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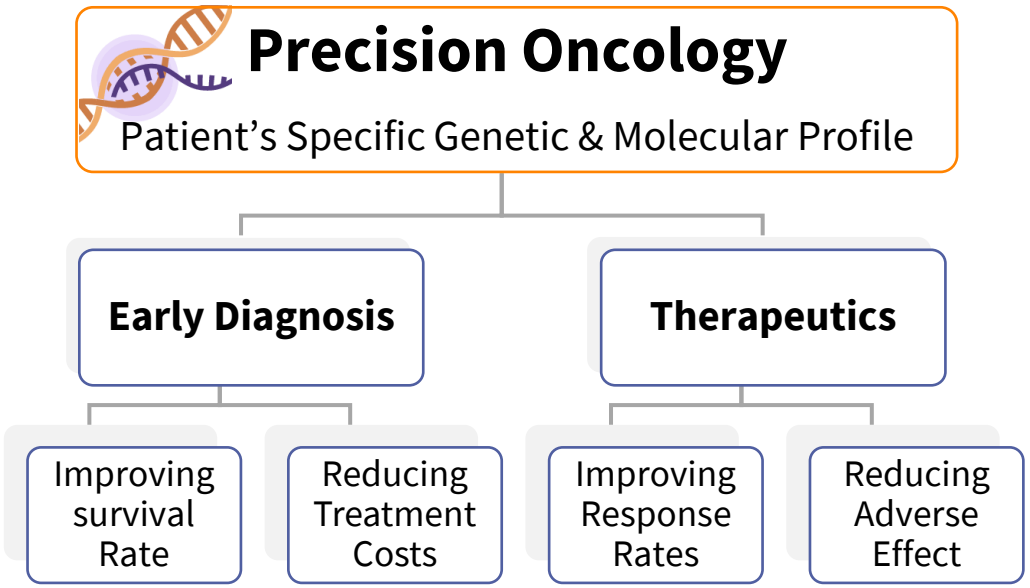
AI-Powered RNA Analytics Driving Innovation in Precision Medicine

Noushin Hadadi
Director of Data Science and Bioinformatics

Life Science Industry Meets Data Science

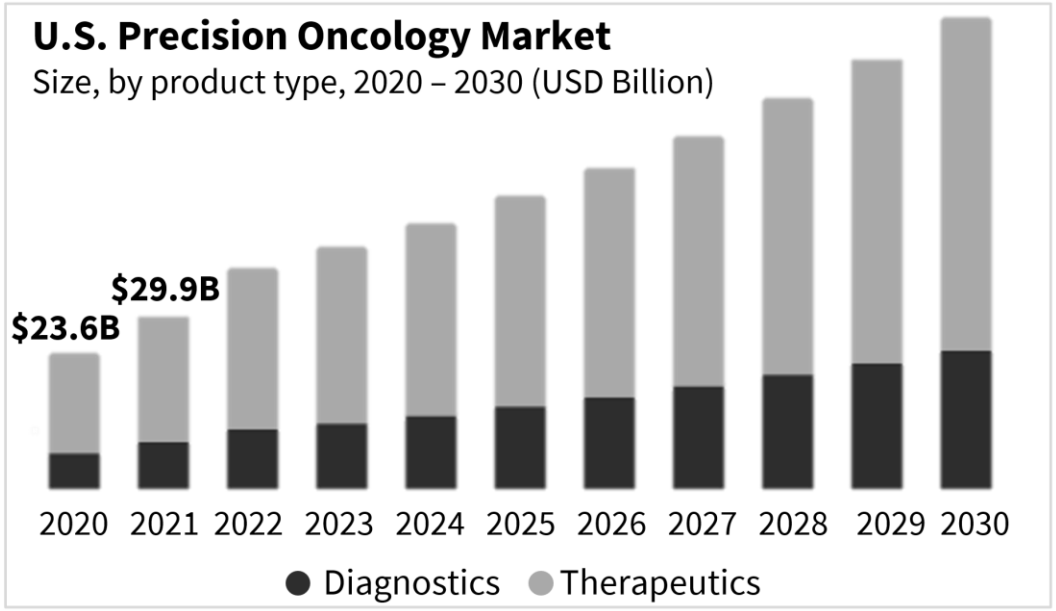
5th September 2024

Precision Oncology



five-year survival rate for early-stage bladder cancer is about **95%**, compared to just **5%** for advanced stage

20-30% of patients receiving immunotherapy achieve durable results, while **20-25%** develop severe immune-related adverse events (irAEs).



https://www.grandviewresearch.com/

Bladder Cancer

- Notably high mortality in advanced stages
- Among the most challenging and expensive cancers to manage
- Over half face cancer recurrence post-treatment

Precision Oncology in Practice: Novigenix's History

2014

Company founded

2015

colox

Colorectal cancer qPCR assay commercialization

2017

Immuno-transcriptomic NGS value proposition

2018-2019

platform development (RNA sequencing)

2019

RadioMedix™ INNOVATING THERANOSTICS

1st BioPharma Contract
for precision oncology
Accelerating Biopharma Clinical Utility

2020

Database Expansion
Immunotherapy of cancer
CRC early detection & recurrence monitoring

2021

LITOseek™
Application Development

- ✓ LITOseek I/O: therapy response prediction
- ✓ LITOseek *ColoxNGS: CRC screening*
- ✓ LITOseek *Digital Cytometry:* cellular deconvolution
- ✓ LITOseek *Platform Augmentation: scale up*

2022

Development of Biopharma Commercial Solutions

2023

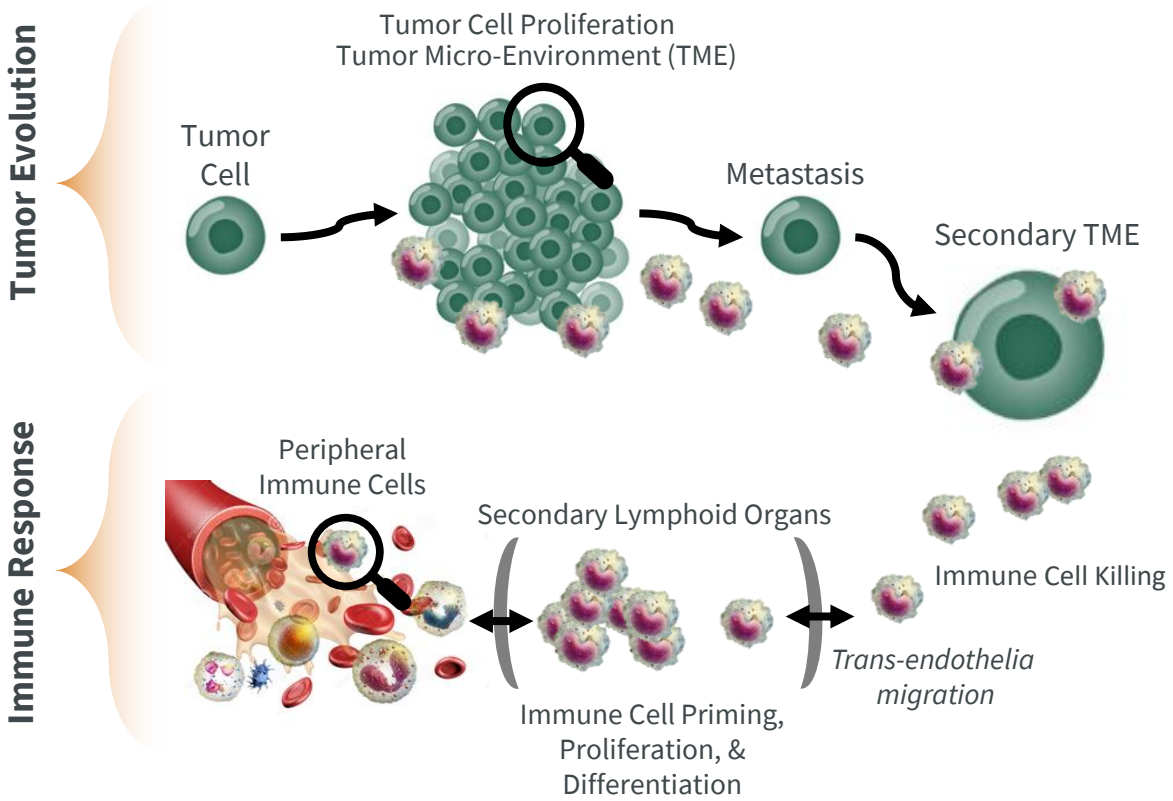
LITOseek™
Biopharma & Clinical Scale-Up

- ✓ **Immunotherapy Response Prediction in Bladder, Prostate, and Melanoma**
- ✓ **Early Detection of Cancer**
- ✓ **Digital Cytometry Utility**
- ✓ **Drug Target Discovery**

2024

LITOseek™ Biopharma Applications Market Launch

Capturing Host Immune Response Dynamics and Tumor Interactions



NOVIGENIX LBx 360

Host response mRNA LBx captures systemic immune response & patient heterogeneity (180˚)

+

Tumor-informed cfDNA LBx captures tumor evolution & patient heterogeneity (180˚)

NOVI 360 LBx multiomic platform provides comprehensive assessment of disease progression with predictive capabilities

LBx solution can be efficiently implemented in global clinical trials to detect early response to therapy, and leverage multiomic LBx biomarkers to support clinical development of novel therapies

It’s Prime Time for Harnessing the Power of RNA & AI

AI-driven RNA Analytics for

- ✓ Early Disease Detection
- ✓ Therapy Response Prediction
- ✓ Drug Target Discovery

Key Challenges with NGS Blood RNA-seq Data Generation & Analysis

Technical Noise

Sources of unwanted variability & interference that affect the accuracy and reliability of RNA from blood samples : sample handling, RNA extraction, sequencing depth, batch effects, etc.

Capturing Weak Signal in Blood

Clinically relevant RNA signals in blood samples are frequently weak, posing challenges in capturing robust biomarkers associated with immune response to cancer, particularly in the early stages of disease.

Curse of Dimensionality & Low Sample Size

Curse of dimensionality from analyzing thousands of genes in relatively low number of samples which can result reduce statistical power

Population Heterogeneity

Biological diversity and population variations, e.g., genetic heterogeneity, age, gender, and underlying health conditions that affect the biomarker discovery methods.

LITOSeek™

Precise & Predictive Patient Profiling

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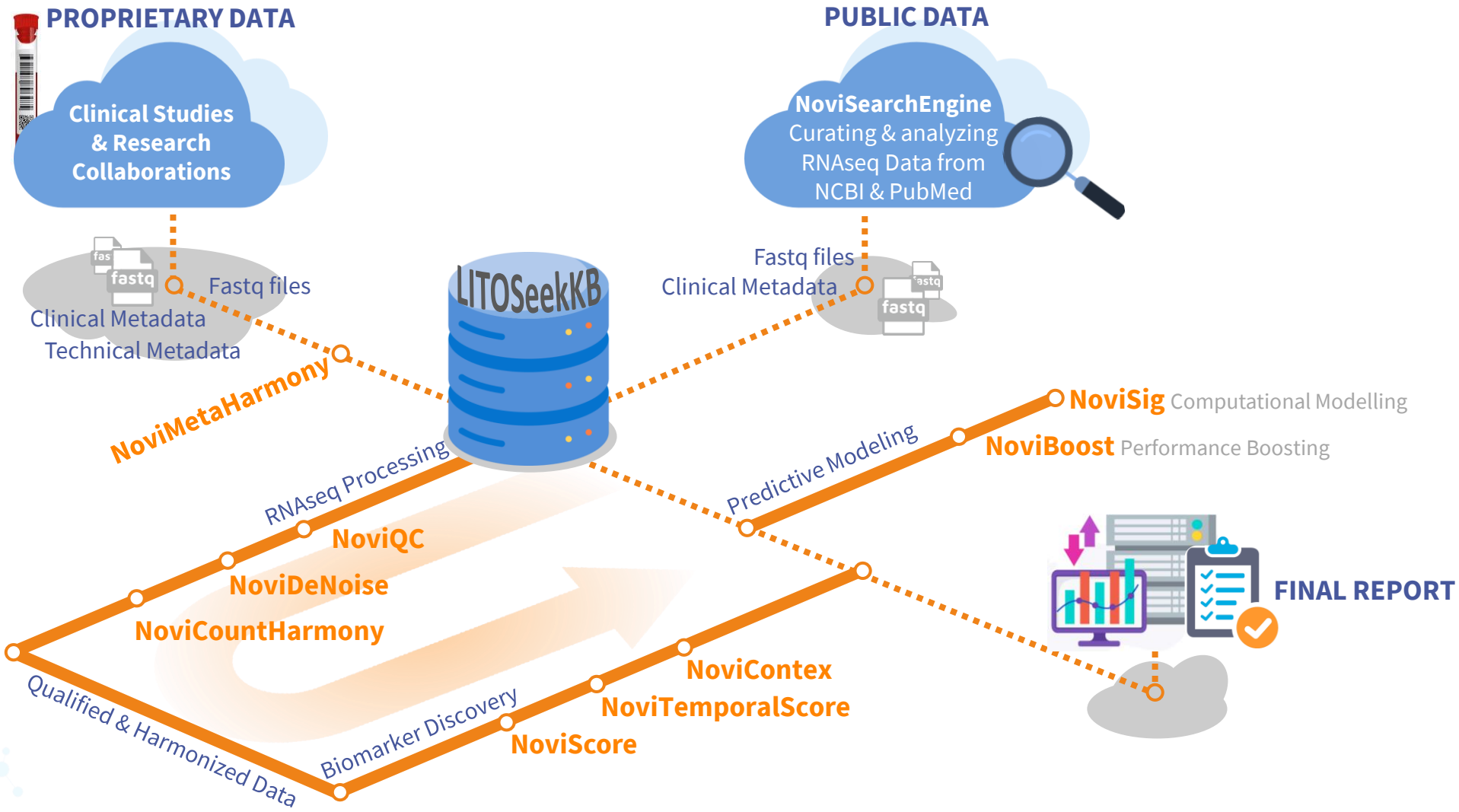
LITOSeek™

Liquid ImmunoTranscriptOmic Platform

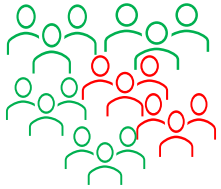


LITOSeek™ Modules

1 Raw Data Generation

Partners

Clinical Cohort

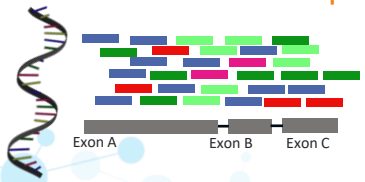


Blood & Tissue Samples

2.5ml Whole blood
PAXgene tube stability
3 days at 25 °
5 days at 2-8 °C
Long-term at -80 °C

RNA Extraction & Sequencing

Spike-in & Standard Samples



2 Data Quality Control

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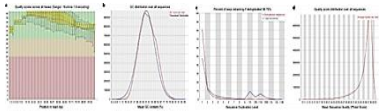
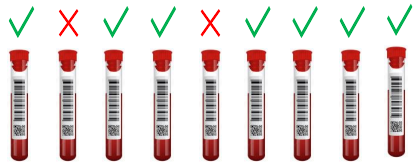
Fastqs to Gene Counts



RNAseq Quantification

Sample Quality Assessment

NoviQC



- Summarizes QC measurements from sequencing & bioinformatics.
- Assigns confidence scores to samples using a machine learning model trained on known-quality samples.

3 Data Structuring

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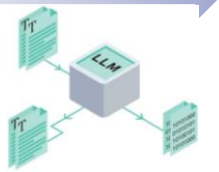
Metadata Structuring & Standardizing

NoviMetaHarmony

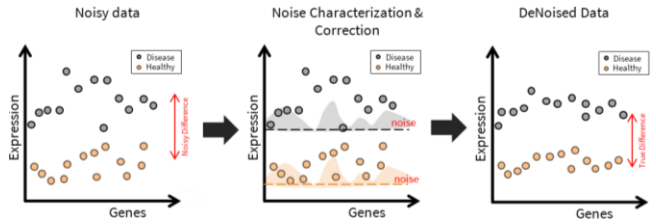
Heterogeneous Clinical & Technical Metadata Files



Harmonized Metadata

Gene Expression Denoising

NoviDeNoise

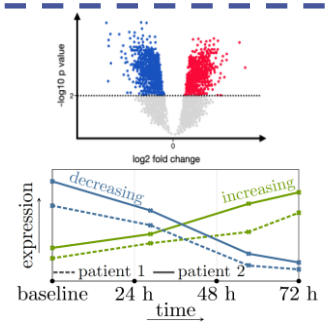


Gene Expression Harmonization

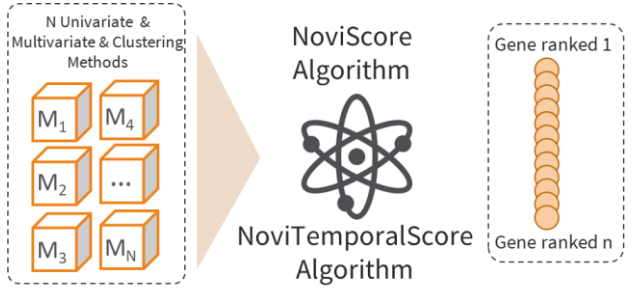
NoviCountHarmony

4 Data Analytics

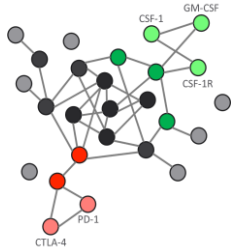
Feature (Biomarker) Discovery



NoviScore
NoviTemporalScore

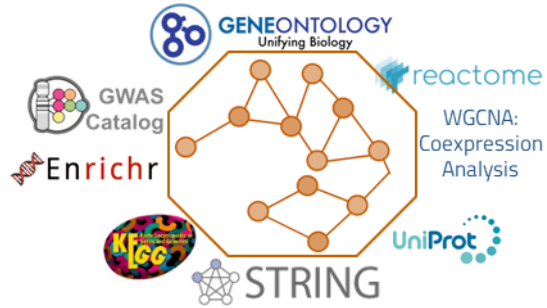


Biomarker Biological Interpretation & Contextualization

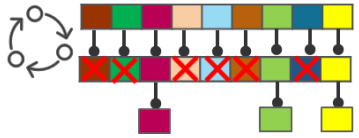


NoviContext

Automated Pathway Knowledge Retrieval



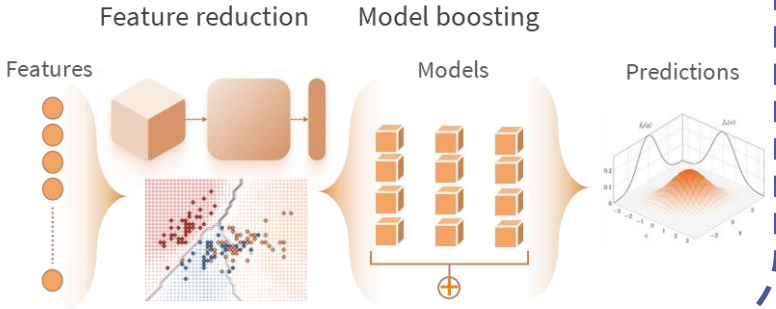
ML-based Feature Reduction



NoviSig

Model Development Training & Evaluation

NoviBoost



LITOSeek™ Case Study

Immunotherapy Clinical Benefit Prediction

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Clinical Application of Monitoring Peripheral Blood Biomarkers

Discovery cohort **(n = 33)**

Biomarker discovery and model training

Test cohort **(n = 37)**

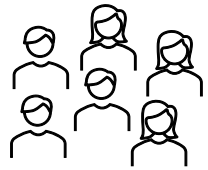
Model testing and parameters optimization

Validation cohort #1 **(n = 21)**

Model validation on a blinded cohort

Validation cohort #2 **(n = 150)**

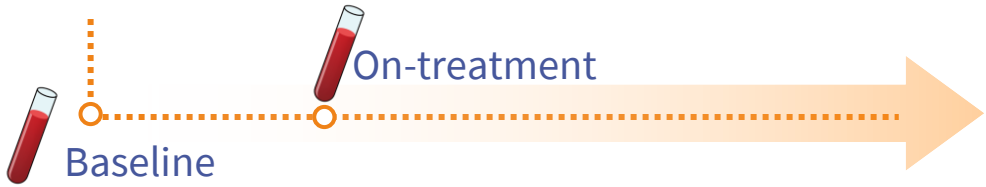
*Sample collection planned



Metastatic bladder cancer patients (**N=91**)

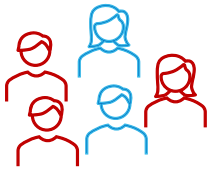
Goal: identify **biomarkers** of early response to treatment and craft **predictive models** of clinical benefit

Immune-checkpoint inhibitors (ICI)



Patient follow-up and clinical benefit assessment (months)

LITOSeek™ platform

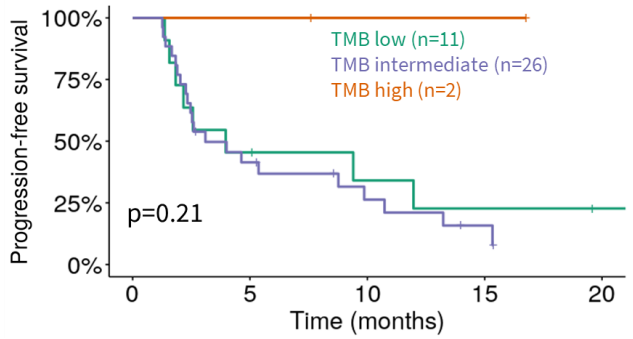


Cohort stratification

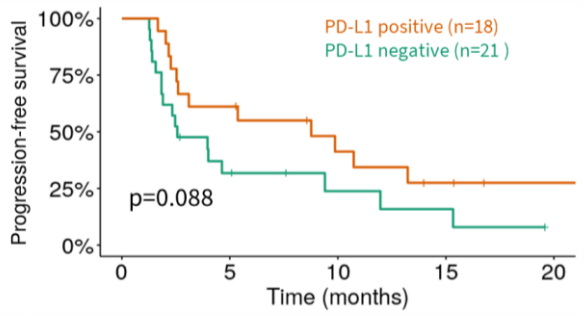
Superior Predictive Performance of Immuno-Transcriptomic Biomarkers

Typical tumor-centric biomarkers fail to predict clinical benefit to ICI

Tumor Mutation Burden



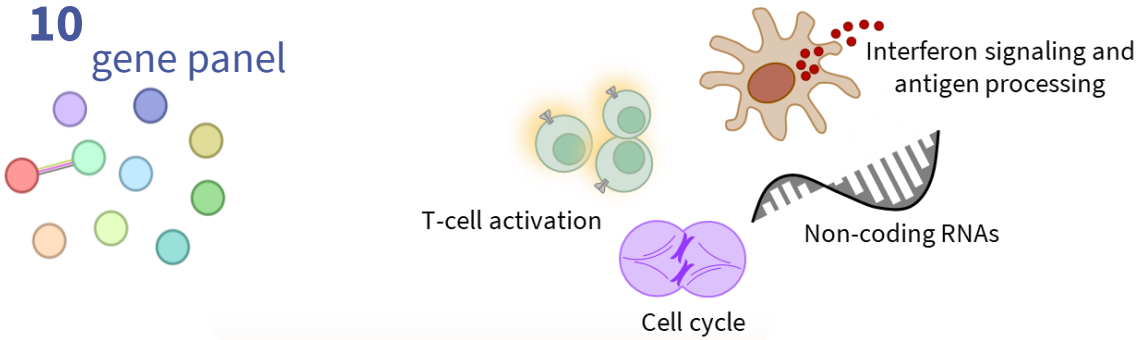
PD-L1 score

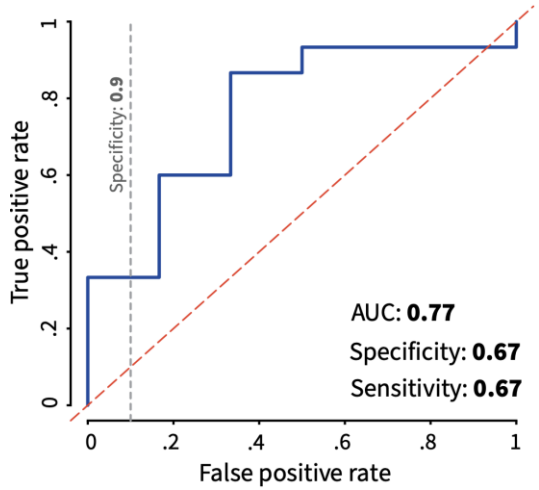


In collaboration with Prof. Niven Mehra and colleagues, Radboud University Medical Center, Nijmegen, Netherlands

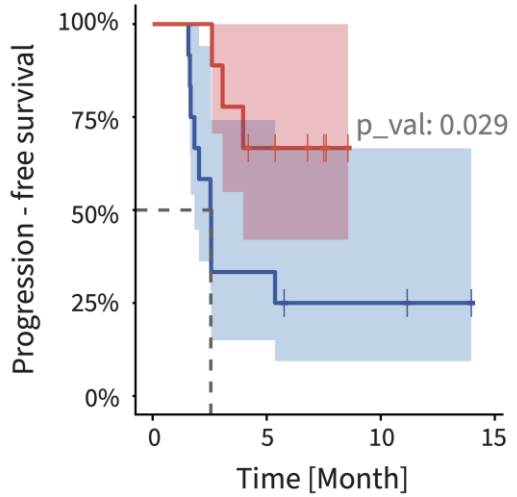
LITOSeek™ platform

A 10 gene panel contains both functionally relevant and novel biomarkers



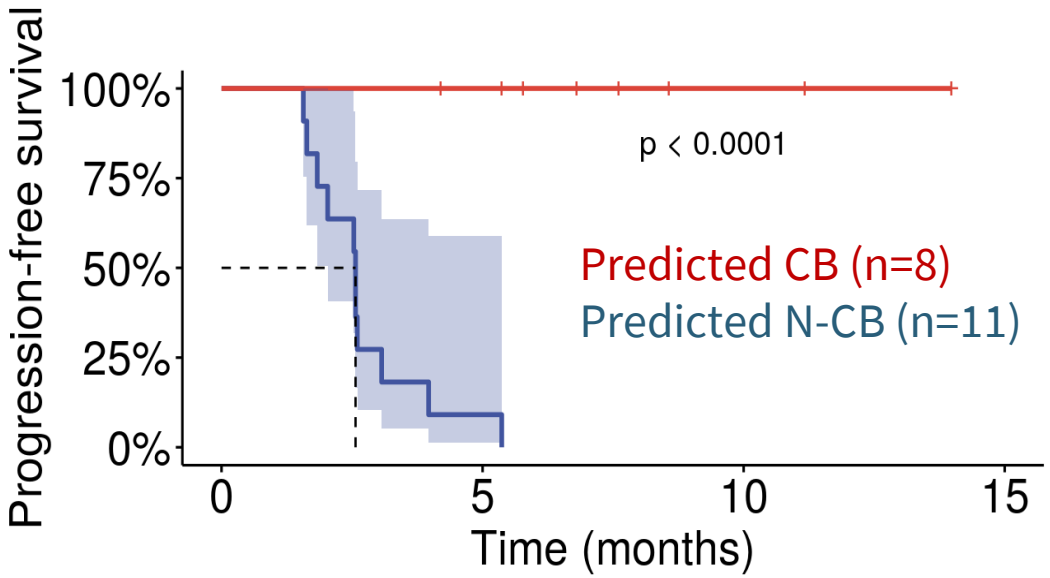


Predicted clinical benefit (CB) (n=9)
Predicted no clinical benefit (N-CB) (n=12)



Multimodal Prediction

Modelling approach	Immunotranscriptome		ctDNA		**Multimodal**	
Cohort	Test	Validation	Test	Validation	Test	Validation
Number of patients	29	21	32	23	27	19
Specificity	79%	67%	**87%**	**100%**	**100%**	**100%**
Sensitivity	**73%**	**67%**	59%	56%	**72%**	**79%**



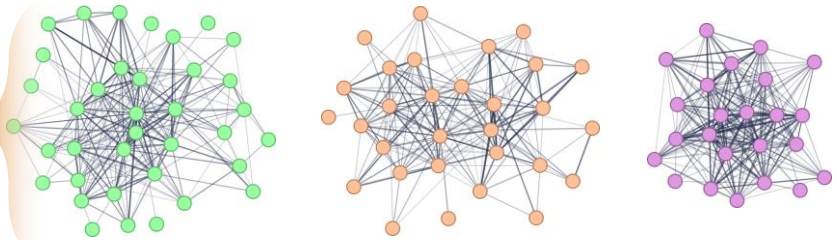
Pancancer Application & Patient Journey Guidance

Bladder

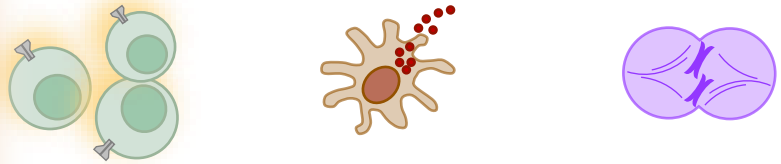
Melanoma

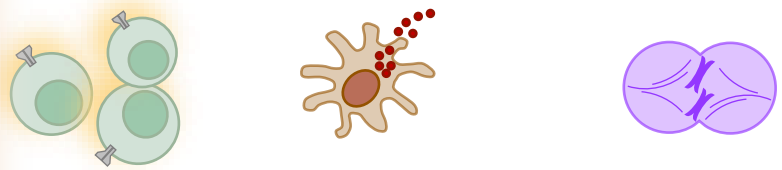
Prostate

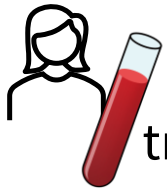
Biomarker discovery



Function







Immuno-trascriptome

- **CtDNA**
- PD-L1
- TMB

LITOseek™ platform

Treatment B

Toxicity

Clinical benefit

Treatment A

Take-home Messages

- LITOSeek™ is a powerful and versatile platform providing clinically relevant insights from non-invasive liquid-biopsies through AI-driven immuno-transcriptomics
- LITOSeek™ has been optimized with well-established analytical pipelines and QC measures to overcome historical limitations associated with blood RNAseq real-world data
- Multimodal integration of RNA and ctDNA data showed an unprecedented accuracy in predicting clinical benefit
- Although precision oncology is still in its infancy, it holds great promise for the future, offering personalized therapies that **save lives** and **reduce healthcare costs**

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Thank you

LITOSeek™

Precise & Predictive Patient Profiling

Partner with us in
Development of Innovative,
Cancer Therapies