Know Your Proteome: Exploring personalized proteomics in precision health

Felicia K. Ooi, Monica Ghaly, Santosh Bhosale, Stephen A. Whelan, Susan M. Mockus
Precision Biomarker Laboratories, Cedars-Sinai Medical Center, Beverly Hills, CA

Precision Biomarker Laboratories

Cedars Sinai

Introduction

The study of the proteome allows for the gathering of information to bridge the gap between genomic signatures and potential disease phenotypes.

Personalized proteomics builds on the foundation pioneered by personalized genomics, wherein the genetic information provides a baseline for information while the proteomic signature gives insight into how a disease might manifest physiologically in different individuals.

These insights are key for the future of personalized medicine, both for early preventive screening of disease biomarkers as well as for designing unique treatments to halt progressive disease.

On a more personal level, having access to one's proteome allows for better informed decisions on lifestyle changes to improve health as well as for monitoring the outcome of said changes.

Study Design

10 diverse phenotypically-healthy participants:

- Control (no change)
- Intervention (lifestyle change e.g. diet, exercise)

3 sample collection timepoints over ~1 month:

- Baseline, midpoint, final

3 sample types:

- Plasma – venous (traditional phlebotomist visit)
- Plasma – capillary (lancet finger prick)
- Dried blood spots (Neoteryx Mitra device)

Immunoassay data was generated using:

- Olink® Target 48 Cytokine Panel
- Alamar Bio NULISAseq Inflammation 250 Panel

LC/MS-MS data was generated in DIA mode:

- EvoSep One coupled with Orbitrap Exploris 480

Results

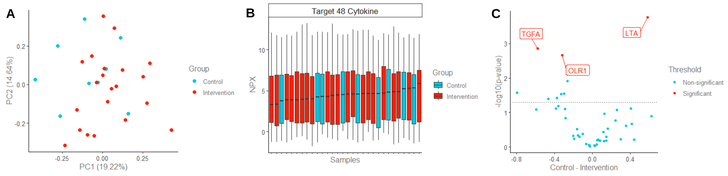


Figure 1_The control and intervention groups display some differential protein expression

A. PCA plot of control vs intervention groups shows some overlap across both groups;
B. As does the sample distribution of all 45 proteins assayed
C. Expression of LTA is slightly higher in control individuals, while TGFA and OLR1 are elevated in the intervention group

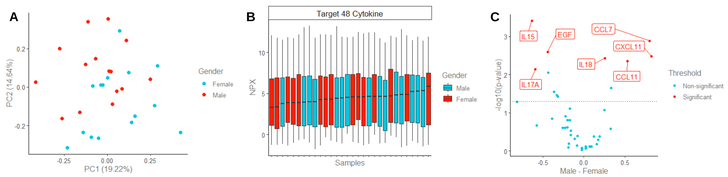


Figure 2_Gender appears to be a distinguishing factor in protein expression

A. PCA plot of male vs female groups does not show obvious clustering;
B. Neither does the sample distribution of all 45 proteins assayed
C. EGF, IL15, IL17A are slightly elevated in females, while CCL7, CCL11, CXCL11, IL18 are slightly elevated in males

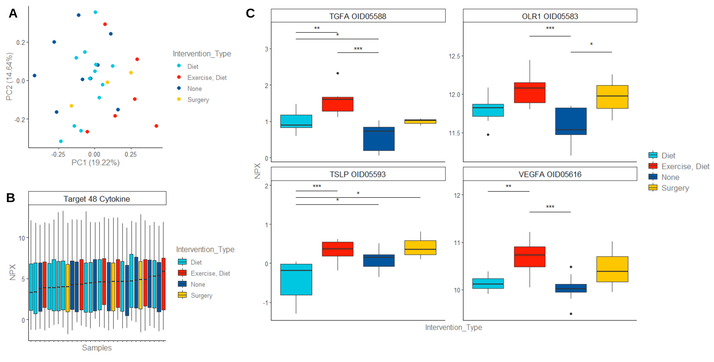


Figure 3_The type of lifestyle change also plays a role in differential protein expression

A. PCA plot of the different intervention types shows some slight clustering;
B. Which can also be observed in the sample distribution of all 45 proteins assayed
C. TGFA, OLR1, TSLP and VEGFA are differentially expressed across the intervention groups

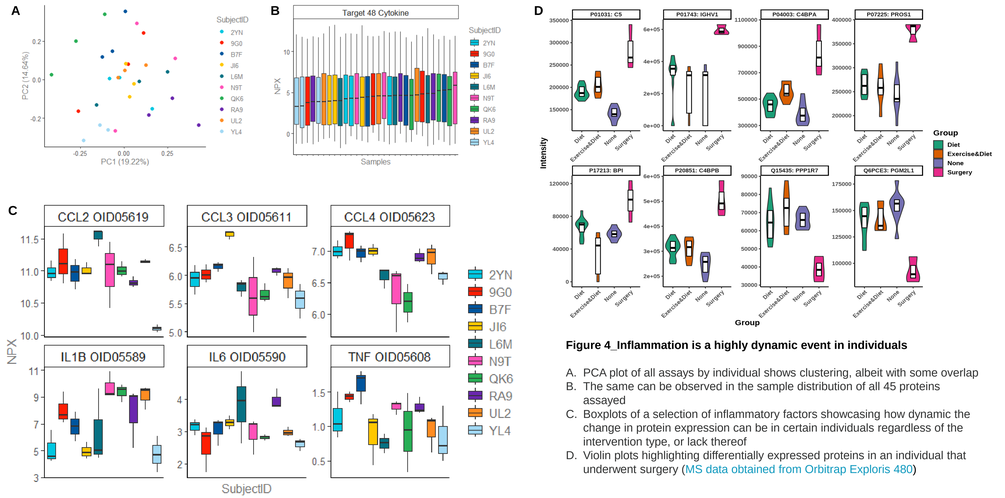


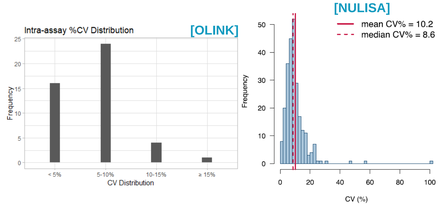
Figure 4_Inflammation is a highly dynamic event in individuals

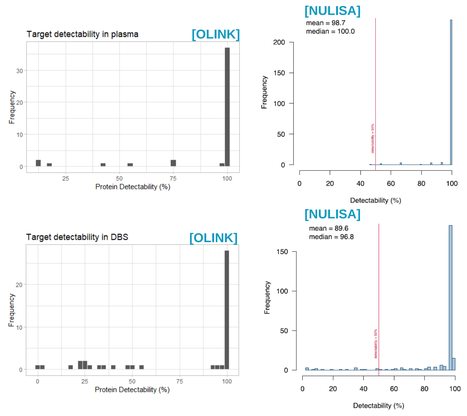
A. PCA plot of all assays by individual shows clustering, albeit with some overlap
B. The same can be observed in the sample distribution of all 45 proteins assayed
C. Boxplots of a selection of inflammatory factors showcasing how dynamic the change in protein expression can be in certain individuals regardless of the intervention type, or lack thereof
D. Violin plots highlighting differentially expressed proteins in an individual that underwent surgery (MS data obtained from Orbitrap Exploris 480)

QC Comparison → Olink Target 48 vs NULISAseq Inflammation 250

In a cross-platform validation study, the same set of samples previously run on the Olink Target 48 and Orbitrap Exploris-DIA were also run on the Alamar Biosciences NULISAseq Inflammation 250 panel. Data analysis is still ongoing, but highlighted below are some QC metrics of interest:

Panel	Olink Target 48 Cytokine	NULISA Inflammation 250
Number of targets	45	250
Total target % detectability (Plasma)	88.9	99.6
Total target % detectability (DBS)	71.1	93.2
Mean intra-assay %CV	7	10.2
Volume of sample (Plasma)	1µL	10µL
Volume of sample (DBS)	1µL	40µL
Quantification	Normalized, absolute	Normalized





Conclusions

We are generally pretty healthy!

- Given the small study population, protein expression tended to cluster on an individual basis
- Despite the short time frame, some individuals exhibited highly dynamic changes in response to events like exercise or surgery
- In a diverse population, biological gender does play a small role in inflammatory protein expression
- Immunoassays like Olink and NULISA can detect changes in low-abundance proteins to complement those detected in MS

Acknowledgements

All members of Precision Biomarker Labs at Cedars-Sinai Medical Center

Contact Information: Felicia.Ooi@cshs.org

Conflict of Interest: No conflict of interest to declare

NULISA data collected in conjunction with ALAMAR BIOSCIENCES