

ENHANCED PLASMA PROTEOMICS: NANOPARTICLE ENRICHMENT APPLIED TO A COHORT OF BECKER MUSCULAR DYSTROPHY PATIENTS

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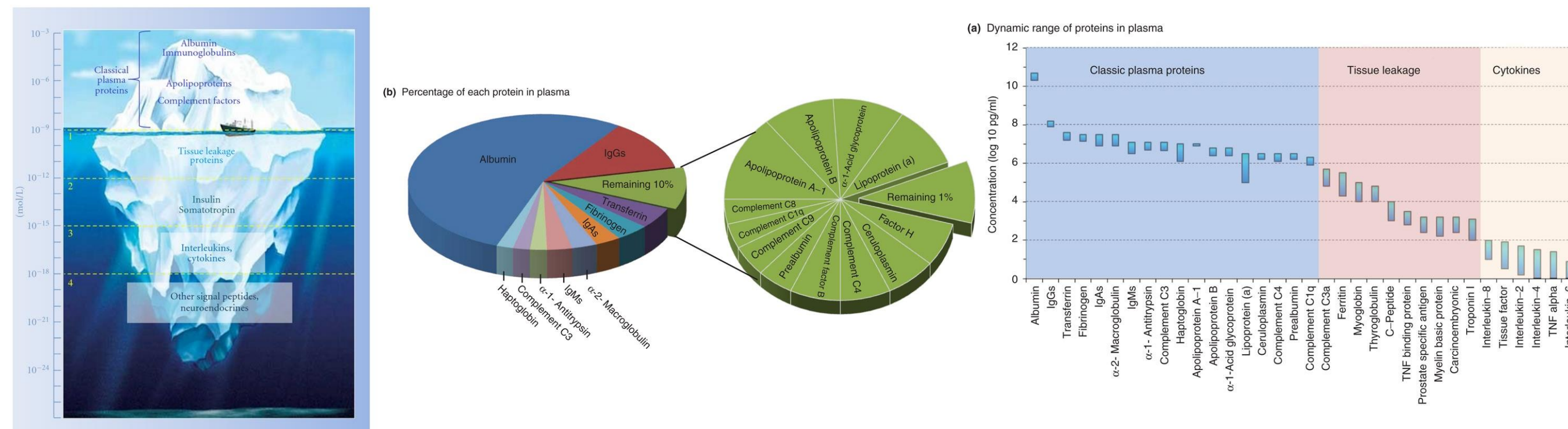
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INTRODUCTION

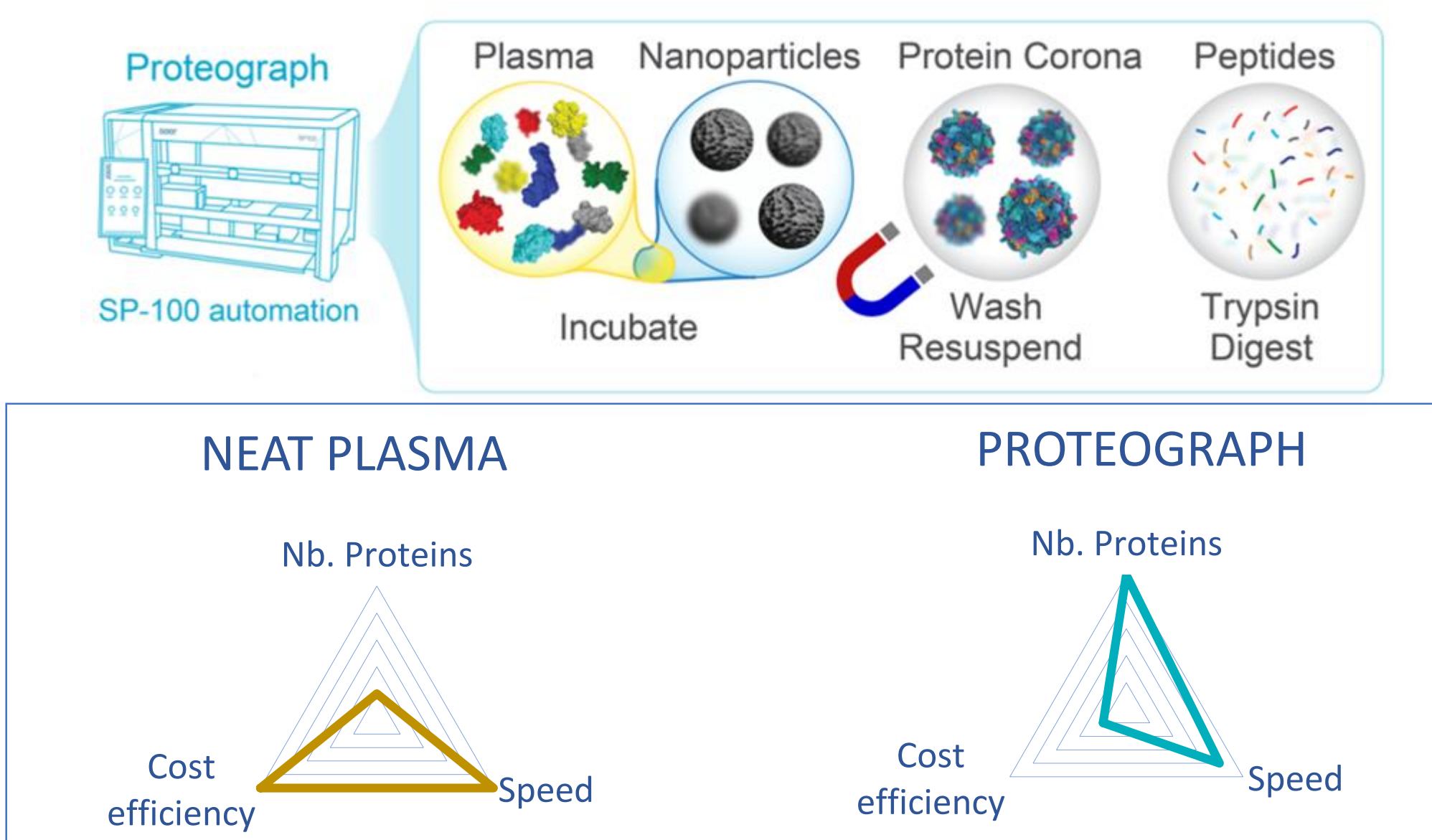
Becker muscular dystrophy is a genetic disorder causing progressive muscle weakness in need of reliable plasma biomarkers for early diagnosis, monitoring, and treatment follow-up.

THE CHALLENGE: HIGH DYNAMIC RANGE

99% of plasma proteome comes from the 22 most abundant proteins

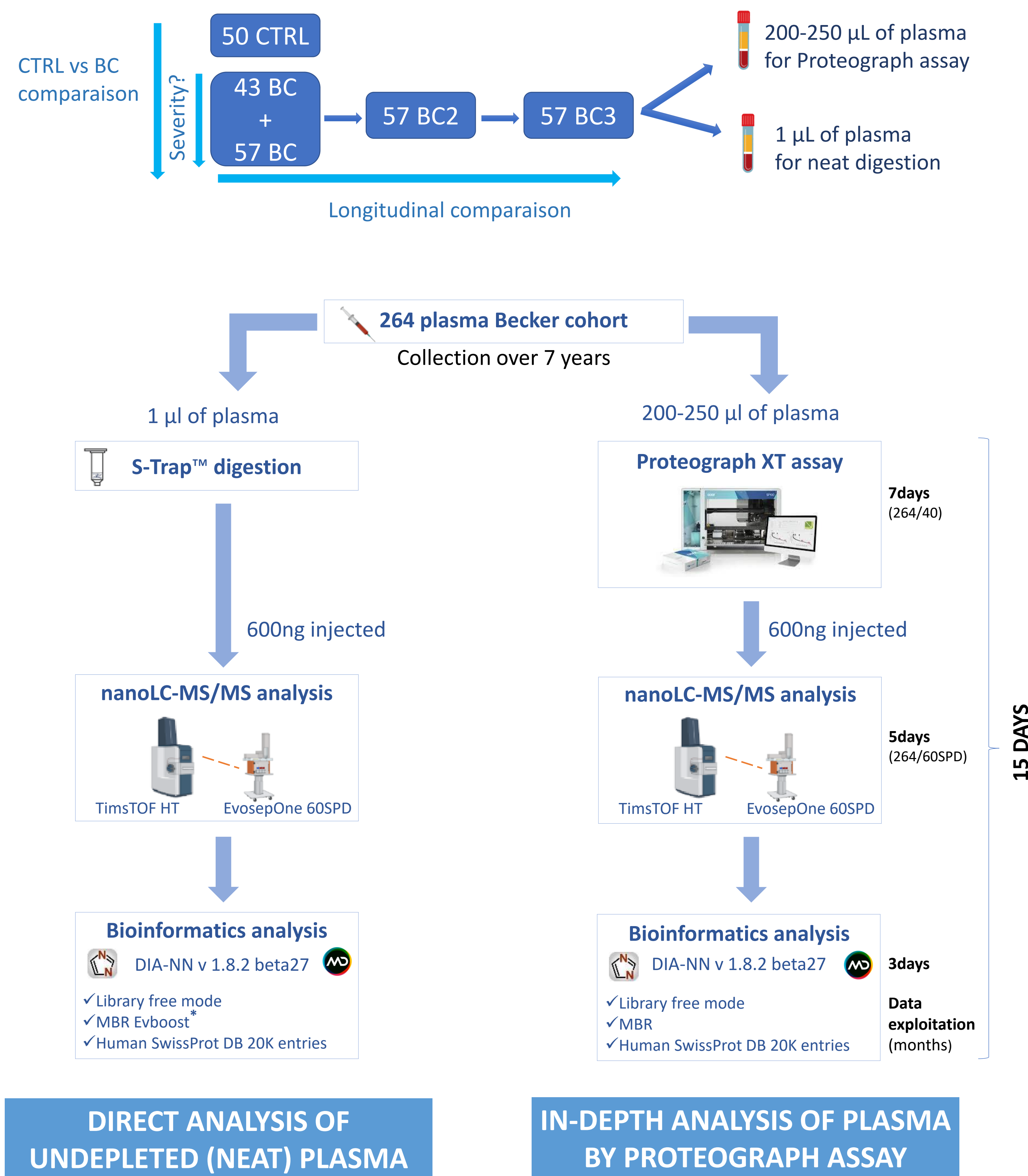


RECENT APPROACH TO OVERCOME THE CHALLENGES



MATERIALS AND METHODS

WORKFLOW



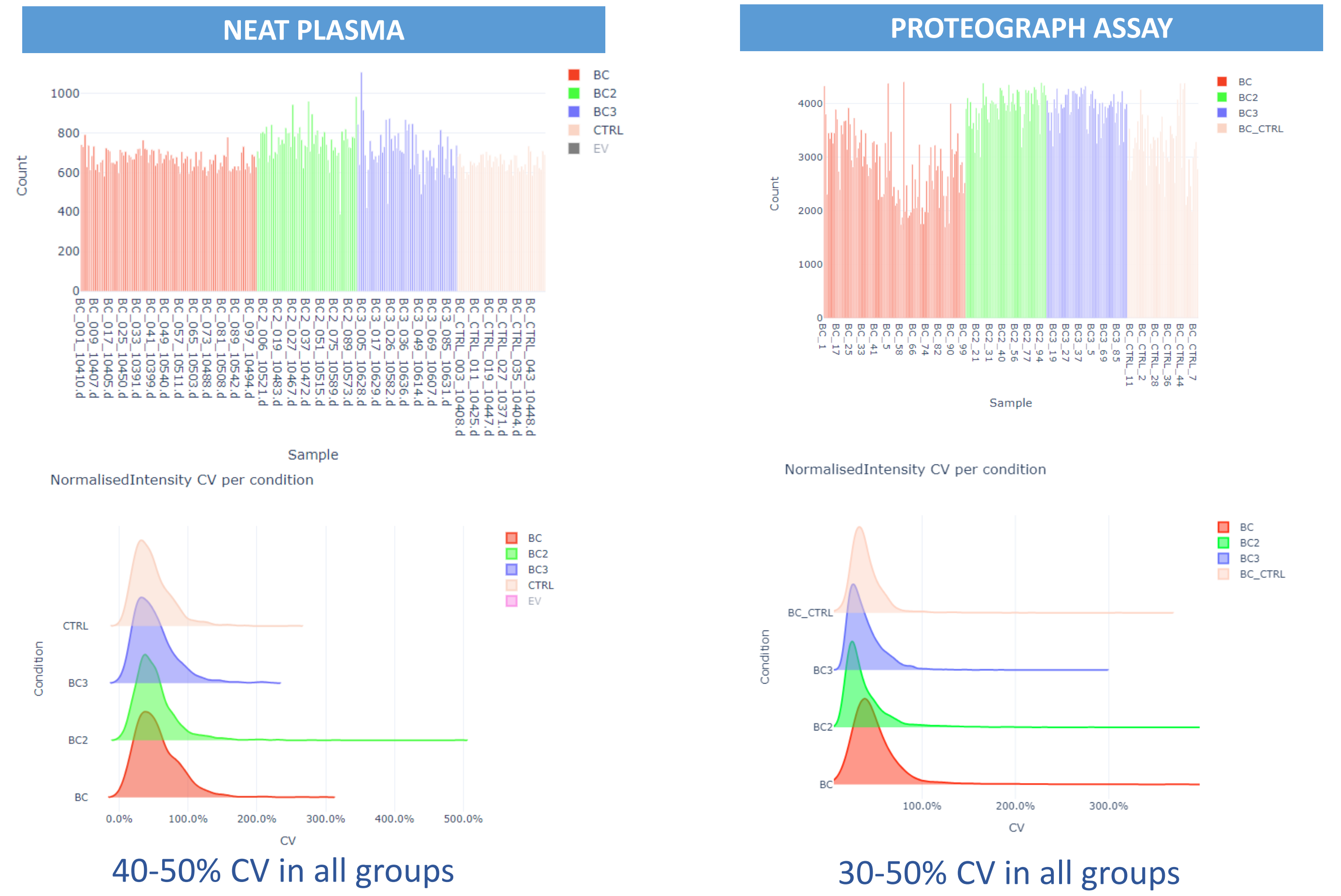
DIRECT ANALYSIS OF UNDEPLETED (NEAT) PLASMA

IN-DEPTH ANALYSIS OF PLASMA BY PROTEOGRAPH ASSAY

AIM : IDENTIFY BIOMARKERS OF PROGNOSIS AND EARLY CARDIOPATHY

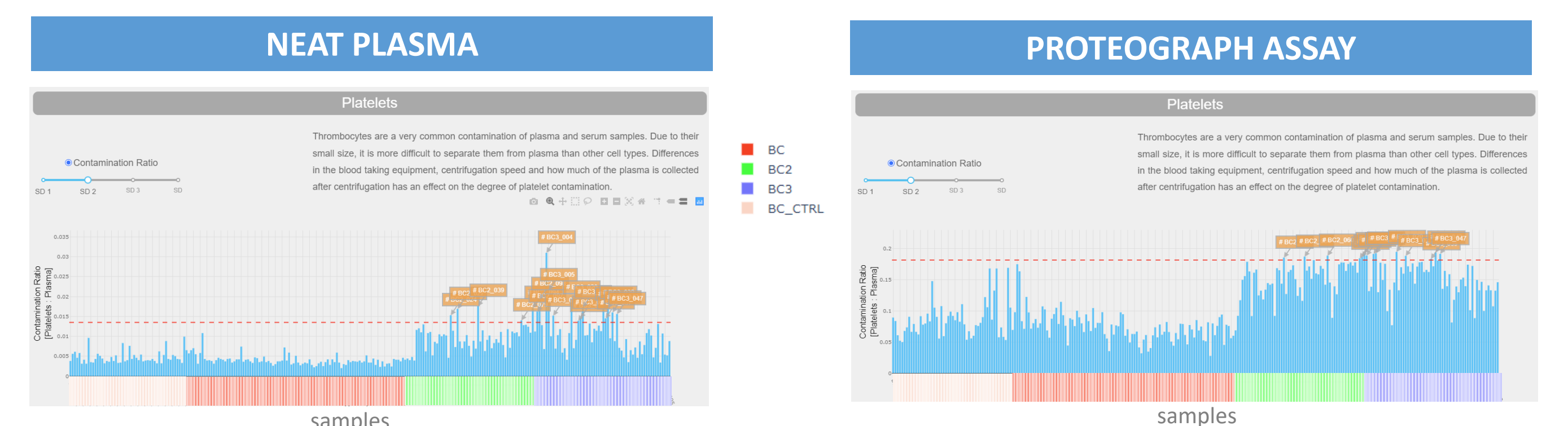
RESULTS

NUMBER OF PROTEINS & CV



- ❖ An average of 657±95 PG IDs in neat plasma using EV-boost approach.
- ❖ An average of 3366 ±720 PG ID (Ca. 4x increase in number of proteins identified) using Proteograph assay.
- ❖ CVs of 40-50% in neat and 30-50% in NP-enrich plasma.

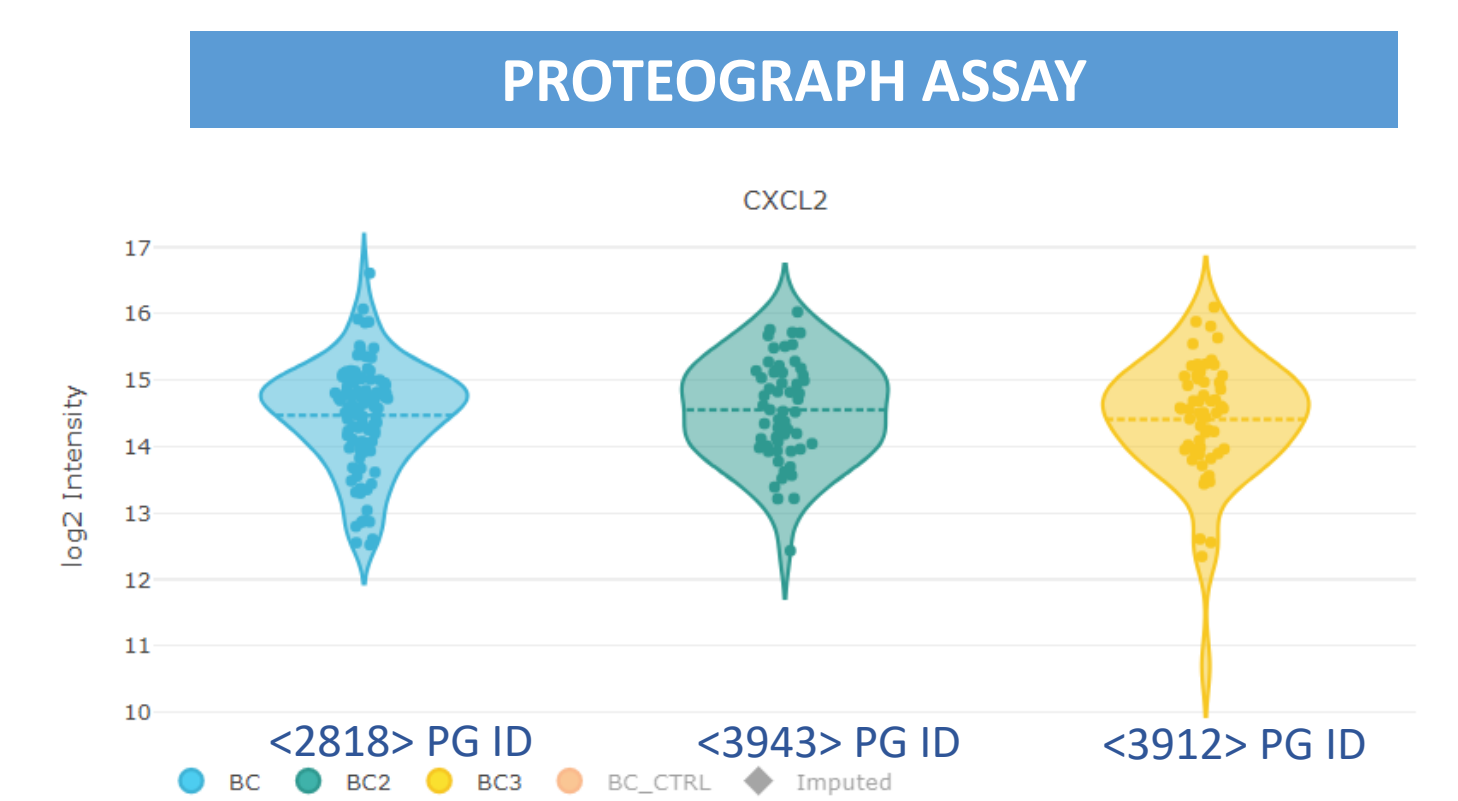
PLASMA CONTAMINATION



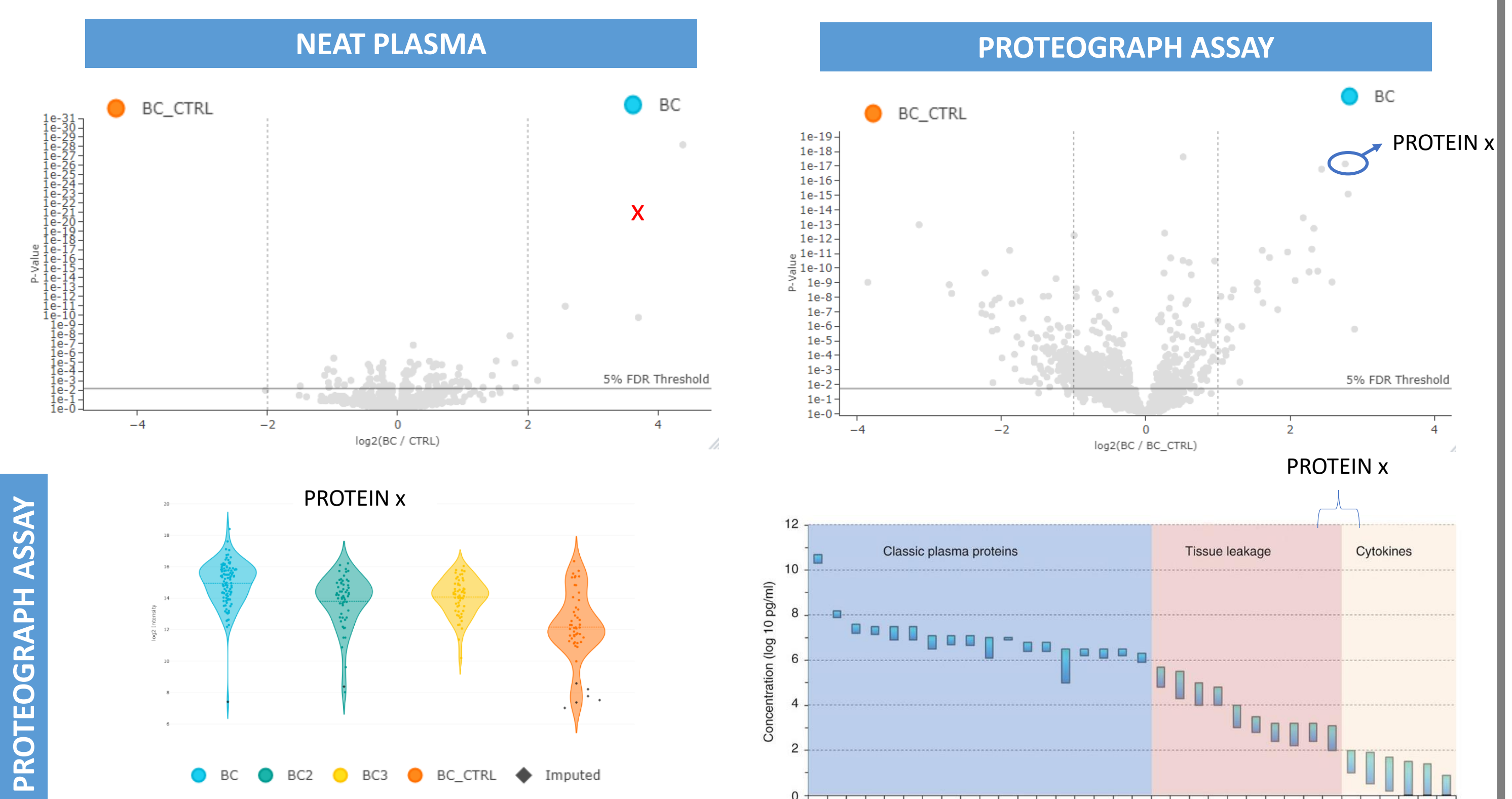
- ❖ The number of proteins ID correlated with contamination from plasma cells and coagulation factors.

CHEMOKINES DETECTION IN PROTEOGRAPH ASSAY

- ❖ The Proteograph assay enables the identification of low abundance proteins.
- ❖ Notably, the detection of these proteins is independent of the number of proteins IDs and of the platelet contamination level.



SIGNIFICANTLY DIFFERENTIAL PROTEINS



- ❖ The analysis with NP-enriched samples allows to detect clear markers of muscle damage at levels as low as 100pg/mL.

CONCLUSION

Nanoparticle (NP)-based enrichment compresses the dynamic range of plasma and enhance proteome coverage without compromising quantification. The NP analysis allows to detect proteins of known low abundance, such as tissues leakage derived proteins and chemokines. This detection seems independent of the platelet contamination and the number of proteins identified.

Nanoparticle (NP)-based enrichment allowed to identify higher levels of pertinent markers currently under validation.