MagExo™ EV Isolation Enables High-Purity, Reproducible Capture of the Senescence-Associated Secretory Proteome for Aging Biomarker Profiling

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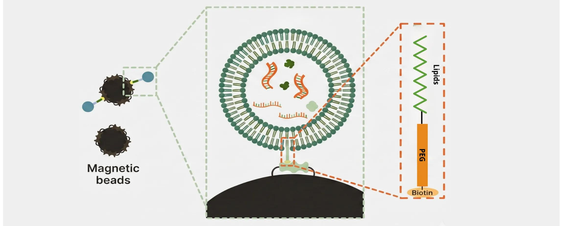
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Introduction

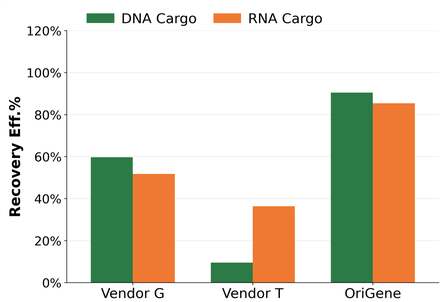
Liquid biopsy promises to track disease and biological aging from a routine blood draw, but disease specific biomarker detection and accurate measurement in plasma is critical. Extracellular vesicles (EVs) carry senescence-associated secretory phenotype (SASP) cargo within a protective lipid bilayer, reflecting senescent cell burden with cell-type specificity — making them ideal for minimally invasive biological aging assessment. However, abundant plasma protein contaminants compromise EV isolation and downstream analysis, requiring a high-purity, robust method.

MagExo™, a lipid nanoprobe-based magnetic bead system, enriches plasma EVs through lipid–lipid membrane interactions. purity and recovery were confirmed by immunoassay and LC-MS, as well as benchmarked against leading commercial reagents. EV proteome depth was assessed by LC-MS versus parallel blood proteomic workflows. EVs from 12 healthy donors aged >65 years were profiled by 127-plex NuLISA covering established SASP markers (GDF15, CXCL8, IGFBPs, TIMP3). Aging related markers were enriched and measured while not detectable in neat plasma.

Mechanism

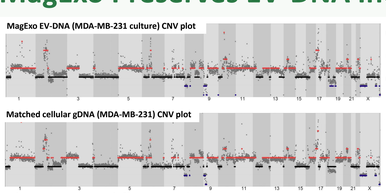


High Recovery of EV Nucleic Acid Cargo



MagExo™ recovers >80% of EV-associated DNA and RNA from plasma, exceeding two benchmark isolation reagents (Vendor G, Vendor T). Recovery efficiency was calculated as (EV-spiked plasma − unspiked plasma) / total yield from pure EVs × 100%, quantified by Qubit DNA/RNA HS assay.

MagExo Preserves EV-DNA Integrity

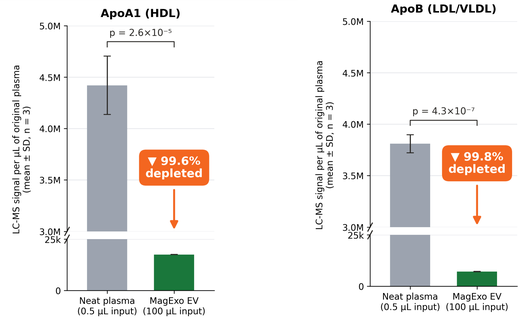


Copy number variation (CNV) analysis from NGS demonstrates that EV DNA profiles strongly resemble the cellular genomic DNA from the donor cell line.

CNV PCC=0.92

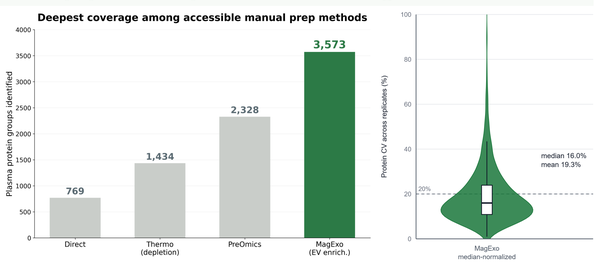
The same workflow applied to plasma recovers intact EV cargo — protein, miRNA, and DNA — preserving the signatures that plasma biomarker discovery depends on.

High Purity and Minimal Contamination



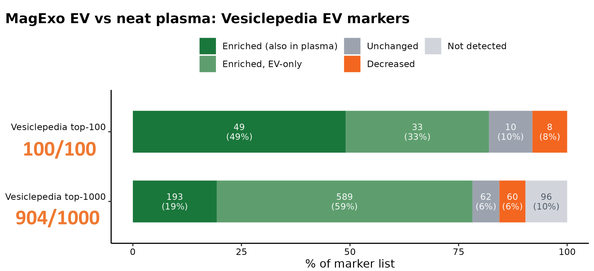
MagExo EV isolation achieves near-complete, statistically significant removal of both HDL-associated (ApoA1) and LDL/VLDL-associated (ApoB) apolipoproteins per unit of starting plasma, confirming effective lipoprotein contaminant depletion during EV enrichment.
Peptide-level LC-MS/MS quantification (DIA-NN output) for ApoA1 and ApoB was summed per protein and normalized to plasma input volume (Neat Plasma: 0.5 µL; EV Fraction: 100 µL).

Deep plasma protein coverage



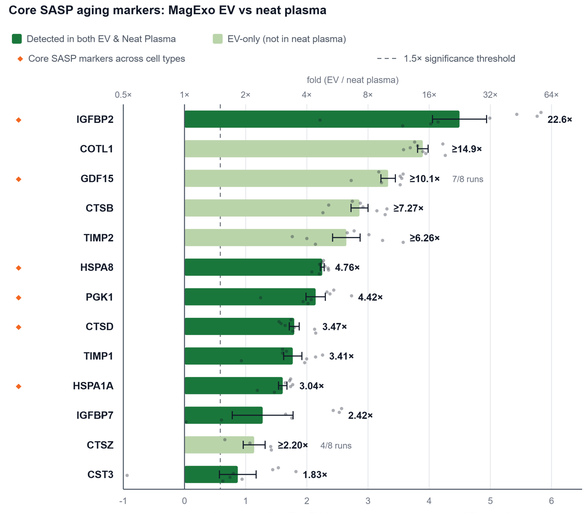
LC-MS analysis of MagExo™-isolated EVs from as little as 100 µL plasma identifies >3,500 protein groups — substantially deeper coverage than direct blood/plasma processing methods (329–2,328 protein groups) — demonstrating exceptional EV proteome depth.
MagExo protein CV was computed across 4 independent preparations of the same pooled plasma. The violin shows the median CV is 16.0% and mean CV 19.3% from MagExo. The box shows the median and interquartile range with whiskers 1.5 × IQR.

MagExo Genuinely Enriches EVs



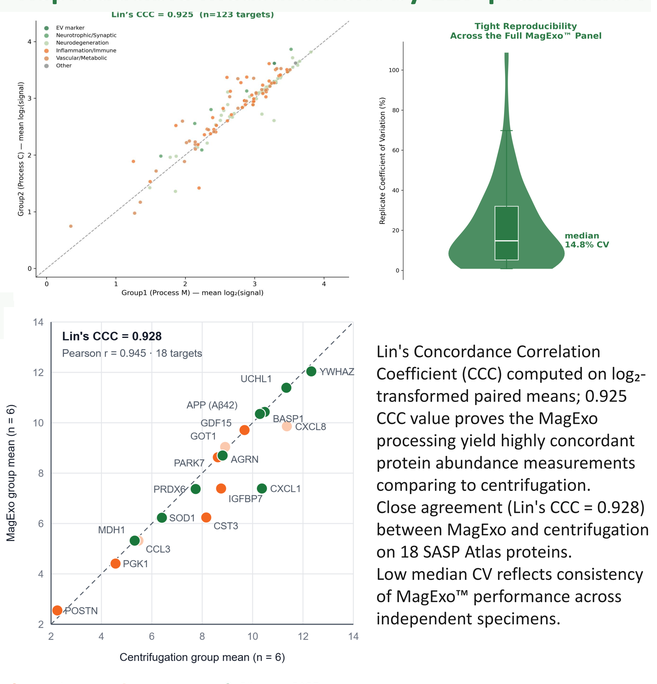
Of the 100 most frequently reported EV proteins in Vesiclepedia, MagExo detects all 100, and 82 are clearly more abundant than in the same amount of plain plasma. Across the top 1,000, it detects over 90% reported EV proteins, of which 82% are significantly enriched ≥1.5-fold.

Core Aging Biomarkers Enriched by MagExo



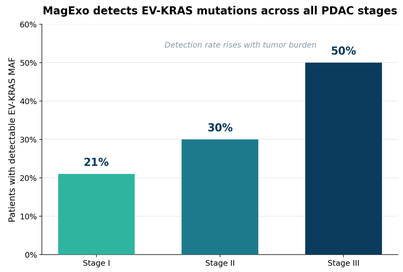
The core senescence-associated secretory phenotype (SASP) proteins were reported as aging markers in all three fibroblast senescence models (irradiation, oncogenic RAS, atazanavir; SASP Atlas, *Basisty et al. 2020*). They also increase significantly with age in human plasma (*Tanaka et al. 2018*, SomaScan, n ≈ 240). Of these 25 proteins, MagExo detects 24; the 13 shown are significantly enriched in the MagExo EV fraction vs neat plasma.

Reproducible measurement by 127-plex NuLISA



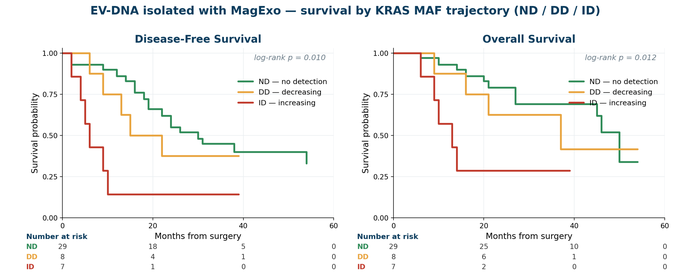
Lin's Concordance Correlation Coefficient (CCC) computed on $\log_2$-transformed paired means; 0.925 CCC value proves the MagExo processing yield highly concordant protein abundance measurements comparing to centrifugation.
Close agreement (Lin's CCC = 0.928) between MagExo and centrifugation on 18 SASP Atlas proteins.
Low median CV reflects consistency of MagExo™ performance across independent specimens.

EV-KRAS Mutations by PDAC Stages and Survival



Using MagExo isolation followed by droplet digital PCR, tumor-specific KRAS mutations (*G12A, G12S, G12C, G12V, G12R, and G12D*) were measured in circulating EVs at different disease stage — EV associated KRAS mutation rate more than doubled from Stage I to Stage III, demonstrating EV-KRAS MAF as a real-time surrogate of disease load.

44 patients with confirmed KRAS-mutated PDAC, neoadjuvant therapy + surgery (2019–2021)
Plasma sampled at diagnosis, post-NAT, and 1-month post-surgery.



Restricted-mean survival separated cleanly by group. The **ID** (increasing) group had the shortest disease-free and overall survival, while **ND** (no detection) patients fared best.
Both splits were statistically significant (Disease free survival p=0.010; Overall survival p=0.012), and increasing MAF independently predicted worse survival on multivariable analysis.

MagExo™: Infrastructure for Biomarker Discovery from liquid Biopsy

- Overcomes key barriers to plasma biomarker work:
  - high recovery: >90% EV capture and nucleic acid recovery
  - high purity: >99.5% removal of contaminants per volume of plasma
  - strong reproducibility: 86.7% detectability and a median CV <20%
- Captures the aging secretome. MagExo™ detects 94% of the core SASP Atlas proteins (vs 60% in neat plasma) and enriches key aging markers.
- Gives a consistent SASP signature in adults over 65. NuLISA results agree across all 12 donors.
- Supports multi-omics (LC-MS, NuLISA, NGS) from minimal plasma use.

We welcome collaboration with investigators applying MagExo™ to aging cohorts and biomarker validation studies.

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Reference

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