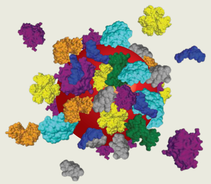

Nanoparticle-protein complex

ASMS Poster

Efficient and scalable profiling of a median of 1,779 plasma proteins in 288 subjects with multi-nanoparticle (NP) Proteograph™ platform enables robust detection of early-stage non-small cell lung cancer (NSCLC) and classification vs. healthy and co-morbid subjects

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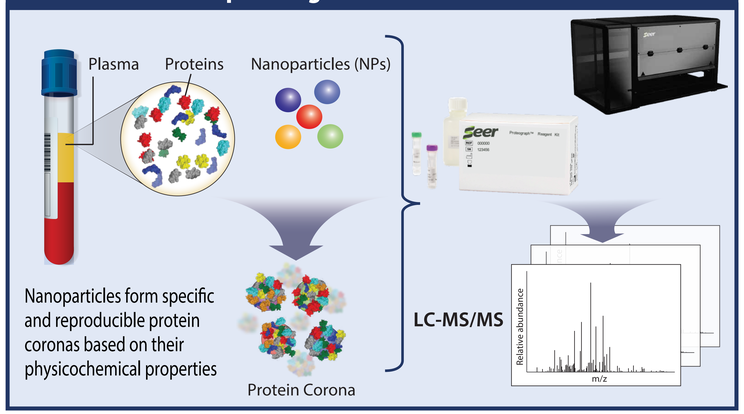
Overview

Liquid biopsy screening tests for detection of non-small cell lung cancer (NSCLC) have not yet achieved the performance necessary for clinical utility. The diversity of protein molecules is vast and proteins change within cells, tissues, and at the organ sytems level in response to physiology, environmental and disease-state factors. The information content from proteins is relatively unexplored compared to genomic information. Unbiased protein profiling maximizes the possibility of finding novel, clinically useful markers for test and therapeutic development. Proteograph, a multi-nanoparticle platform for deep, unbiased, precise and efficient protein profiling, makes large-scale studies feasible for the first time. **We have used Proteograph to rapidly profile a median of 1,779 proteins across 288 subjects and demonstrate robust classification of early stage (Stage 1-3) NSCLC, late stage (Stage 4) NSCLC, healthy and co-morbid controls.**

Proteograph

Enabling deep, unbiased, precise and efficient protein profiling for the first time

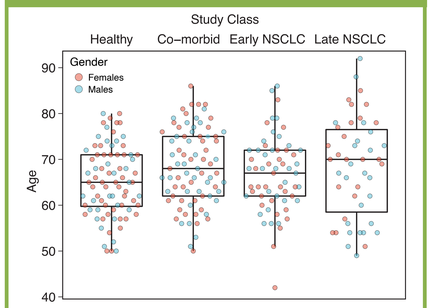


Experimental Design and Processing

Sample Collection and Processing

- 288 samples collected at 24 IRB-approved sites
  - Healthy (82) and co-morbid (81) controls
  - Early (50) and late (75) NSCLC with pathology-confirmed diagnosis
- Subjects were initially profiled with a panel of 10 NPs
- The subset of 5 NPs that are part of our commercial proteomics suite were used for classification analysis
- Proteomic data were collected with data-independent acquistion mode on Sciex LC/MSMS with 2.5 hr cycle time per 5 NP sample
- Total time for 5 NP sample processing and MS data acquistion was 3.5 weeks
- Random-forest machine learning was employed with10 rounds of 10-fold cross-validation
- Permuations tests with 10 rounds of random class assignments were to confirm that original models were significant.

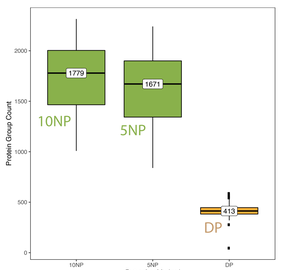
Balanced Study Subject Classes



288 age- and gender-matched samples collected in 4 classes: healthy, co-morbid, early- and late-stage NSCLC

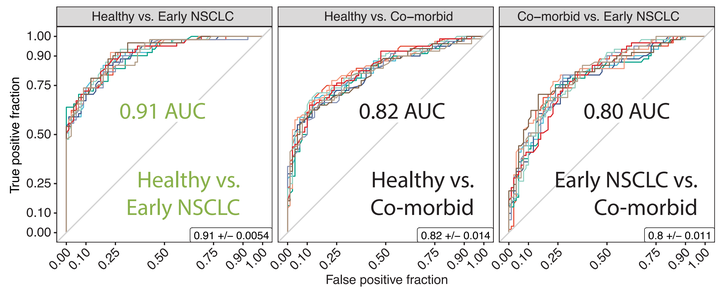
Proteograph data enables superior performance for clinically relevant classification

Proteograph detects 4x more proteins than comparator method



Protein counts across 288 study subjects. Median values are 10NPs - 1,779, 5NPs -1,671, and Depleted Plasma (DP) 413. Both 10NP and 5NP results are >4x the DP median.

Proteograph plasma-profiling enables high-performance early NSCLC classifiers (AUC 0.91)

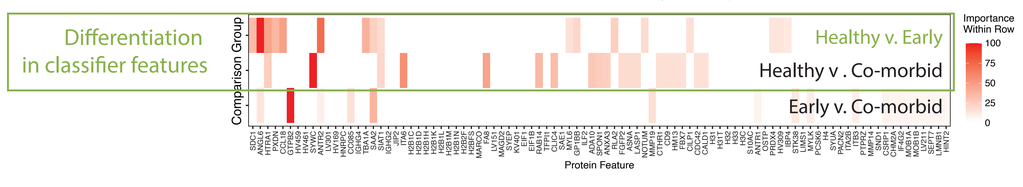


ROC plots from random forest classification after10 rounds of 10-fold cross-validation. Healthy vs Late NSCLC 0.98 AUC not shown.

More information

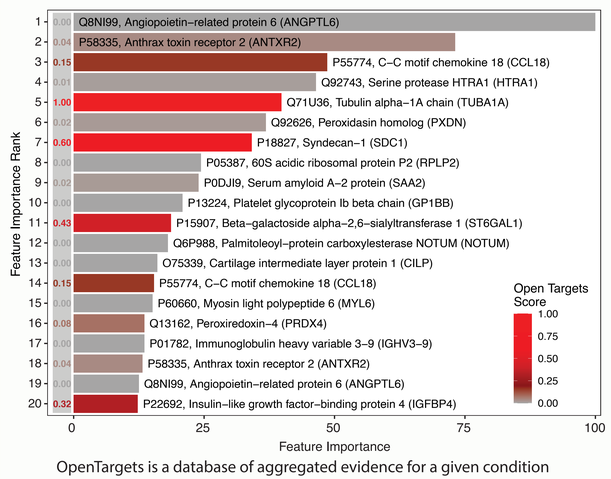
please visit seer.bio/publications or scan the QR code

Differentiation in classifier components enabled by deep profiling maximizes potential for broad clinical utility in larger population



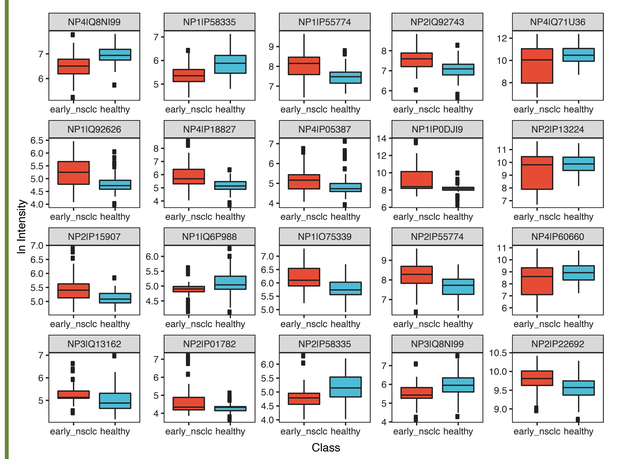
Proteograph discovers high performance, novel combinations of known and unknown markers as a result of unbiased profiling

Healthy vs early NSCLC most important classifier features include proteins known (e.g., Taxol-target tubulin, Syndecan-1) and unknown to be targets



OpenTargets is a database of aggregated evidence for a given condition

Proteograph provides highly-multiplexed quantification of detected proteins, enabling rapid downstream validation



Top 20 Healthy vs Early NSCLC important classifier feature intensity changes

For more details see Blume, et. al., "Rapid, Deep and Precise Profiling of the Plasma Proteome with Multi-Nanoparticle Protein Corona", Nature Communications (2020) in press