOP
 p.F102C
 VF=1.6%