

Supplementary Notes

Supplementary Note 1. Visualizing location of platform-discordant protein-altering genetic variants in protein structures

Upon visualizing consequences of each of the platform-discordant protein altering variants (PAVs) in AlphaFold predicted protein structures, we observed the majority of platform-discordant PAVs encode amino-acid changes on the surface of the protein, supporting the notion that these variants may reflect interference with affinity probe binding (Supplementary Figure 36- Supplementary Figure 53).

Supplementary Note 2. Impact of adjustment for platform-discordant PAVs pQTL on inter-platform correlation (across all probe pairs)

For the 18 proteins associated with a platform-discordant PAV *cis*-pQTL across all probe pairs (Supplementary Data 6; Supplementary Figure 13), we adjusted each platform's measures for copies of the PAV, and computed inter-platform correlation estimates with residual measures. Prior to PAV-adjustment, the mean inter-platform correlation estimate for these proteins was 0.37, with estimates ranging from -0.39 to 0.66. Post PAV-adjustment, the mean inter-platform correlation increased to 0.51, with estimates ranging from 0.15 to 0.76 (Supplementary Data Table 6; Supplementary Figure 13).

Supplementary Note 3. Adjustment for platform-discordant PAV pQTL in *cis*-pQTL mapping

On SomaScan, 2 *cis*-pQTL signals, for 2 unique proteins (ACP1 and CPPED1), become significant only upon using PAV-adjusted protein measures in pQTL mapping (Supplementary Data 23, Supplementary Figure 17, Supplementary Figure 18).

Additionally, a subset of 8 signals for 8 proteins on SomaScan (APOL1, APOE, CLU, CTSH, KDR, PGLYRP2, PLAUR, RNASE6) (Supplementary Data Table 21), and 4 signals for 4

proteins on Olink (CTSH, CTSS, HNMT, and PILRA) increased in significance following adjustment for platform-discordant PAV (Supplementary Data Table 22), (Supplementary Figures 19-27). For example, when mapping pQTL using PAV-adjusted PILRA measures, an alternate non-coding genetic signal, driven by chr7:10048786:C:G, exhibited increased significance for Olink's PILRA measures (without PAV Adjustment $P=3.70 \times 10^{-15}$, with PAV Adjustment $P=1.67 \times 10^{-23}$) (Supplementary Figure 15). Similarly, mapping pQTL with suPAR measures adjusted for the platform-discordant PAV results in increased significance of an independent, platform-concordant signal driven by chr19:43652320:T:C on SomaScan (without PAV Adjustment $P=2.94 \times 10^{-14}$, with PAV Adjustment $P=1.49 \times 10^{-21}$) (Supplementary Figure 16).

Supplementary Note 4. Additional examples of ancestry-differentiated, platform-discordant PAV *cis*-pQTL

In addition to suPAR, two additional proteins -- apolipoprotein 1 (APOL1) and Calcineurin Like Phosphoesterase Domain Containing 1 (CPPED1) – are associated with platform-discordant PAVs most prevalent among participants clustering with the African (AFR) ancestry reference population.

APOL1

APOL1 associates with an ancestry-differentiated, platform-discordant PAV (rs2239785, chr22:36265284:G:A, Glu166Lys, EAF $X^2=449.8$, X^2 $p=3.47 \times 10^{-97}$) (Supplementary Figure 20, Supplementary Figure 29, Supplementary Figure 38) common across all ancestry clusters contributing to this study, but most common among individuals clustering with the African ancestry reference (EAF=0.63). Following adjustment for this PAV, correlation improved to the largest extent among individuals in the AFR ancestry group (Pearson's r without PAV Adjustment=0.34, Pearson's r with PAV Adjustment = 0.47). (Supplementary Figure 29) Additionally, pQTL mapping using APOL1 measures adjusted for copies of the platform-

discordant PAV resulted in improved strength of a *cis*-pQTL association driven by a noncoding variant, chr22:36251719:A:T (Supplementary Figure 20).

Given the proximity of rs2239785 to APOL1 G1 and G2 kidney disease genotype risk factors, we further examined whether rs2239785 was independent of these variants by adjusting for APOL1 risk haplotypes in pQTL mapping (with non-PAV adjusted APOL1 measures). While adjustment for APOL1 G1/G2 risk haplotype slightly attenuated the PAV signal, the signal was still present, suggesting independence from known risk variants in the region (Supplementary Figure 30).

CPPED1

CPPED1 associates with an ancestry-differentiated, platform discordant PAV (rs3748976, chr16:12803721:G:T, A19D, EAF $X^2=299.2$, EAF X^2 $p=1.45 \times 10^{-64}$) (Supplementary Figure 18, Supplementary Figure 40) most common among individuals of AFR ancestry (EAF=0.60). While adjustment for this PAV improves CPPED1 measures across all participants from inter-platform Pearson's r -0.14 to 0.47, interestingly, the largest improvement is not among individuals of AFR ancestry (Pearson's r improvement from -0.06 to 0.27 post-adjustment), but rather, individuals clustering with AMR references (r improvement from -0.06 to 0.45 with PAV adjustment), suggesting interplay of other genetic variants or technical/environmental factors (Supplementary Figure 31). However, adjustment for this platform-discordant PAV results in a new *cis*-pQTL signal on SomaScan, led by chr16:12768150:A:C (PAV-Adjusted lead variant p -value= 1.78×10^{-55}) (Supplementary Figure 18).

Supplementary Note 5. Adjustment for platform-specific pQTL

Adjustment for platform specific PAVs also, on average, modestly improved assay correlation (mean difference 5.1×10^{-2} for 256 Olink-specific PAVs, mean difference 1.5×10^{-2} for

SomaScan specific PAVs; see Supplementary Figure 14), but differences were generally minor compared to the large improvements seen for the smaller number of platform discordant PAVs. The overall impact of using protein measures adjusted for platform-specific PAV in epidemiological models was minimal; the correlation of phenotypic effect sizes obtained from models with measures not adjusted for PAVs vs. PAV-adjusted measures was similar (Supplementary Figure 34; Supplementary Figure 35). Full results from these analyses can be found in Supplementary Data 24 and Supplementary Data 25. Similarly, adjustment for SomaScan-specific pleiotropic *trans*-pQTL among associated proteins proteins did not have an impact on inter-platform correlation (Supplementary Data 28).

Supplementary Note 6. Summary data tables

A key summarizing correlation, per-ancestry correlation estimates, and pQTL summary statistics per platform can be found in Supplementary Data 29. pQTL and LOD result summaries and credible sets corresponding to results from considering all probes for the 2,157 platform overlapping proteins can be found in Supplementary Data 2, Supplementary Data 6, Supplementary Data 19-35.

Supplementary Methods

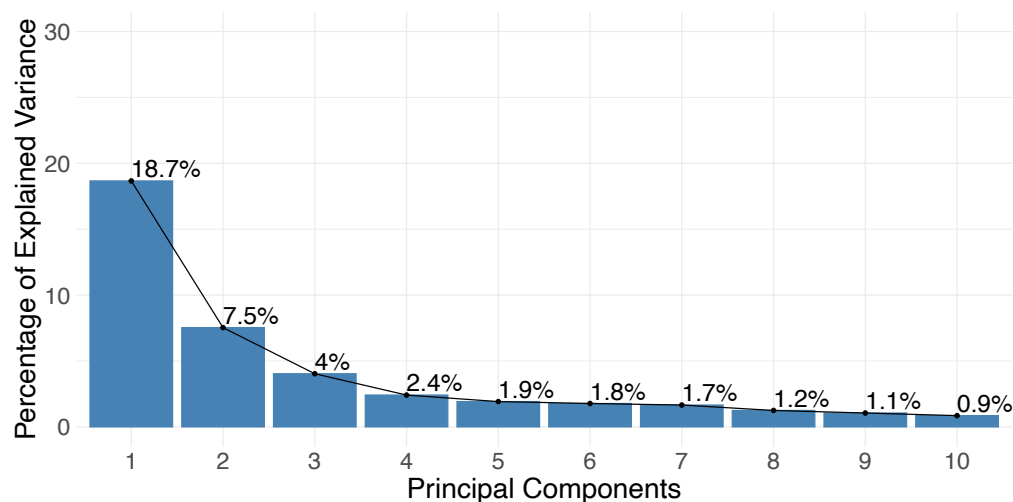
Visualizing location of platform-discordant PAVs in protein structures

Protein FASTA sequences were obtained from UniProt (www.uniprot.org/)¹ and modified to reflect the isoform encoded by each platform-discordant PAV. FASTA sequences were then input into the AlphaFold Server powered by Alpha Fold 3 (<https://alphafoldserver.com/>)² to obtain predicted structure models. Structures were visualized and images were generated in Pymol³.

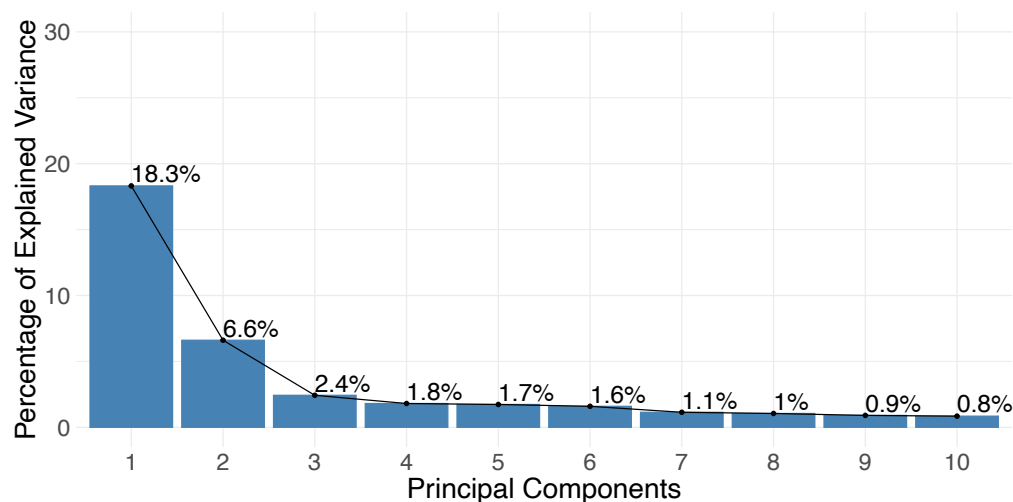
Adjustment for APOL1 G1 and G2 kidney disease risk alleles

APOL1 G1 (rs73885219, chr:36269595:AATAATT:A) and G2 (rs71785313, chr22:36265860:A:G) risk alleles were extracted from TOPMed Freeze 8 (due to missingness in TOPMed Freeze 10). G1 was coded as 0, 1, or 2, based on copies of the minor allele (the deletion). Similarly, G2 was coded as 0, 1, or 2, based on copies of the minor allele (the G allele). The following allele combinations were considered as high risk: G1=1 and G2=1; or G1=2 and G2=0; or G1=0 and G2=2. All other combinations were considered low risk. Risk status was adjusted for as a covariate in APOL1 pQTL mapping (performed as reported in main analysis methods). Resulting pQTL association statistics were used to determine the robustness of the platform-discordant PAV signal to the APOL1 risk alleles.

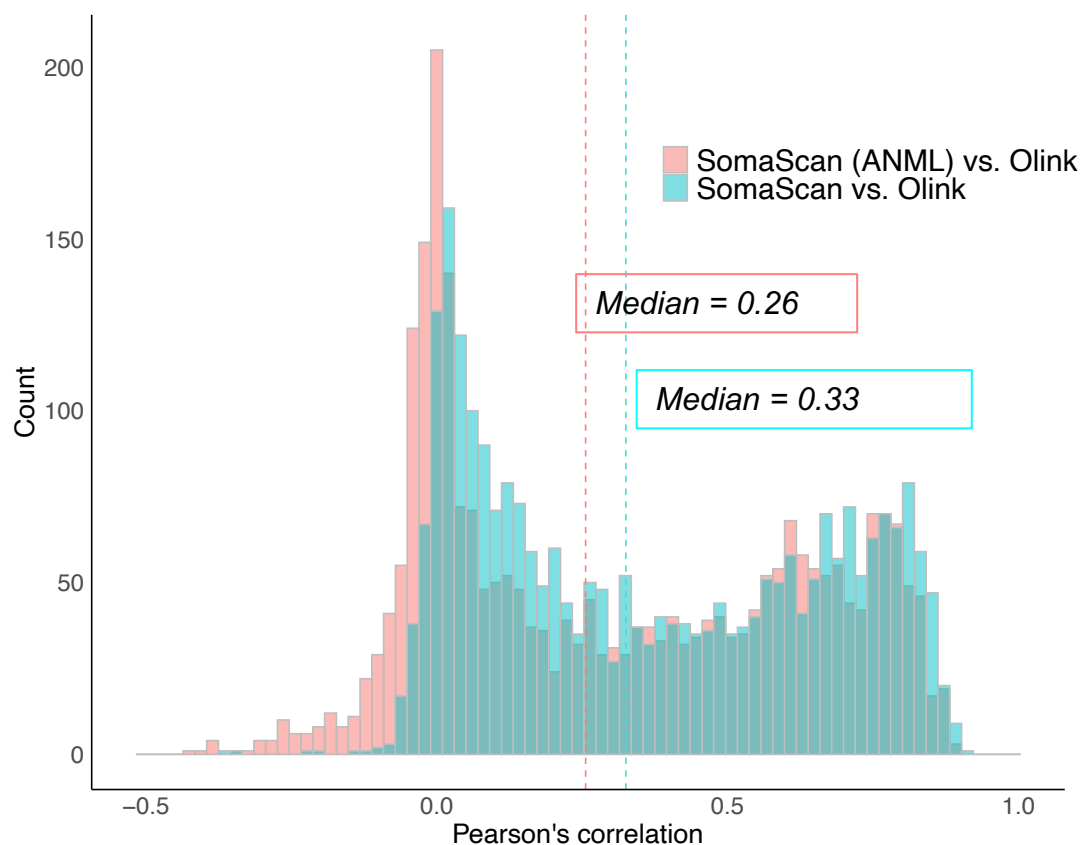
(A) SomaScan 7k



(B) Olink Explore 3072

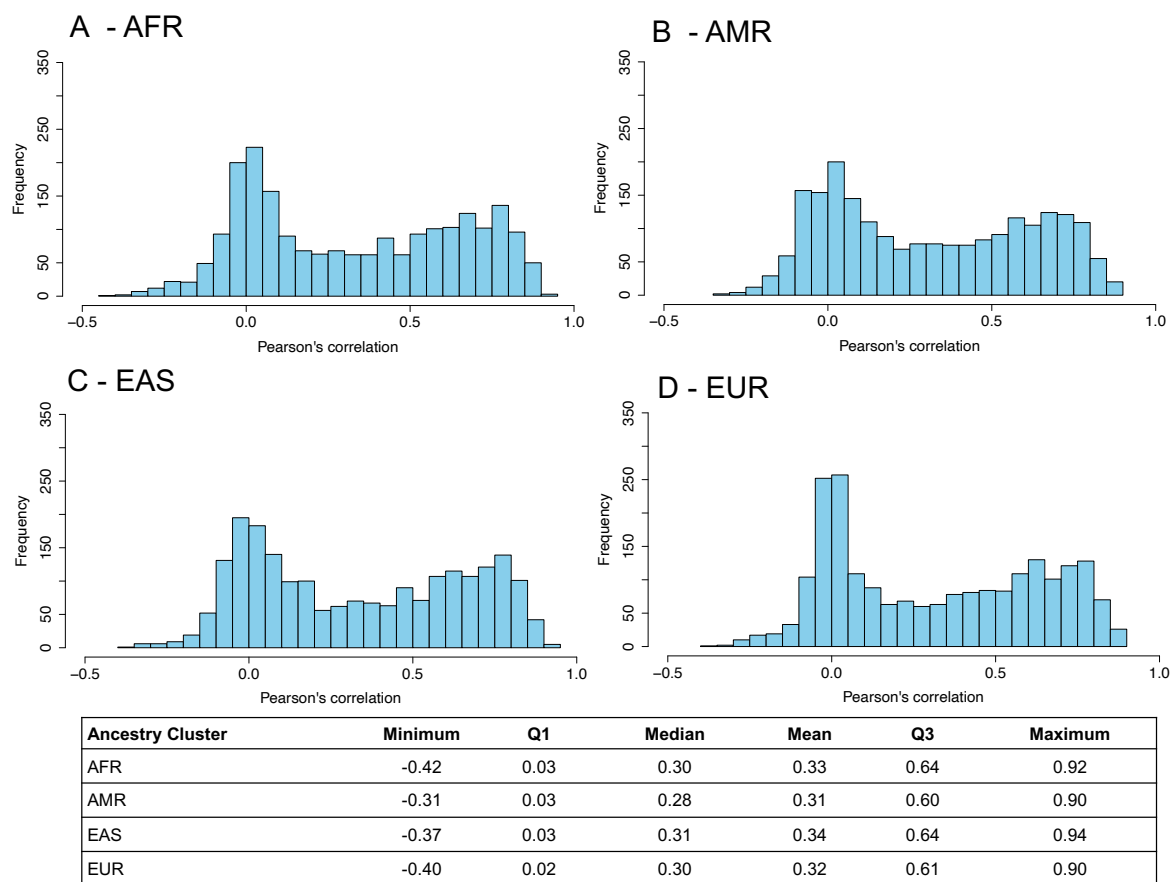


Supplementary Figure 1. Scree plot depicting percentage of variance explained by protein principal components on (A) SomaScan 7k (using sample measures with adaptive-normalization by maximum likelihood) and (B) Olink Explore 3072 in 1,923 MESA participants. Principal component analyses were performed across all proteins analyzed on each platform. Source data is available as Source Data File 1.

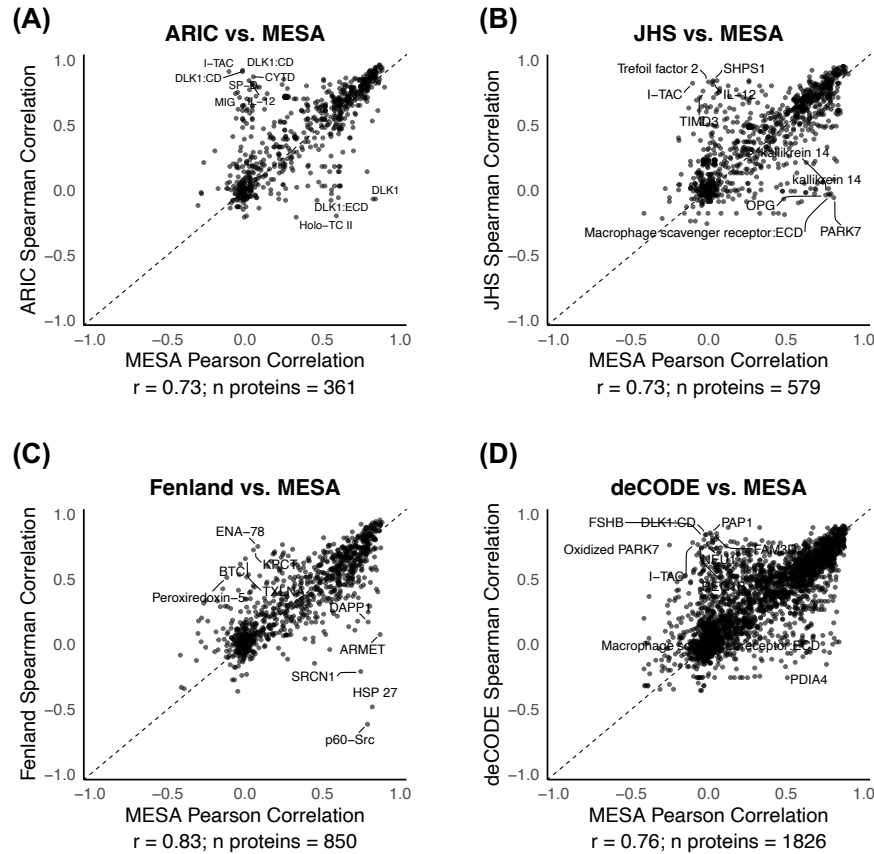


	Minimum	Median	Mean	IQR	Maximum
SomaScan (ANML) vs. Olink	-0.42	0.26	0.31	[0.01, 0.61]	0.90
SomaScan vs. Olink	-0.37	0.32	0.37	[0.08, 0.65]	0.91

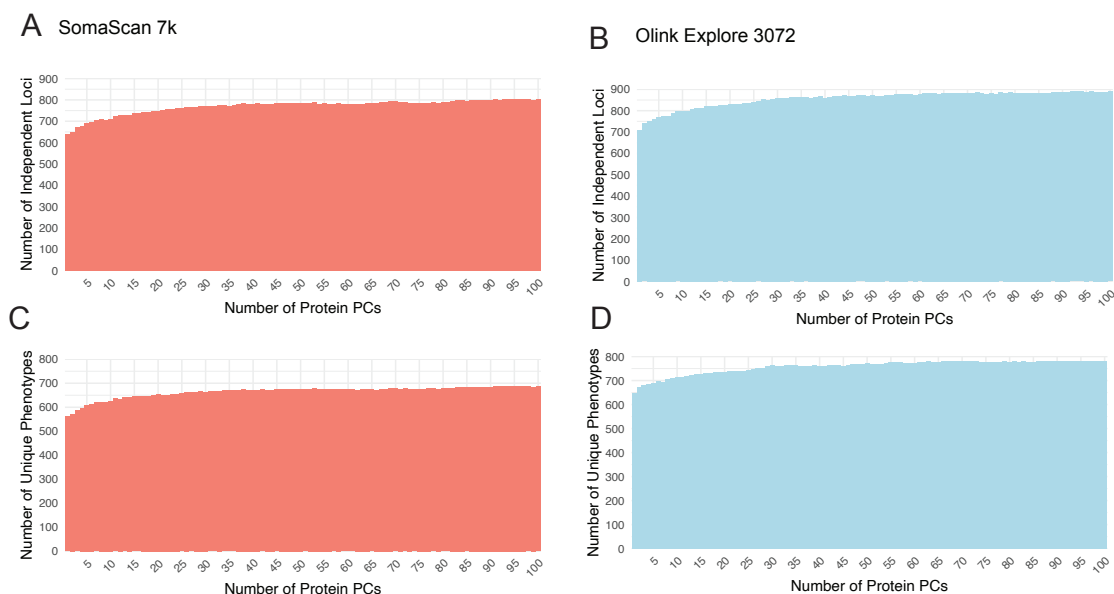
Supplementary Figure 2. Inter-platform Pearson's correlation estimates for 2,708 SomaScan 7k and Olink Explore 3072 affinity probe pairs, corresponding to 2,157 UniProt targets assayed on both platforms from 1,930 MESA participants with plasma samples measured on both platforms. Correlation (Pearson's r) estimates from comparison of SomaScan measures with adaptive-normalization (ANML-SMP) performed across all samples shown to Olink measures displayed in pink, whereas estimates from comparison of SomaScan measures with ANML performed in quality control samples only (ANML-QC) to Olink measures shown in blue. Source data is available in Supplementary Data Table 2.



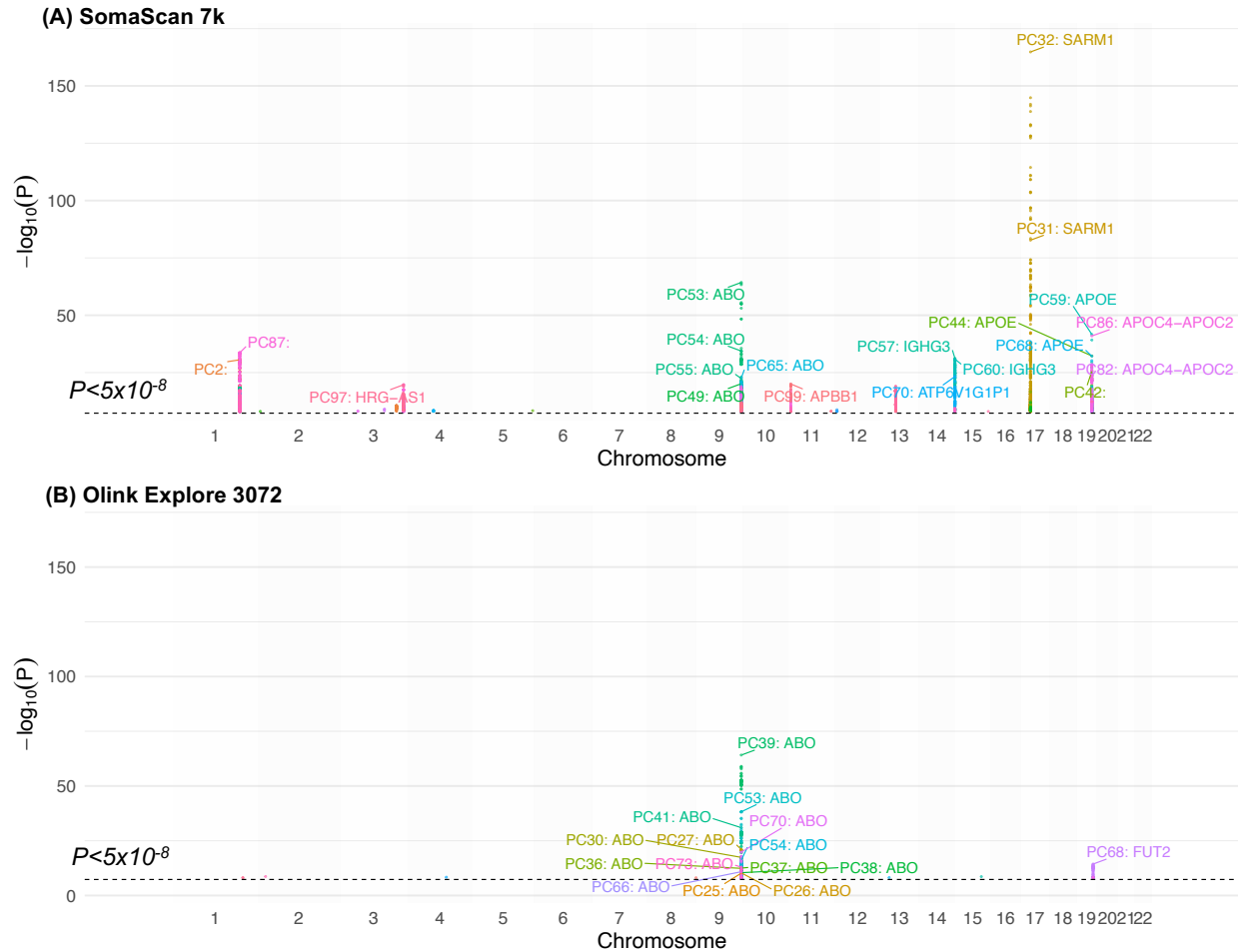
Supplementary Figure 3. Inter-platform Pearson correlation estimates by ancestry for 2,157 SomaScan SeqIDs and 2,157 Olink IDs targeting the 2,157 UniProt IDs measured on both platforms from 1,852 MESA participants with protein measures, whole genome sequencing data available, and ancestry group assigned (433 African ancestry (AFR), 220 Admixed American (AMR), 267 East Asian (EAS), and 932 European (EUR)). Table displays values of the minimum, first quartile (Q1), median, mean, third quartile (Q3), and maximum Pearson's r value observed within individuals of each ancestry cluster. Source data is available in Supplementary Data Table 2.



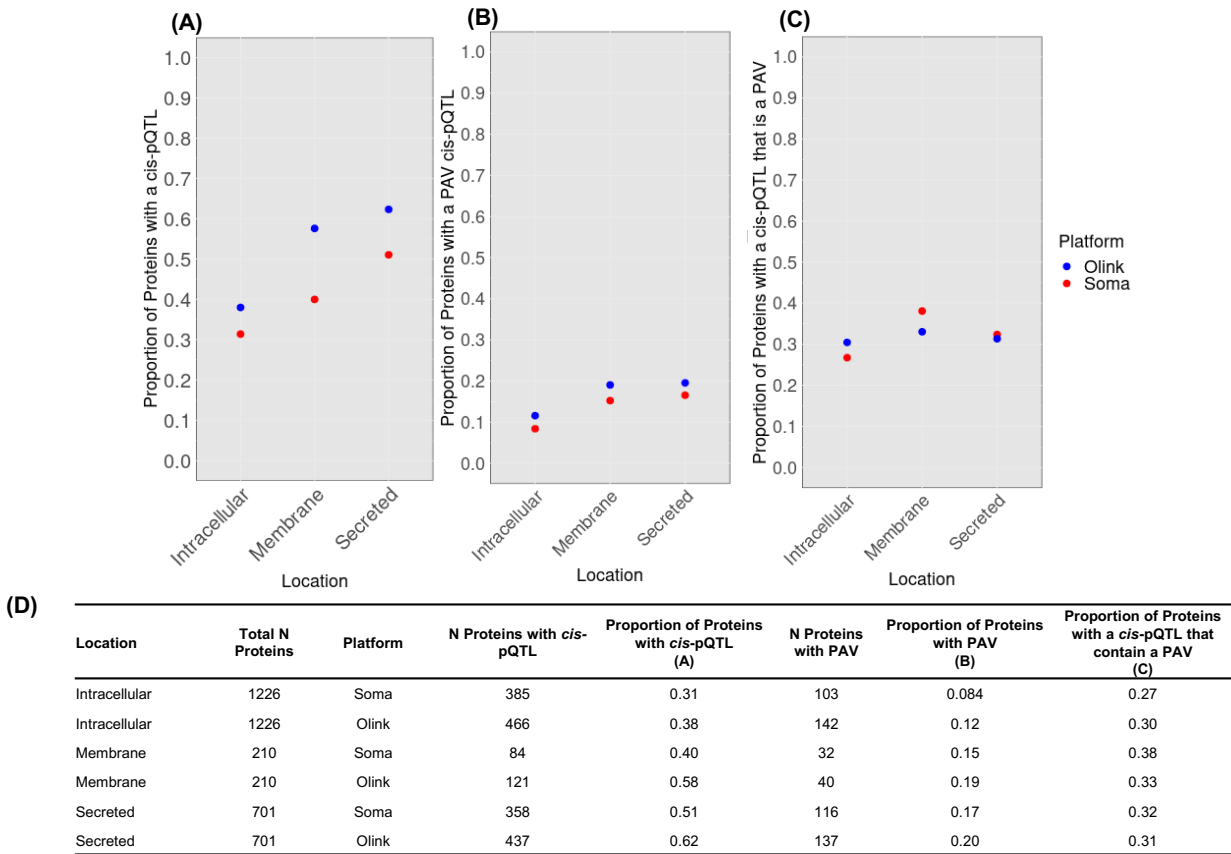
Supplementary Figure 4. Comparison of SomaScan 7k vs. Olink Explore 3072 Pearson's r correlation coefficients observed in 1,930 MESA participants in present study compared to protein measure correlation coefficients observed (A) for 361 proteins measured on SomaScan v4 and Olink in 427 ARIC participants in Rooney et al., (2023), (B) for 579 proteins measured on SomaScan 1.3k and Olink Explore 1.5k in 568 JHS participants in Katz et al., (2022), (C) for 850 proteins measured on SomaScan v4 and Olink in 485 Fenlad study participants in Pietzner et al., (2021), (D) for 1,826 proteins measured on SomaScan v4 and Olink Explore 3072 in 1514 deCODE participants in Eldjarn et al., (2023). Source data is available in Supplementary Data Table 2.



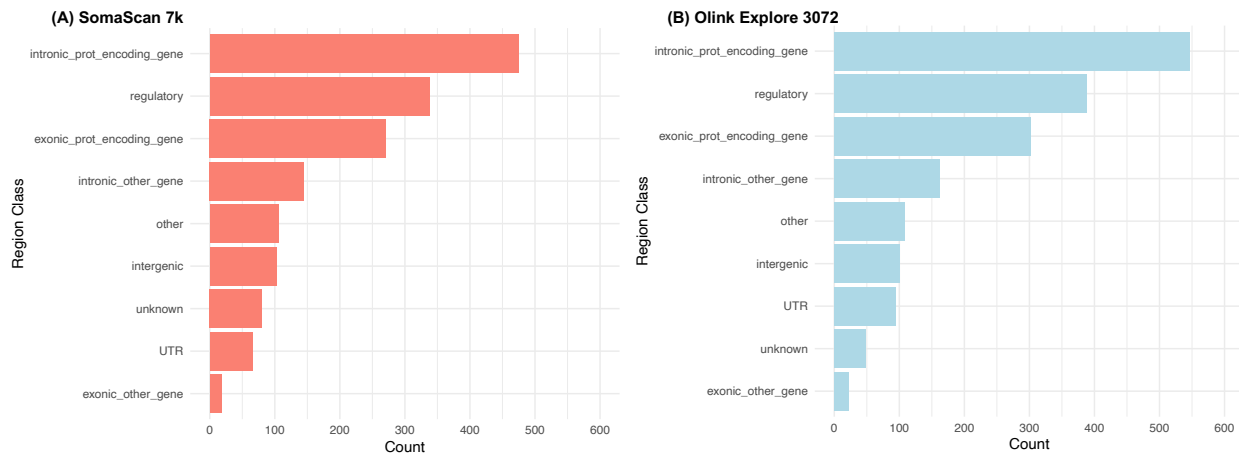
Supplementary Figure 5. Impact of the number of protein principal components (PCs) adjusted for in *cis*-pQTL mapping on the number of significant lead *cis*-pQTL (p < 5 × 10⁻⁸, 500 kilobase distance threshold) identified on (A) SomaScan and (B) Olink in 1,889 unrelated MESA participants, as well as the number of probes with a significant lead *cis*-pQTL on SomaScan and Olink in analyses including one probe per UniProt ID, per platform. pQTL were generated with linear regression under an additive model, two-sided test of significance. Source data is available on Zenodo 10.5281/zenodo.17642644 (<https://zenodo.org/records/17642645>).



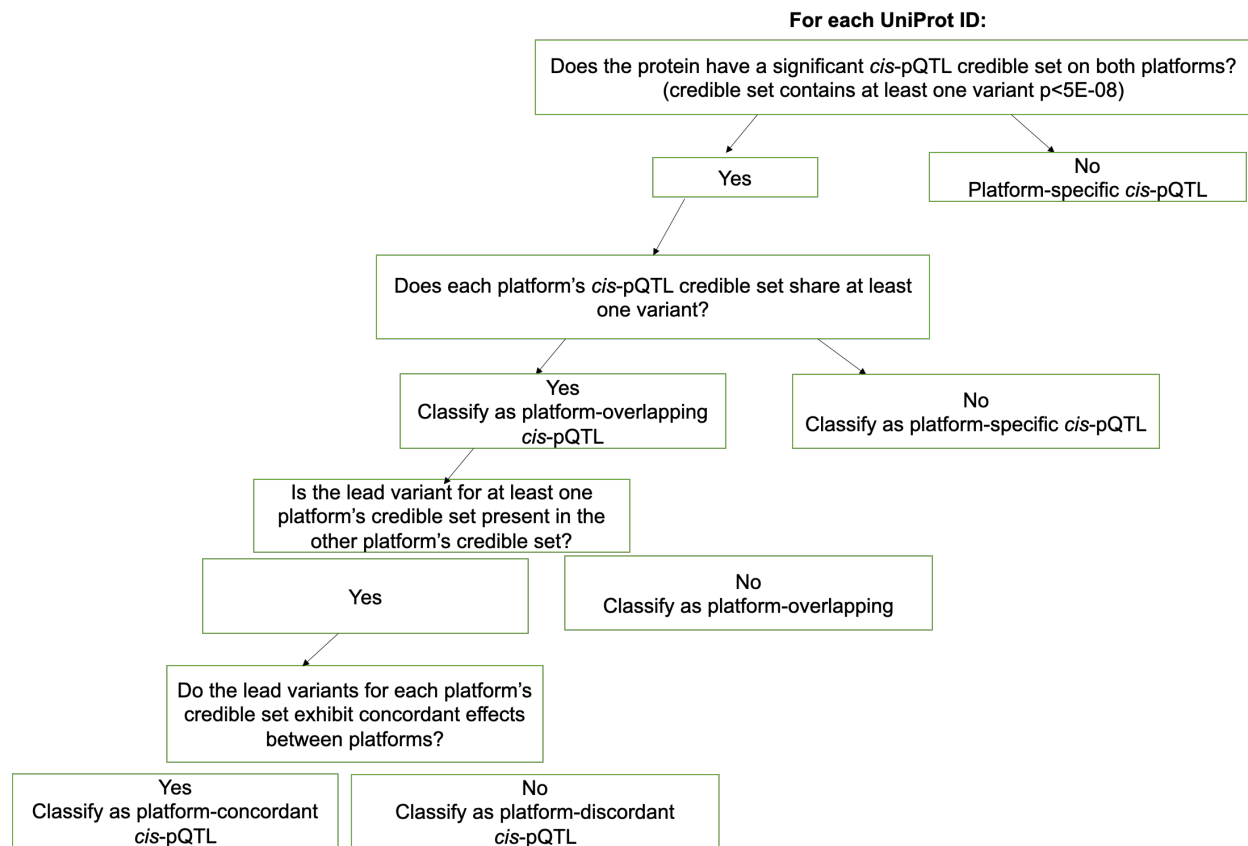
Supplementary Figure 6. Genetic associations for protein principal components (PCs), at a genome-wide significance threshold of $p < 5 \times 10^{-8}$ for (A) SomaScan 7k protein PCs and (B) Olink Explore 3072 protein PCs. Genetic variant associations with protein principal components were generated with linear regression under an additive model, two-sided test of significance. Source data is available on Zenodo 10.5281/zenodo.17642644 (<https://zenodo.org/records/17642645>).



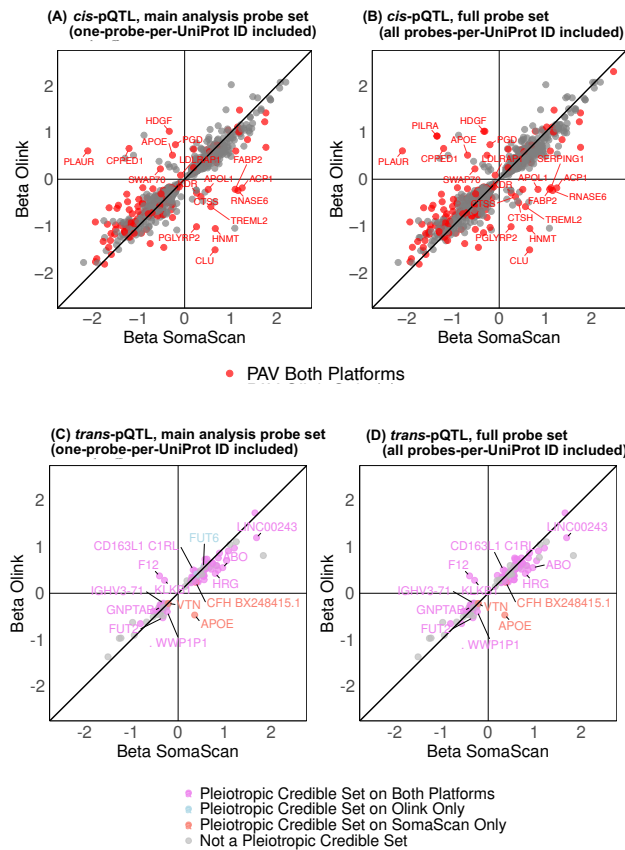
Supplementary Figure 7. Protein *cis*-pQTL status according to subcellular location. The 2,157 proteins measured on both SomaScan 7k and Olink Explore 3072 were classified as intracellular, membrane, or secreted (according to Human Protein Atlas reported location, see Methods). Within each category and platform, we determined the proportion of proteins (A) associated with a significant *cis*-pQTL (SuSiE credible set with at least one variant at genome-wide significance, $p < 5 \times 10^{-8}$), (B) associated with a *cis*-pQTL containing a PAV, and (C) associated with a *cis*-pQTL PAV relative to total number of proteins associated with a *cis*-pQTL. Counts and proportions are reported in (D). Significant *cis*-pQTL were detected for larger proportions of secreted proteins on each platforms, but similar proportions of PAV associations were observed for proteins in each category. Source Data is available in Supplementary Data Table 29.



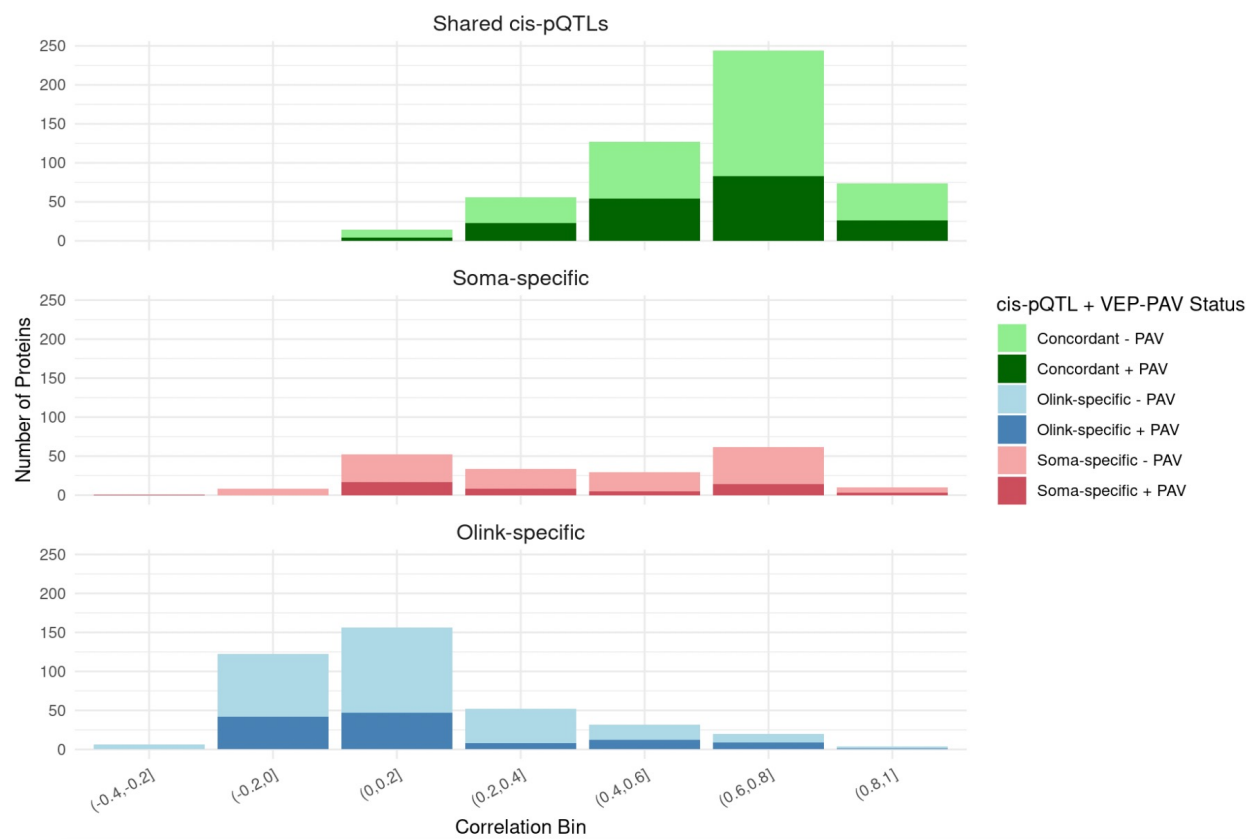
Supplementary Figure 8. Functional consequences for lead *cis*-pQTL variants identified for (A) SomaScan and (B) Olink protein measures, as predicted by Variant Effect Predictor (VEP). Categories (from top row to bottom row) are intronic variant for the protein-encoding gene, regulatory variant, exonic for the protein-encoding gene, intronic for a non-protein gene in the *cis*- window, other, intergenic, unknown, untranslated region (UTR), or exonic for a non-protein encoding gene in the *cis*- window. Regulatory variants are those classified by VEP as “upstream” or “downstream” of a protein-encoding genes. Lead *cis*-pQTL variants for all signals (primary, secondary, tertiary, etc.) were included in each analysis. Source Data is available in Supplementary Data Tables 4 and 5.



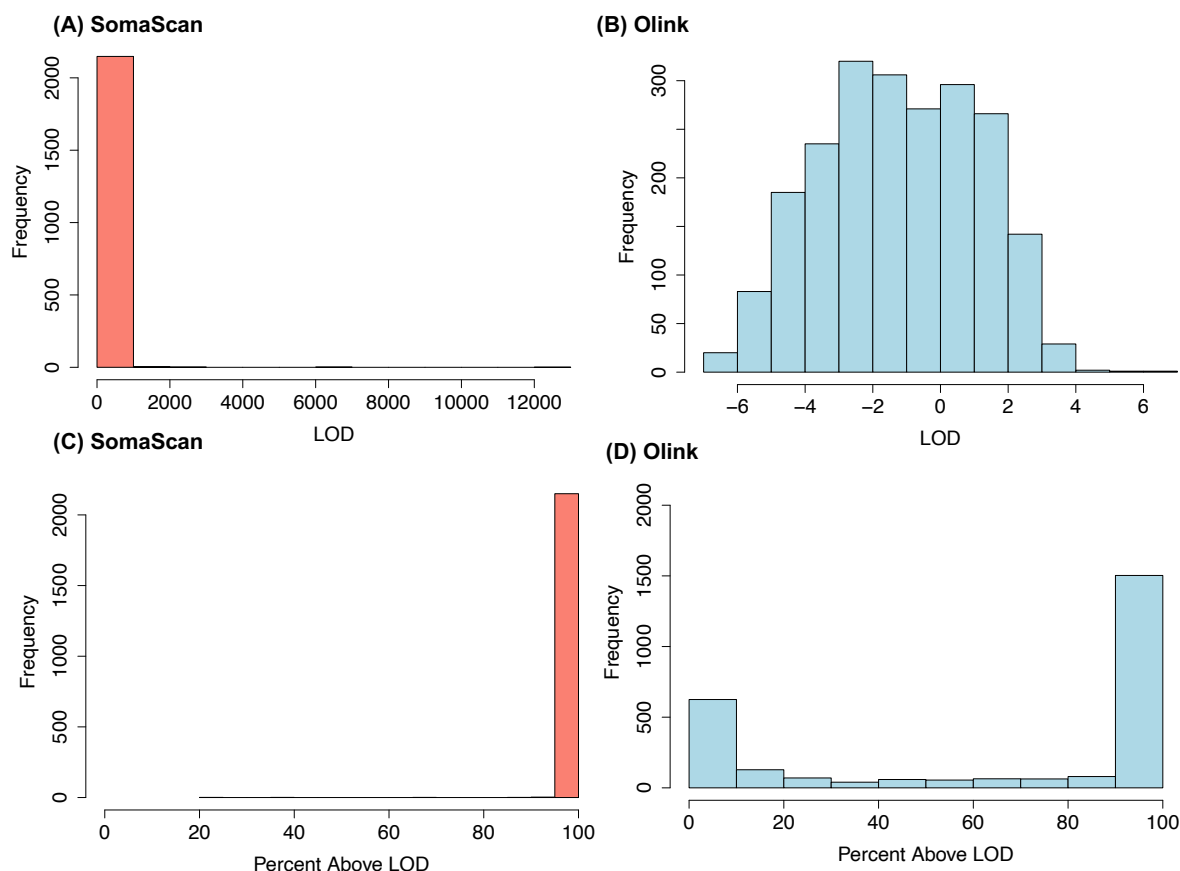
Supplementary Figure 9. Flowchart depicting method for classifying SomaScan and Olink *cis*-pQTL credible sets. Significant credible sets (containing at least one variant significantly associated with the protein at genome-wide significance, $p < 5 \times 10^{-8}$) are classified as platform-concordant, platform-discordant, platform-overlapping, or platform-specific.



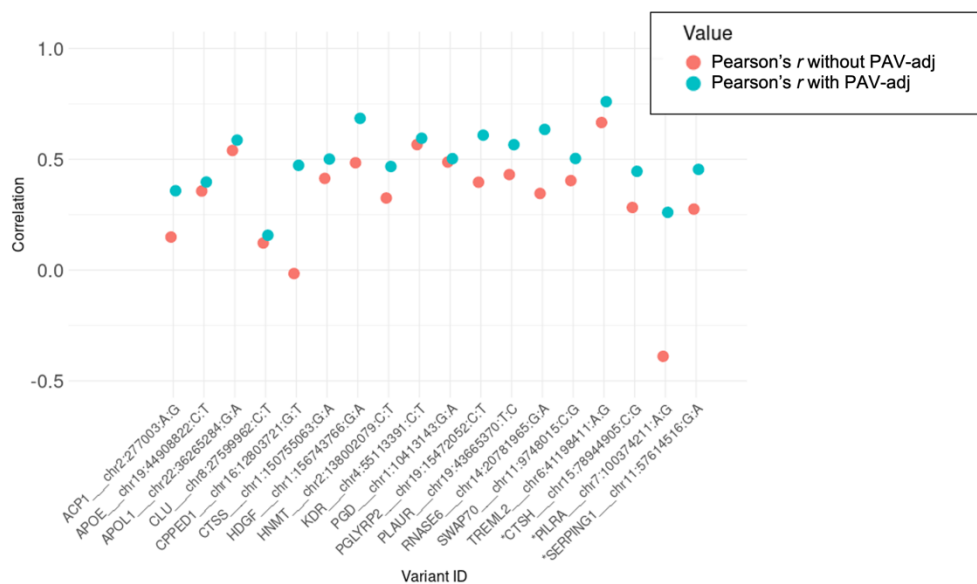
Supplementary Figure 10. (A and B) Lead variant SomaScan and Olink *cis*-pQTL effect-size comparison for all genome-wide significant (at least one SuSiE credible set variant with $p < 5 \times 10^{-8}$) platform-overlapping *cis*-pQTL credible sets (where credible sets overlapped at least one variant, and at least one platform's credible set contained the lead variant for the other platform's credible set), with points colored according to whether a protein-altering variant (PAV) for the protein-encoding gene was present in both platform's credible sets (red) or neither platform's credible set (gray). (C and D) Lead variant SomaScan and Olink *cis*-pQTL effect-size comparison for all significant (genome-wide significance threshold further correcting for 2,708 probe pairs tested 1×10^{-11}) platform-overlapping *trans*-pQTL credible sets, with points colored according to whether the credible set (CS) was pleiotropic (associated with at least 5 proteins) on both platforms, Olink only, SomaScan only, or neither platform. (A & C) Results for platform-overlapping credible sets identified in main analysis of one-probe-per-UniProt ID. (B & D) Results for platform-overlapping credible sets identified in full analysis of all-probes-per-UniProt ID. Source Data is available in Supplementary Data Tables 4, 5, 9, 10, and 12.



Supplementary Figure 11. *cis*-pQTL platform specificity according to protein measure correlation. Number of proteins with a genome-wide significant ($p < 5 \times 10^{-8}$) platform-shared (overlapping signal, concordant directions of effect for SomaScan and Olink signals), SomaScan-specific, or Olink specific *cis*-pQTL according to inter-platform SomaScan and Olink protein measure correlation (Pearson's r). Darker shading within bars represents the number of *cis*-pQTL signals within the category driven by a protein-altering variant (PAV). Source Data is available in Supplementary Data Tables 4 and 5.

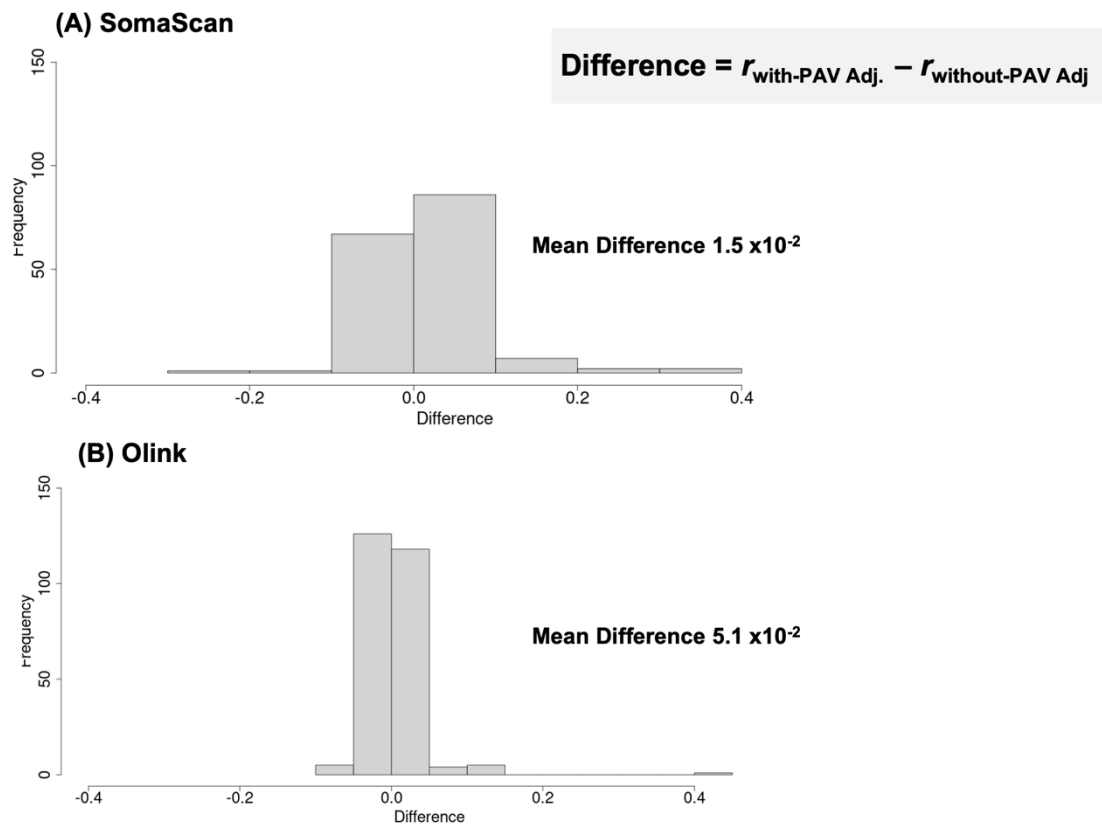


Supplementary Figure 12. (Top panel) Global limit of detection (LOD) values (A) for SomaScan 7k (company-reported values used to define LOD) and (B) for Olink Explore 3072 (calculated from negative controls per company-recommended equation, see methods). (Bottom panel) For each of the 2,157 proteins compared, histogram displaying the distribution of the percentage of (C) SomaScan measures above the SomaScan LOD and (D) Olink measures above the Olink LOD. Source Data is available in Supplementary Data Table 16.

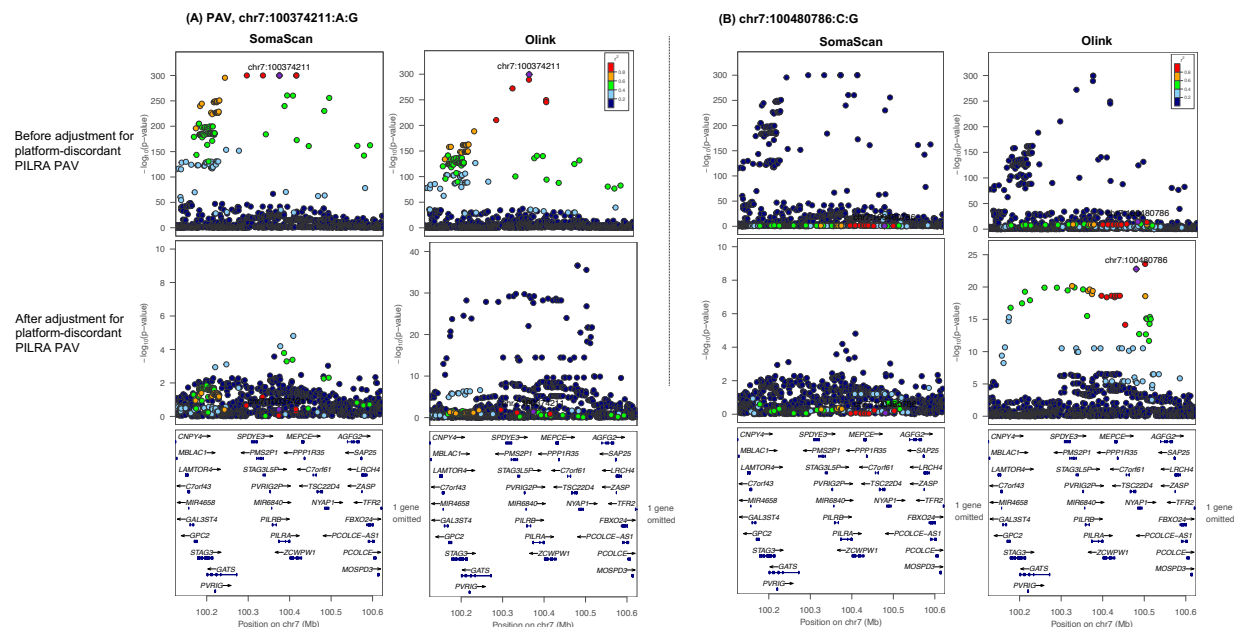


Adjustment	Median correlation
Without Platform discordant PAV-adjustment	0.40
With Platform discordant PAV-adjustment	0.50

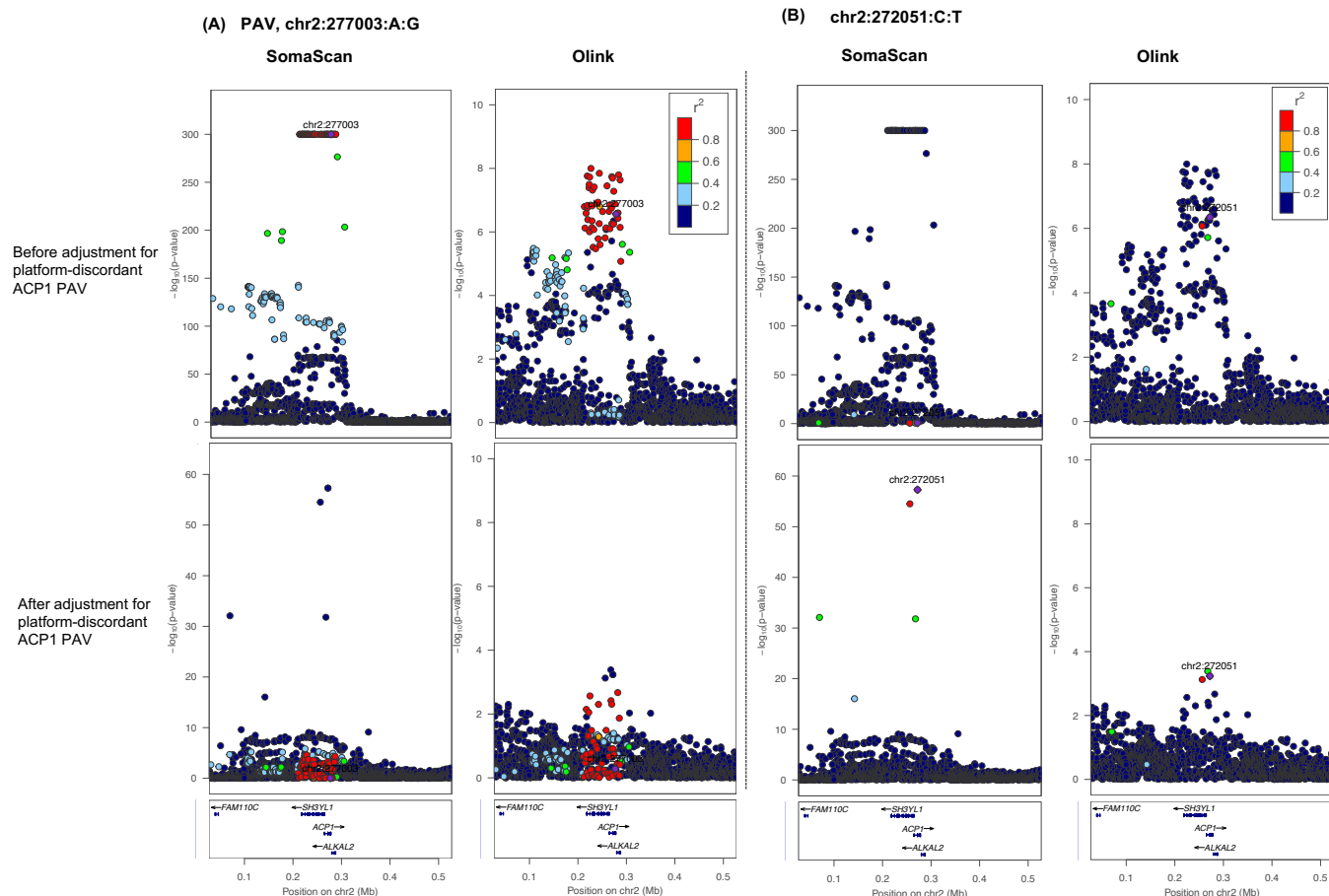
Supplementary Figure 13. Inter-platform correlation without and with adjustment for platform-discordant PAV. 15/18 proteins with a platform-discordant PAV correspond to probes included in main analysis. Protein/PAV pairs marked with asterisk (*) correspond to probes not included in main analysis (which was filtered to the most correlated probe pairs for each UniProt ID), but were included in full analysis of all probe pairs per UniProt ID. Source Data is available in Supplementary Data Table 6.



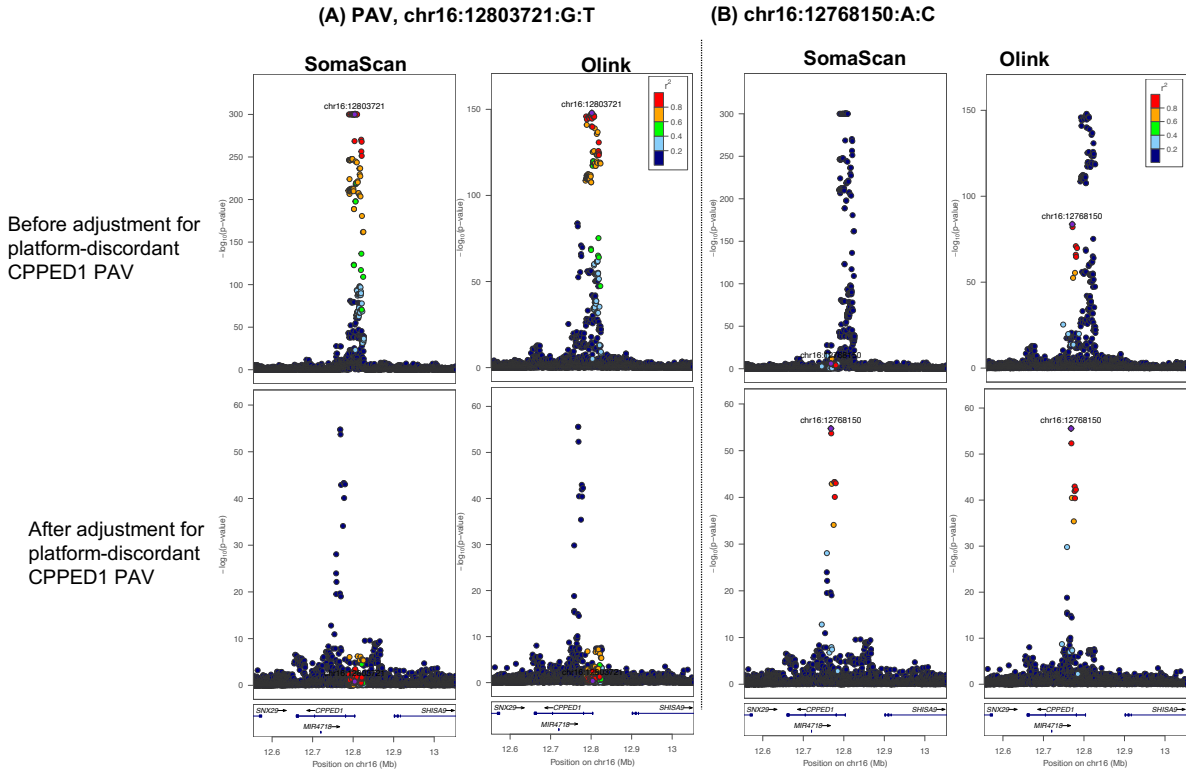
Supplementary Figure 14. Histograms of differences in inter-platform correlation estimates with and without adjustment of protein measures for platform-specific PAVs (difference= correlation of protein measures adjusted for PAV - correlation of protein measures without adjustment for PAV). Difference >0 reflects improved correlation estimate after PAV adjustment. (A) Adjustment for *cis*-pQTL PAV significantly associated with SomaScan measures only. 166 probe pairs assessed. Difference >0 for 97 probe pairs. (B) Adjustment for *cis*-pQTL PAV significantly associated with Olink measures only. 256 probe pairs assessed. Difference >0 for 128/256 probe pairs, although improvements were generally small. Source Data is available in Supplementary Data Tables 24 and 25.



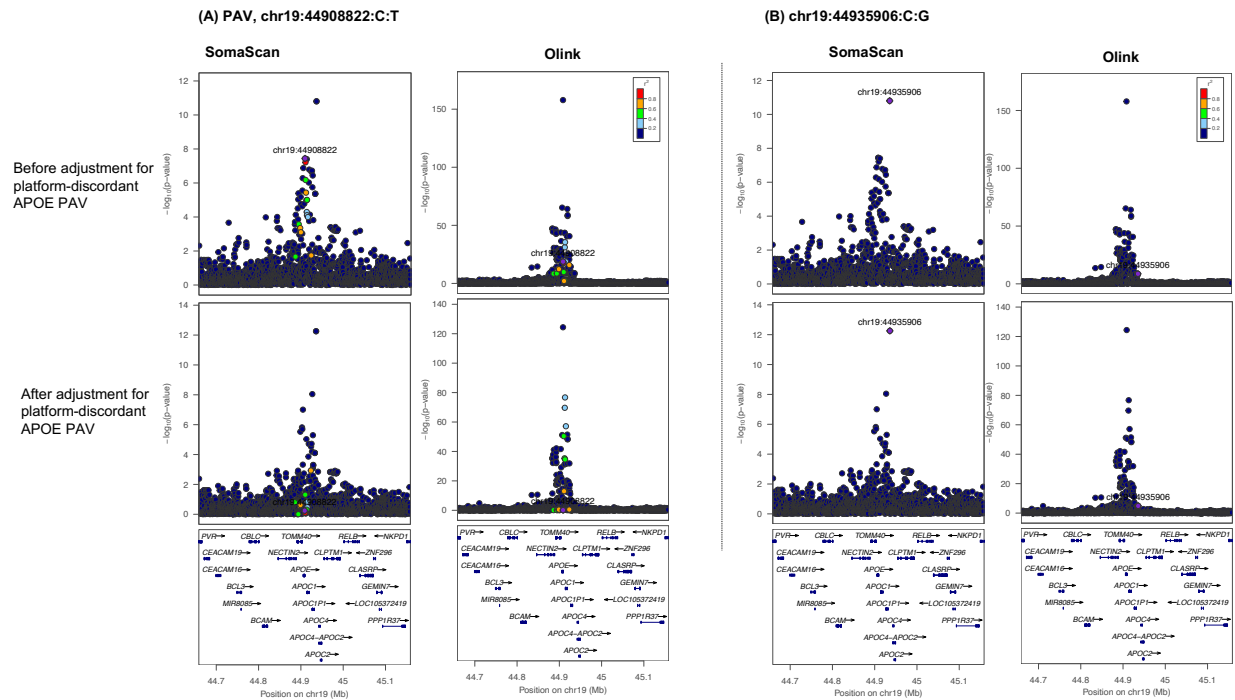
Supplementary Figure 15. Locus Zoom plot displaying the 250KB window around the platform-discordant PILRA PAV before (top) and after (bottom) adjustment for the platform-discordant PAV (chr7:100374211:A:G) on SomaScan vs. Olink, with r^2 values derived in 1,889 MESA study participants. (A, Top) Platform-discordant PAV signal before adjustment on SomaScan and Olink (A, Bottom) Platform-discordant PAV signal after adjustment. As expected, this signal is attenuated to non-significance following adjustment. (B, Top) Prior to adjustment for the PAV, a second, non-coding signal in the region, led by chr7:100480786:C:G, is significantly associated with Olink PILRA measures. (B, Bottom) Following adjustment for the platform-discordant PAV, this signal becomes more significant on Olink. The Y-axes differ in scale between plots. Source data is available on Zenodo 10.5281/zenodo.17642644 (<https://zenodo.org/records/17642645>).



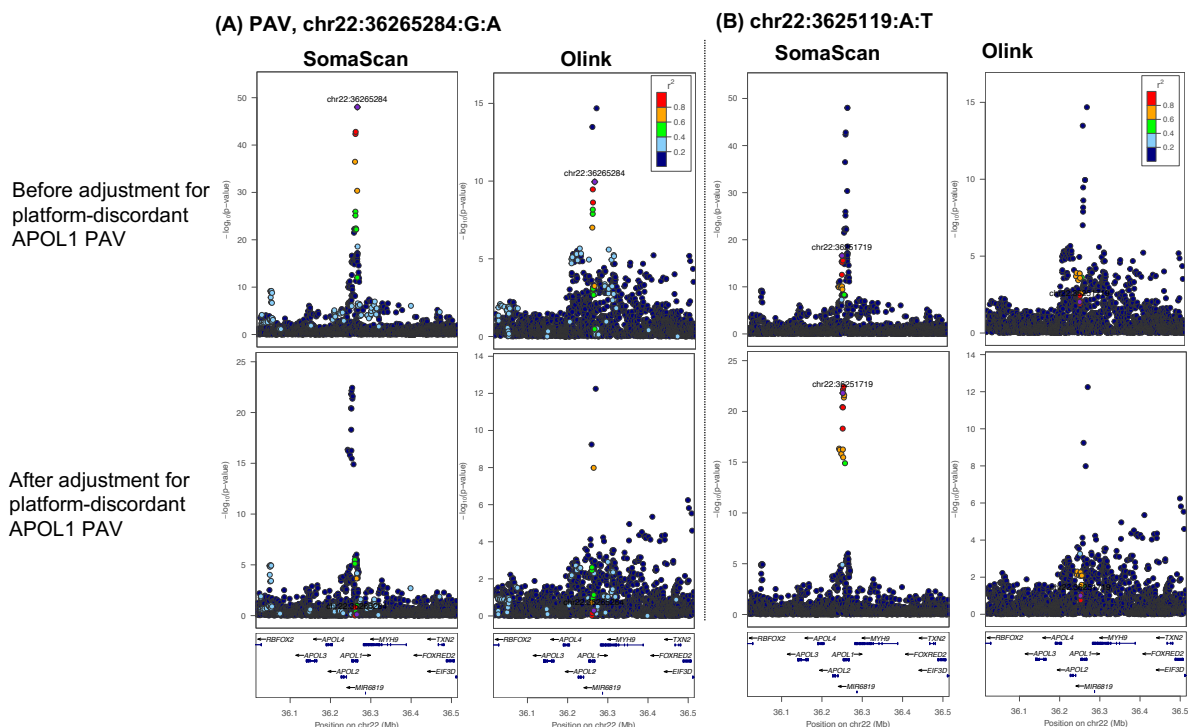
Supplementary Figure 17. Locus Zoom plots displaying the 250KB window around the platform-discordant ACP1 PAV (chr2:277003:A:G) before (top) and after (bottom) adjustment for the platform-discordant PAV on SomaScan vs. Olink. (A) Platform-discordant PAV signal before and after PAV adjustment on SomaScan and Olink, with r^2 values derived in 1,889 MESA study participants. (B, Top) Before adjustment for the PAV, a second, non-coding signal in the region, led by chr2:272051:C:T, is significantly associated with Olink (right), but not SomaScan (left) ACP1 measures. (B, Bottom) Following adjustment for the platform-discordant PAV, this signal becomes significant on SomaScan. The Y-axes differ in scale between plots. Source data is available on Zenodo 10.5281/zenodo.17642644 (<https://zenodo.org/records/17642645>).



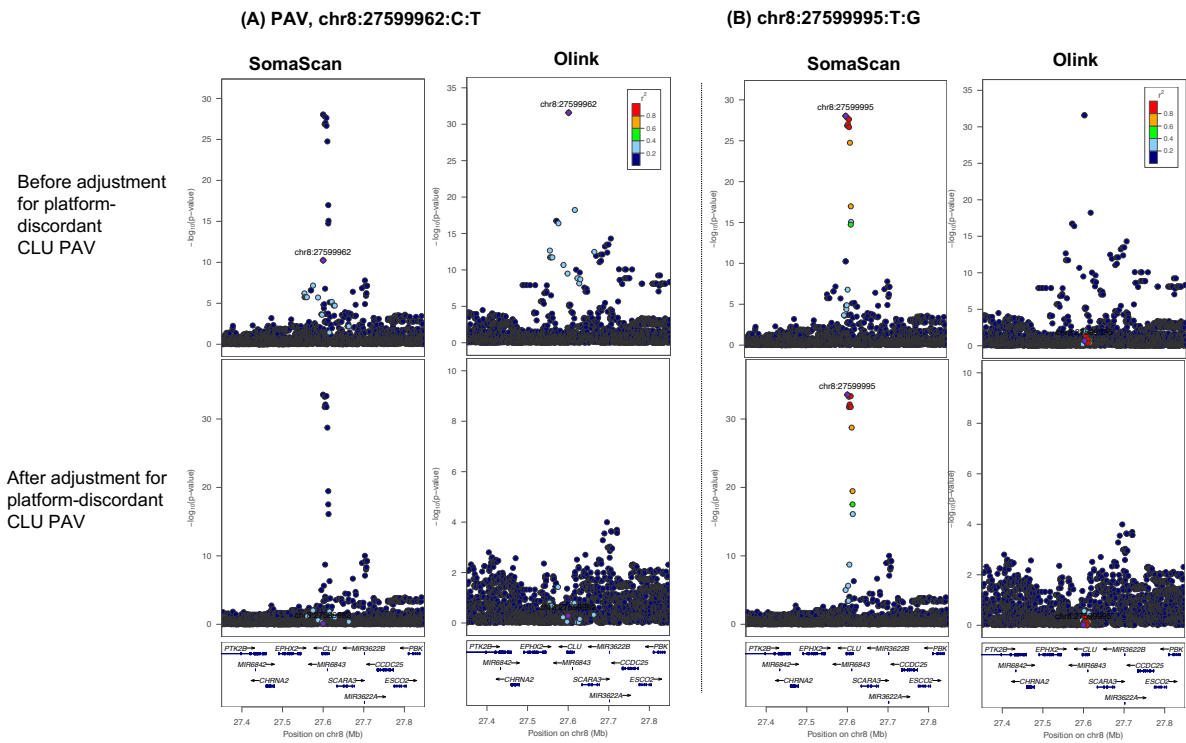
Supplementary Figure 18. Locus Zoom plot displaying the 250KB window around the platform-discordant CPPED1 PAV before (top) and after (bottom) adjustment for the platform-discordant PAV (chr16:12803721:G:T) on SomaScan vs. Olink, with r^2 values derived in 1,889 MESA study participants. (A) Platform-discordant PAV signal before and after PAV adjustment on SomaScan and Olink. (B, Top) Prior to adjustment for the PAV, a second signal in the region, led by a noncoding variant, chr16:12768150:A:C, is significantly associated with Olink (right), but not SomaScan (left) CPPED1 measures. (B, Bottom) Following adjustment for the platform-discordant PAV, this signal becomes significant on SomaScan. The Y-axes differ in scale between plots. Source data is available on Zenodo 10.5281/zenodo.17642644 (<https://zenodo.org/records/17642645>).



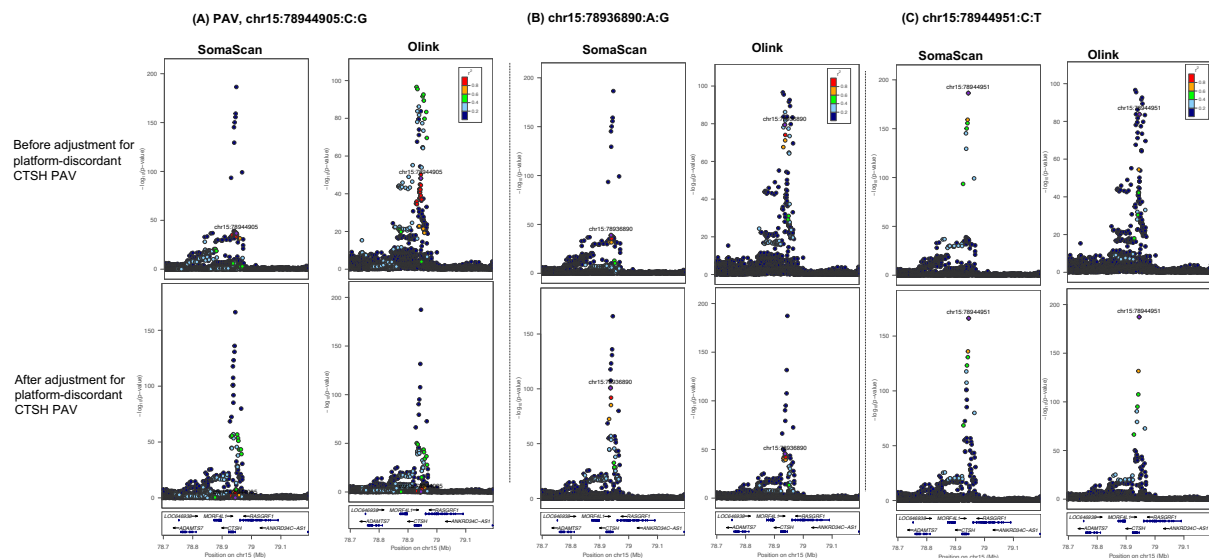
Supplementary Figure 19. Locus Zoom plots displaying the 250KB window around the platform-discordant APOE PAV before (top) and after (bottom) adjustment for the platform-discordant PAV (chr19:44908822:C:T) on SomaScan vs. Olink, with r^2 values derived in 1,889 MESA study participants. (A) Platform-discordant PAV signal before and after PAV adjustment on SomaScan and Olink. (B) A second signal, driven by noncoding variant chr19:44935906:C:G, is significantly associated with both platforms' APOE measures before adjustment for the platform-discordant PAV. (B, Bottom) Following adjustment for the platform-discordant PAV, this signal increases in significance on SomaScan. The Y-axes differ in scale between plots. Source data is available on Zenodo 10.5281/zenodo.17642644 (<https://zenodo.org/records/17642645>).



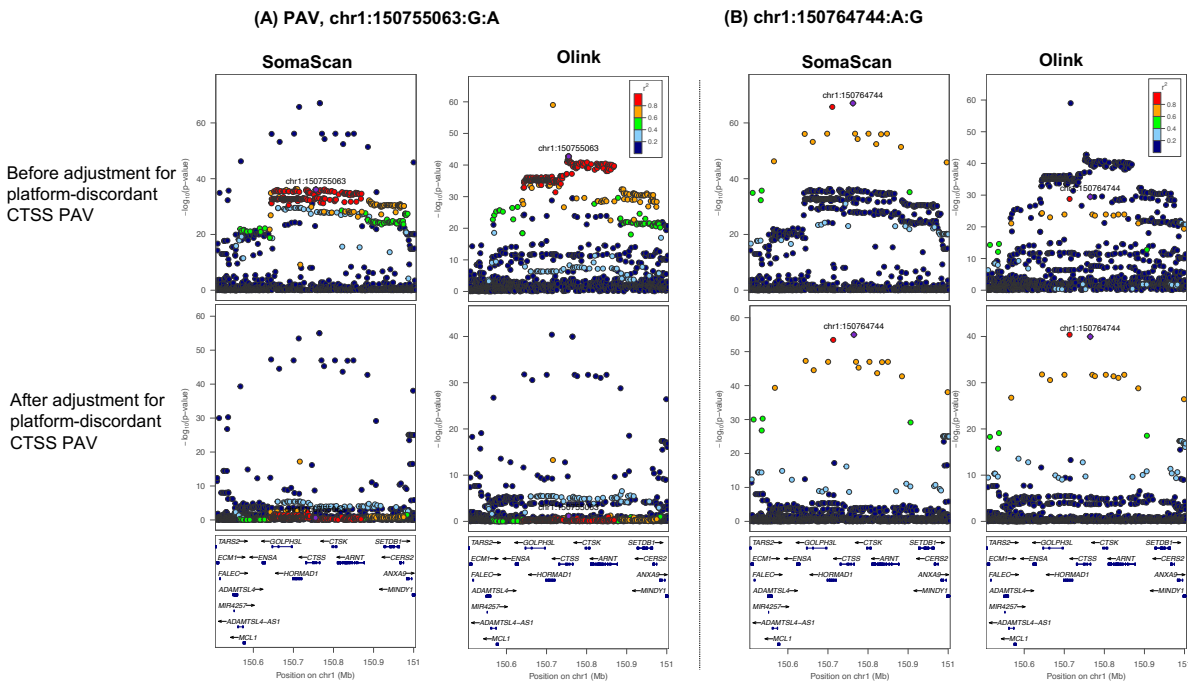
Supplementary Figure 20. Locus Zoom plot displaying the 250KB window around the platform-discordant APOL1 PAV before (top) and after (bottom) adjustment for the platform-discordant PAV (chr22:36265284:G:A) on SomaScan vs. Olink, with r^2 values derived in 1,889 MESA study participants. (A) Platform-discordant PAV signal before and after PAV adjustment on SomaScan and Olink. (B, Top) Prior to adjustment for the PAV, a second, non-coding signal in the region, led by chr22:3625119:A:T, is significantly associated with SomaScan and Olink APOL1 measures. (B, Bottom) Following adjustment for the platform-discordant PAV, this signal becomes more significant on SomaScan. The Y-axes differ in scale between plots. Source data is available on Zenodo 10.5281/zenodo.17642644 (<https://zenodo.org/records/17642645>).



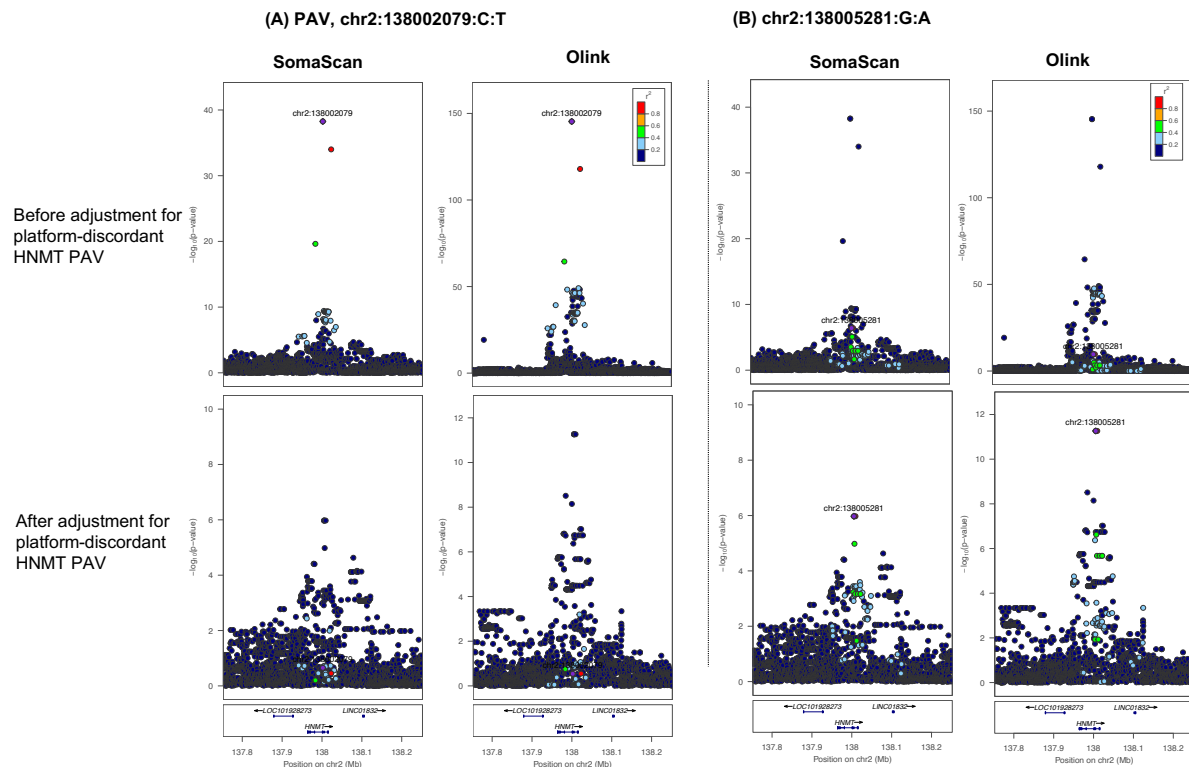
Supplementary Figure 21. Locus Zoom plot displaying the 250KB window around the platform-discordant CLU PAV before (top) and after (bottom) adjustment for the platform-discordant PAV (chr8:27599962:C:T) on SomaScan vs. Olink, with r^2 values derived in 1,889 MESA study participants. (A) Platform-discordant PAV signal before and after PAV adjustment on SomaScan and Olink. (B) Following adjustment for the platform-discordant PAV, an alternate *cis*-pQTL association, associated with SomaScan CLU measures and led by an independent PAV (chr8:27599995:T:G), increases in significance on SomaScan. The Y-axes differ in scale between plots. Source data is available on Zenodo 10.5281/zenodo.17642644 (<https://zenodo.org/records/17642645>).



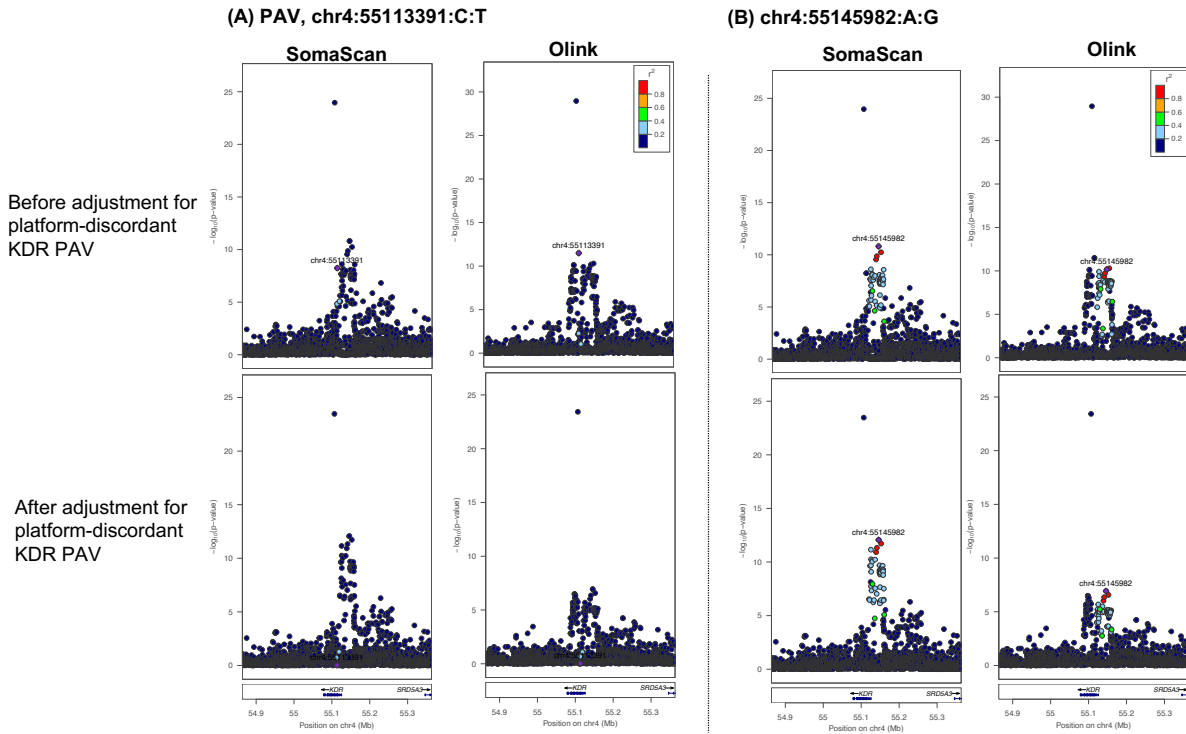
Supplementary Figure 22. Locus Zoom plot displaying the 250KB window around the platform-discordant CTSH PAV before (top) and after (bottom) adjustment for the platform-discordant PAV (chr15:78944905:C:G) on SomaScan vs. Olink. (A) Platform-discordant PAV signal before and after PAV adjustment on SomaScan and Olink, with r^2 values derived in 1,889 MESA study participants. (B) Following adjustment for the platform-discordant PAV, an alternate *cis*-pQTL association, led by an independent, platform-concordant PAV (chr15:78936890:A:G), positively associated with each platform's measures, increases in significance on SomaScan, but not Olink. (C) Following adjustment for the platform-discordant PAV, a second alternate *cis*-pQTL association, led by another, platform-concordant PAV (chr15:78944951:C:T) negatively associated with each platform's CTSH measures, increases in significance on Olink, but not SomaScan. The Y-axes differ in scale between plots. Source data is available on Zenodo 10.5281/zenodo.17642644 (<https://zenodo.org/records/17642645>).



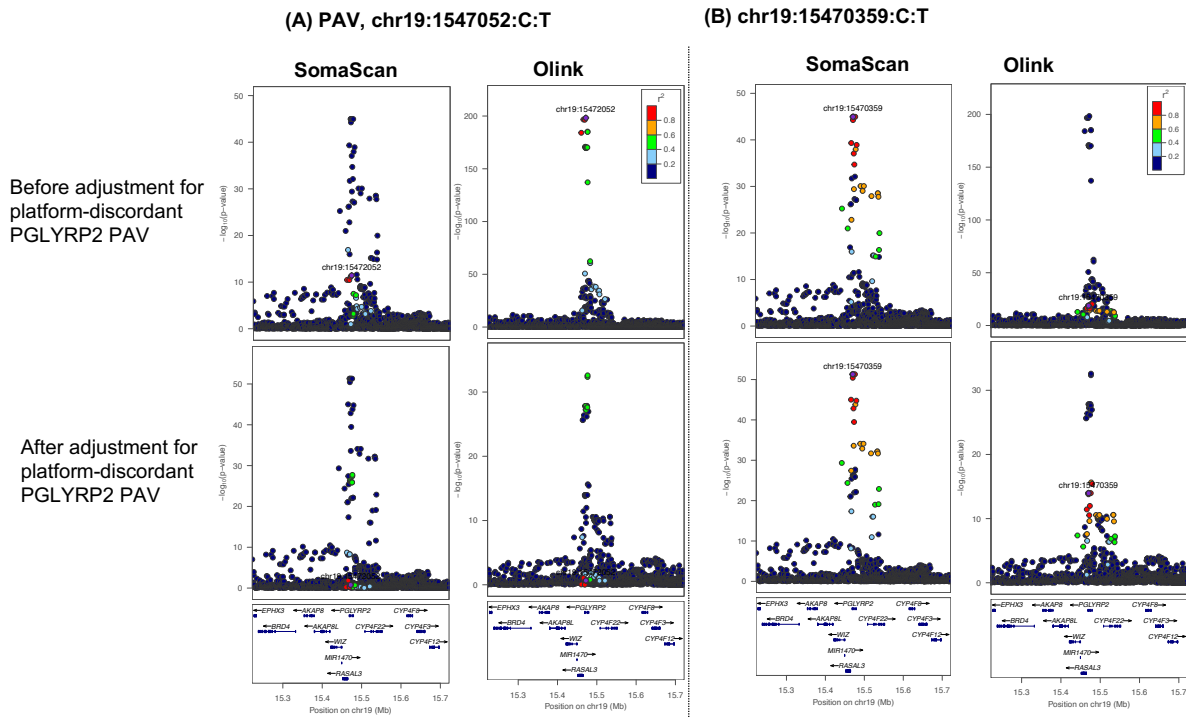
Supplementary Figure 23. Locus Zoom plot displaying the 250KB window around the platform-discordant CTSS PAV before (top) and after (bottom) adjustment for the platform-discordant PAV (chr1:150755063:G:A) on SomaScan vs. Olink, with r^2 values derived in 1,889 MESA study participants. (A) Platform-discordant PAV signal before and after PAV adjustment on SomaScan and Olink. (B) Following adjustment for the platform-discordant PAV, an alternate *cis*-pQTL association, led by an independent, platform-concordant PAV (chr1:150764744:A:G) that is negatively associated with both platform's CTSS measures, increases in significance on Olink, but not SomaScan. The Y-axes differ in scale between plots. Source data is available on Zenodo 10.5281/zenodo.17642644 (<https://zenodo.org/records/17642645>).



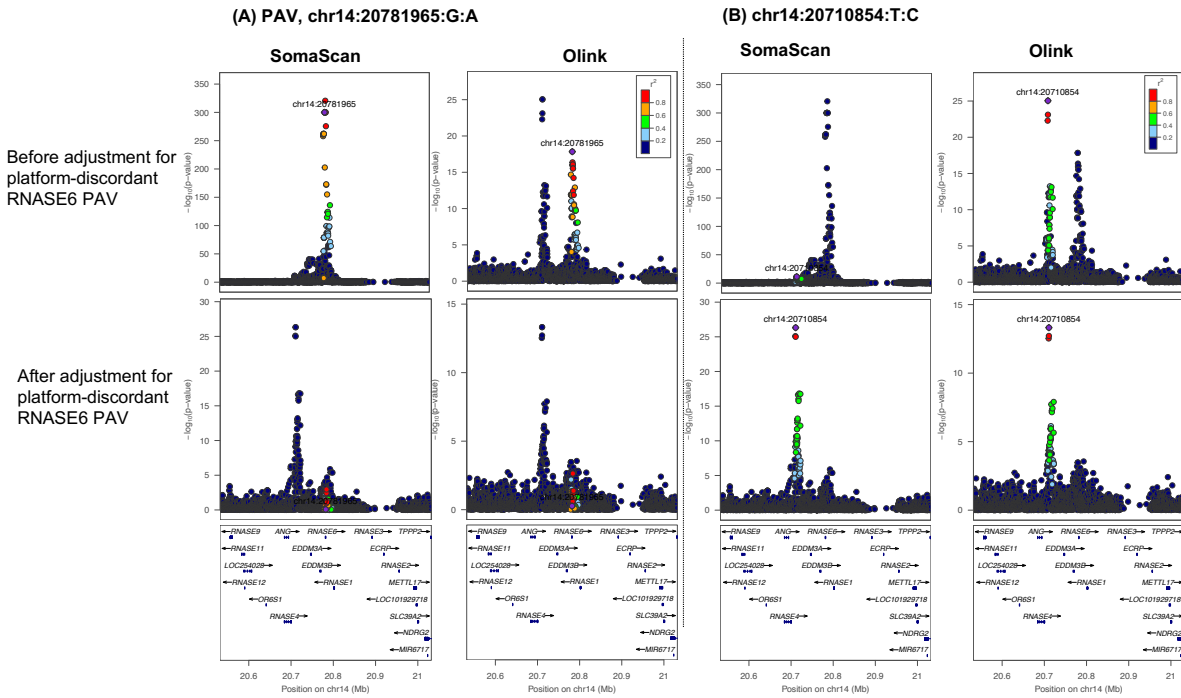
Supplementary Figure 24. Locus Zoom plot displaying the 250KB window around the platform-discordant HNMT PAV before (top) and after (bottom) adjustment for the platform-discordant PAV (chr2:138002079:C:T) on SomaScan vs. Olink, with r^2 values derived in 1,889 MESA study participants. (A) Platform-discordant PAV signal before and after PAV adjustment on SomaScan and Olink. (B) Following adjustment for the platform-discordant PAV, an alternate *cis*-pQTL association, led by a non-coding variant (chr2:138005281:G:A) that is significantly associated with Olink's HNMT measures, increases in significance on Olink, but not SomaScan. The Y-axes differ in scale between plots. Source data is available on Zenodo 10.5281/zenodo.17642644 (<https://zenodo.org/records/17642645>).



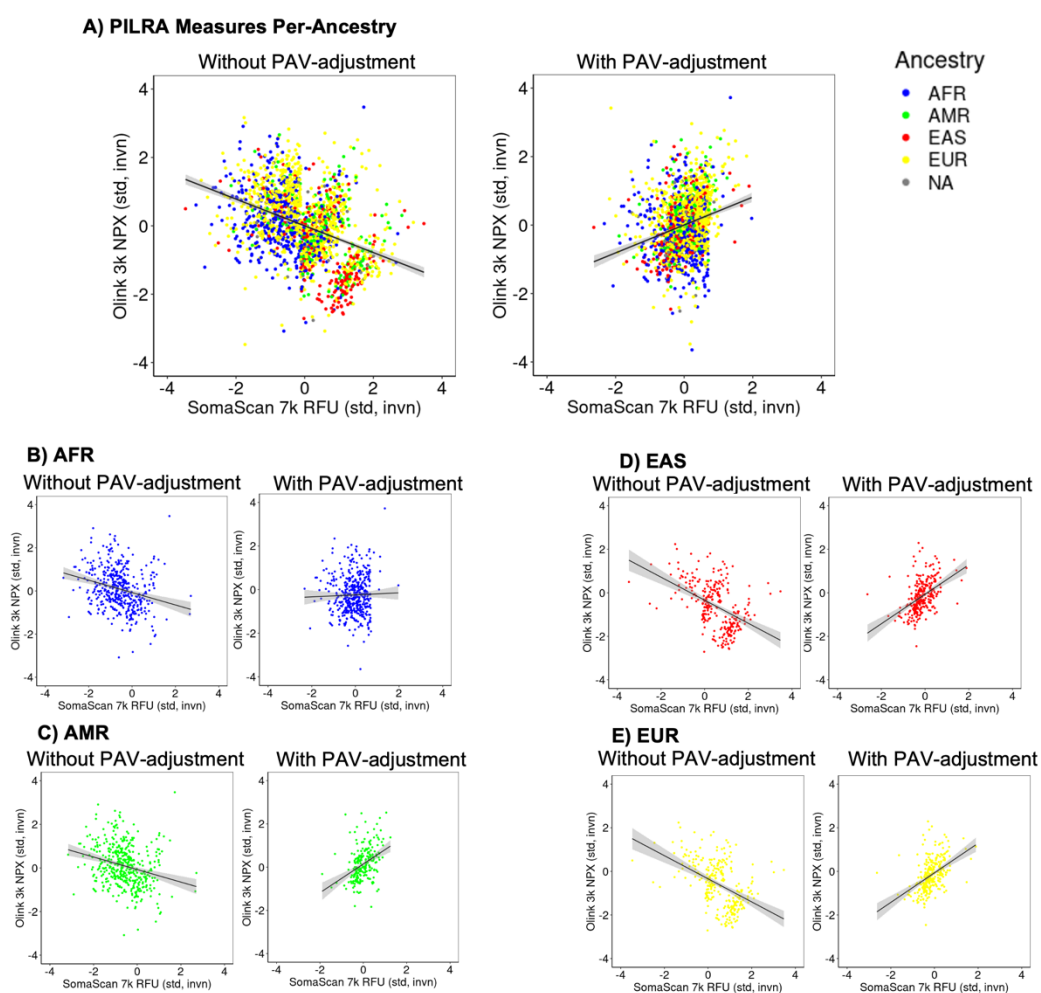
Supplementary Figure 25. Locus Zoom plot displaying the 250KB window around the platform-discordant KDR PAV before (top) and after (bottom) adjustment for the platform-discordant PAV (chr4:55113391:C:T) on SomaScan vs. Olink, with r^2 values derived in 1,889 MESA study participants. (A) Platform-discordant PAV signal before and after PAV adjustment on SomaScan and Olink. (B) Following adjustment for the platform-discordant PAV, an alternate *cis*-pQTL association, led by an alternate, non-coding variant (chr4:55145982:A:G), increases in significance on SomaScan, but not Olink. The Y-axes differ in scale between plots. Source data is available on Zenodo 10.5281/zenodo.17642644 (<https://zenodo.org/records/17642645>).



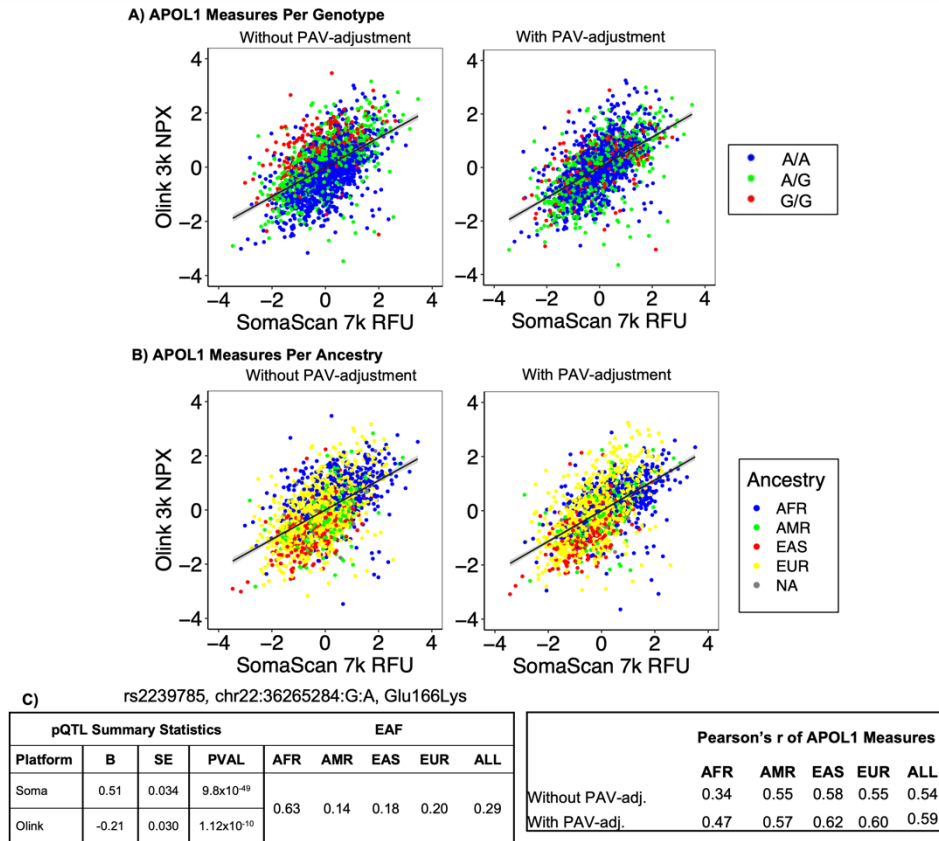
Supplementary Figure 26. Locus Zoom plot displaying the 250KB window around the platform-discordant PGLYRP2 PAV before (top) and after (bottom) adjustment for the platform-discordant PAV (chr19:1547052:C:T) on SomaScan vs. Olink, with r^2 values derived in 1,889 MESA study participants. (A) Platform-discordant PAV signal before and after PAV adjustment on SomaScan and Olink. (B) Before PAV adjustment, an alternate signal, led by noncoding variant chr19:15470359:C:T, is significantly associated with both platforms' measures of PGLYRP2 pre-PAV adjustment. This association becomes more significant on SomaScan post-PAV adjustment. The Y-axes differ in scale between plots. Source data is available on Zenodo 10.5281/zenodo.17642644 (<https://zenodo.org/records/17642645>).



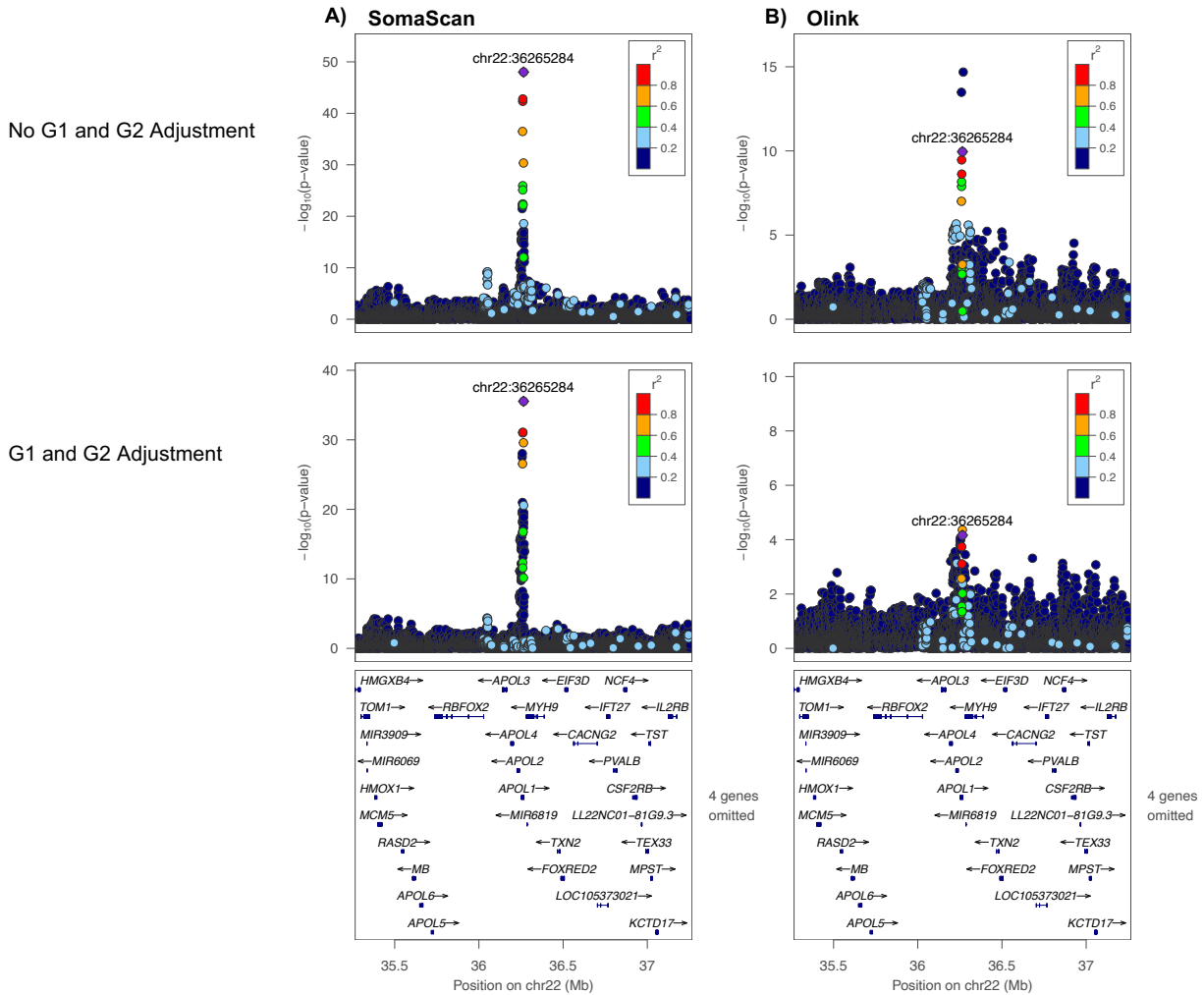
Supplementary Figure 27. Locus Zoom plot displaying the 250KB window around the platform-discordant RNASE6 PAV before (top) and after (bottom) adjustment for the platform-discordant PAV (chr14:20781965:G:A) on SomaScan vs. Olink, with r^2 values derived in 1,889 MESA study participants. (A) Platform-discordant PAV signal before and after PAV adjustment on SomaScan and Olink. (B) A second signal in the region, led by noncoding variant, chr14:20710854:T:C, is significantly associated with both platforms' RNASE6 measures pre-PAV adjustment. This association increases in significance on SomaScan following PAV adjustment. The Y-axes differ in scale between plots. Source data is available on Zenodo 10.5281/zenodo.17642644 (<https://zenodo.org/records/17642645>).



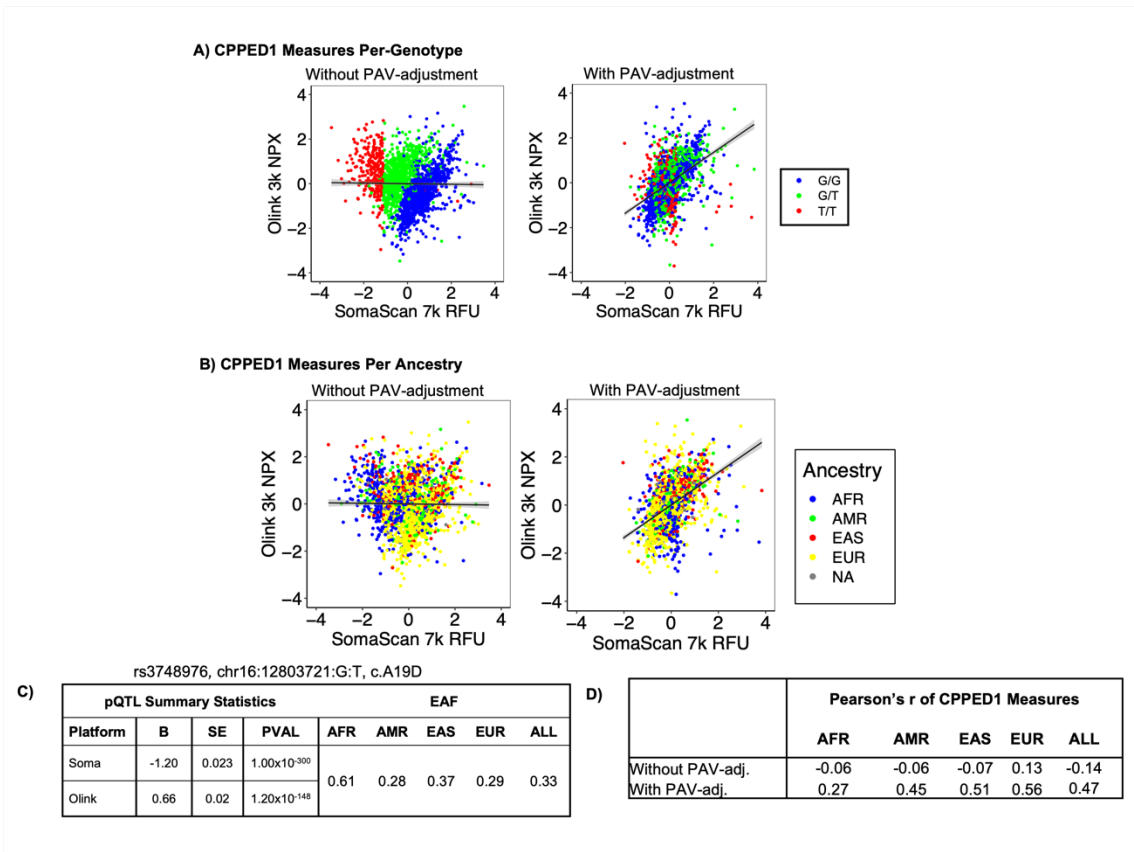
Supplementary Figure 28. PILRA correlation measures by ancestry in 1,889 MESA participants, without and with adjustment for platform-differentiated, ancestry-differentiated PAV (chr7:100374211:A:G). (A) SomaScan and Olink PILRA measures without (left) and with (right) PAV adjustment, with points colored by an individual's ancestry cluster. (B-E) SomaScan and Olink measures from individual ancestry reference groups, with lines of best fit with 95% confidence intervals depicted in gray. Correlation improves to the greatest extent among individuals clustering with EAS ancestry references (shown in plot D). 433 African ancestry (AFR), 220 Admixed American (AMR), 267 East Asian (EAS), and 932 European (EUR) participants. Source data is individual data not available publicly, available through dbGap (<https://dbgap.ncbi.nlm.nih.gov/home>).



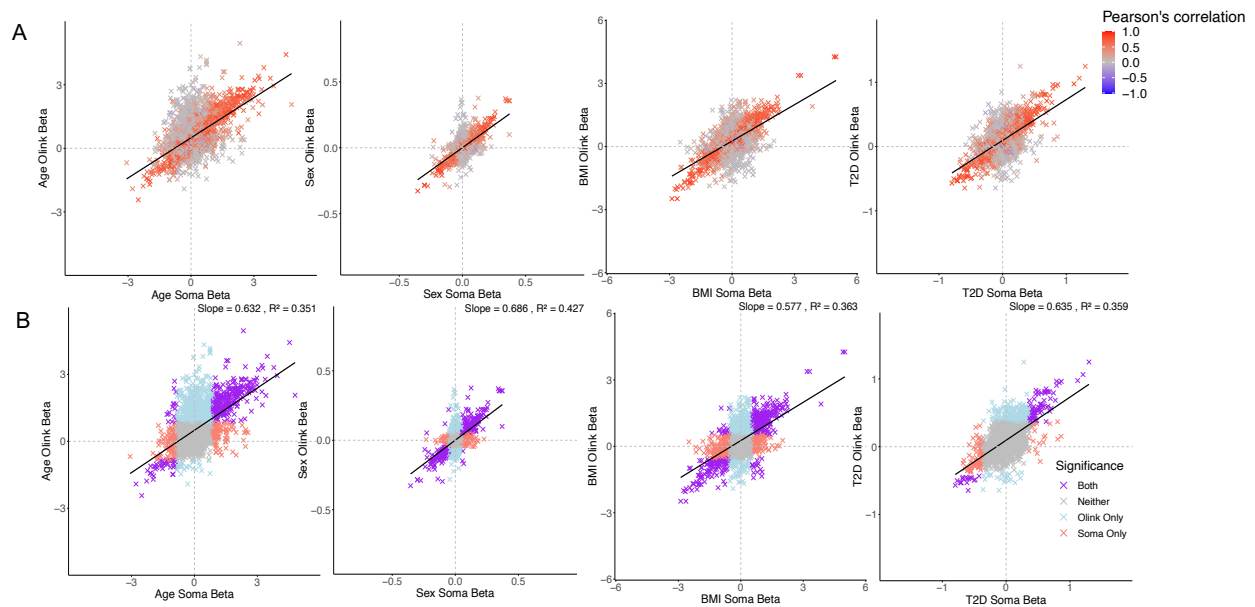
Supplementary Figure 29. APOL1 measures without (left) and with (right) adjustment for platform-discriminant, ancestry differentiated PAV (chr22:36265284:G:A), with points colored (A) by genotype and (B) by ancestry. Shaded bands indicate the 95% confidence interval for the linear regression fit. (C) Ancestry-differentiated PAV summary statistics and effect allele frequencies per-ancestry. The effect allele is significantly more frequent in AFR participants. (D) Pearson's correlation of APOL1 measures per ancestry pre- and post- ancestry differentiated PAV adjustment, with the ancestry group for which highest improvement in inter-platform correlation was observed highlighted in red. 433 African ancestry (AFR), 220 Admixed American (AMR), 267 East Asian (EAS), and 932 European (EUR) participants. Source data is individual data not available publicly, available through dbGap (<https://dbgap.ncbi.nlm.nih.gov/home>).



Supplementary Figure 30. Locus Zoom plot displaying the 1MB window around the platform-discordant APOL1 PAV, chr22:36265284:G:A, with r^2 values derived in 1,889 MESA study participants, before (top plots) and after (bottom plots) adjustment for APOL1 kidney function chronic kidney disease risk variants G1 (rs73885219, chr:36269595:AATAATT:A) and G2 (rs71785313, chr22:36265860:A:G). Platform-discordant PAV signal in APOL1 is attenuated below the significance threshold (5×10^{-8}) post-adjustment for the known APOL1 G1 and G2 risk factors, but is still present. The Y axes differ in scale between plots. Source data is available on Zenodo 10.5281/zenodo.17642644 (<https://zenodo.org/records/17642645>).

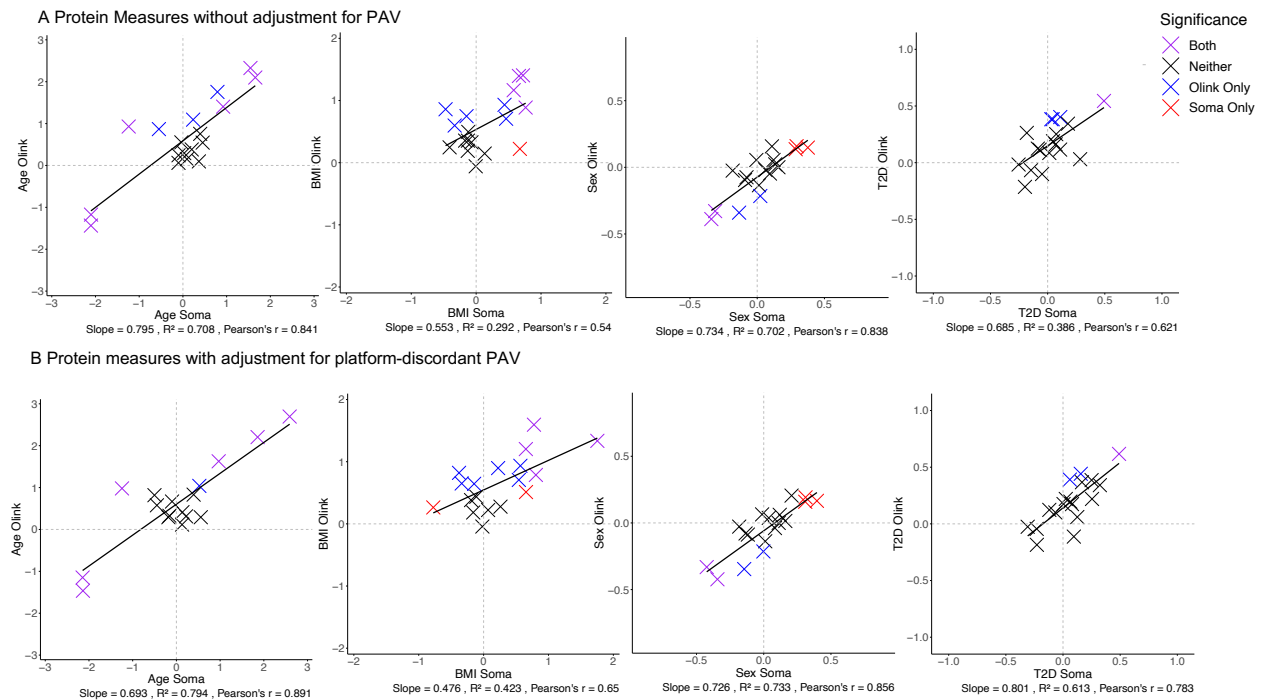


Supplementary Figure 31. CPPED1 measures without (left) and with (right) adjustment for ancestry-differentiated, platform-discordant PAV (chr16:12803721:G:T) in 1,889 MESA participants, with points colored (A) by genotype and (B) by ancestry. Shaded bands indicate the 95% confidence interval for the linear regression fit. (C) Ancestry-differentiated PAV summary statistics and allele frequencies per-ancestry. (D) Pearson's correlation of CPPED1 measures per ancestry pre- and post- ancestry differentiated PAV adjustment. 433 African ancestry (AFR), 220 Admixed American (AMR), 267 East Asian (EAS), and 932 European (EUR) participants. Source data is individual data not available publicly, available through dbGap (<https://dbgap.ncbi.nlm.nih.gov/home>) (A,B). Source data is available in Supplementary Data Tables 4 and 5 (C), and 6 (D).

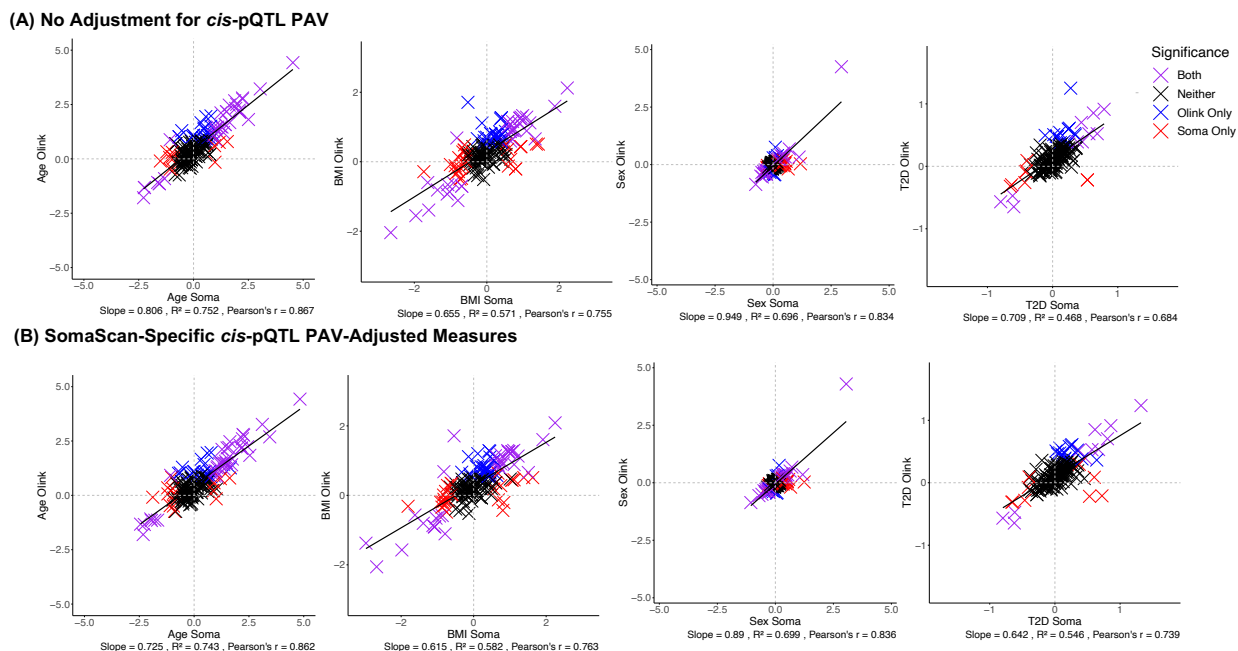


Supplementary Figure 32. Effect size comparison of SomaScan and Olink

phenotype~protein associations, for age, sex, body mass index (BMI), and type 2 diabetes (T2D) in 1,889 MESA participants colored by (A) inter-platform correlation and (B) significance. Associations were significant at $\alpha=0.05$ with correction for 2,708 probe pairs tested ($p<1.8\times10^{-5}$), on both platforms (purple), SomaScan only (red), Olink only (blue), or neither platform. Source data is available in Supplementary Data Table 18.

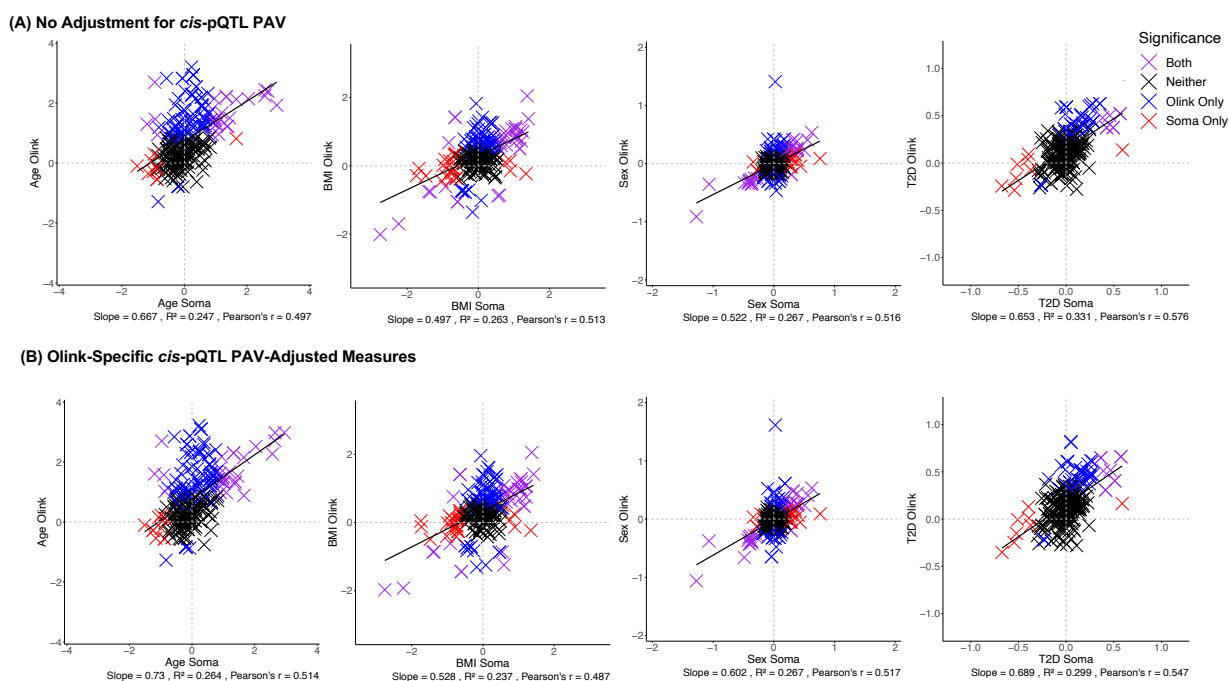


Supplementary Figure 33. Effect-sizes from phenotypic regressions of protein abundance with age, sex, body mass index (BMI), and type 2 diabetes (T2D) in 1,889 MESA participants for the 18 proteins with a platform-discordant PAV association in the full analysis of all probe pairs per overlapping protein target (A) Without PAV adjustment and (B) with PAV adjustment with points colored according to significance of protein-phenotype association on both platforms (purple), SomaScan only (red), Olink only (blue), or neither platform. Associations were significant at $\alpha=0.05$ with correction for 2,708 probe pairs tested ($p < 1.8 \times 10^{-5}$). Source data is available in Supplementary Data Table 6.

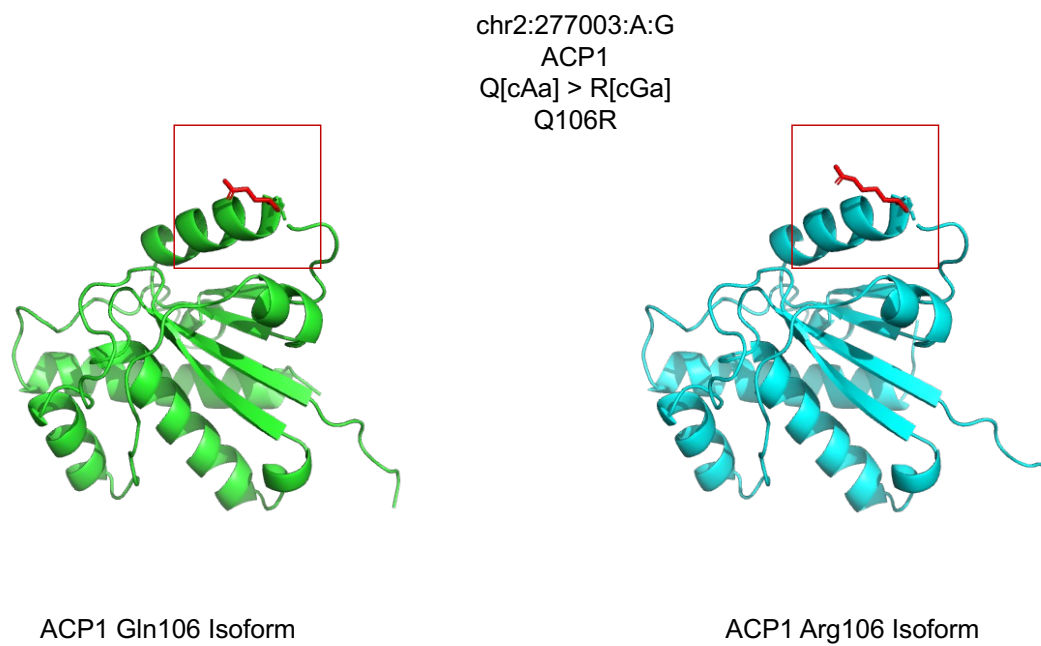


Supplementary Figure 34. Comparison of SomaScan and Olink effect sizes from phenotypic regressions of protein measures with age, sex, BMI, and T2D, without and with adjustment for SomaScan “specific” PAVs in 1,889 MESA participants. Only proteins with a significant PAV-driven *cis*-pQTL on SomaScan are displayed in the plot.

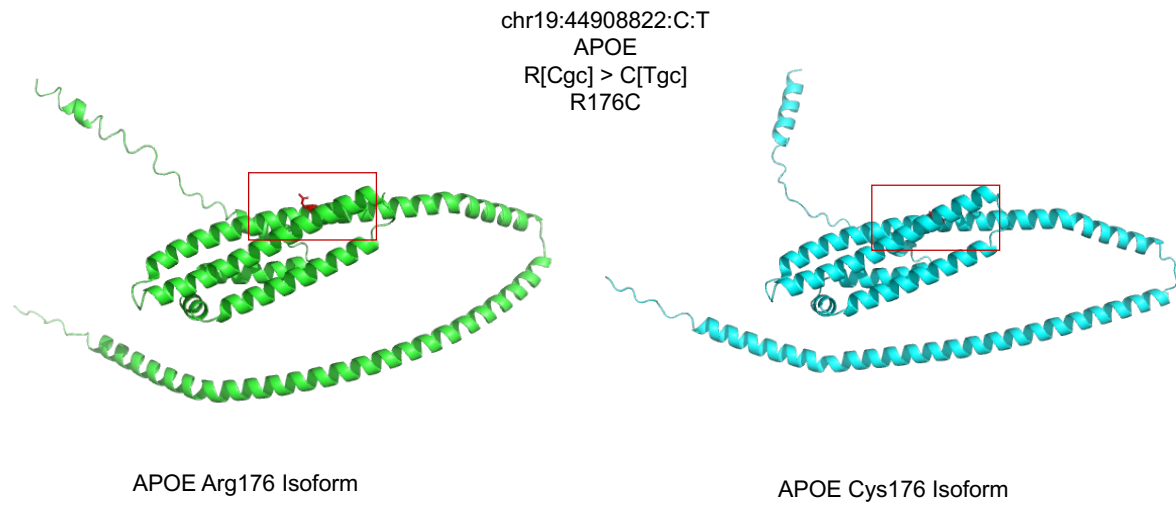
(A) Effect sizes obtained from regression of protein measures without adjustment for SomaScan-specific PAVs (B) Effect sizes obtained from regression of SomaScan-“specific” PAV-adjusted protein measures with each phenotype. In both plots, points are colored according to Bonferroni significance ($p < 1.8 \times 10^{-5}$, $\alpha = 0.05$ with correction for 2,708 probe pairs tested) of protein-phenotype association on both platforms (purple), SomaScan only (red), Olink only (blue), or neither platform. Source data is available in Supplementary Data Table 24.



Supplementary Figure 35. Comparison of SomaScan and Olink effect sizes from phenotypic regressions of protein measures with age, sex, body mass index (BMI), and type 2 diabetes (T2D), without and with adjustment for Olink “specific” PAVs in 1,889 MESA participants. Only proteins with a significant PAV-driven *cis*-pQTL association on Olink are displayed in the plot. (A) Effect sizes obtained from regression of protein measures without adjustment for Olink-specific PAVs (B) Effect sizes obtained from regression of Olink-“specific” PAV-adjusted protein measures with each phenotype. In both plots, points are colored according to Bonferroni significance ($p < 1.8 \times 10^{-5}$, $\alpha = 0.05$ with correction for 2,708 probe pairs tested) of protein-phenotype association on both platforms (purple), SomaScan only (red), Olink only (blue), or neither platform. Source data is available in Supplementary Data Table 25.

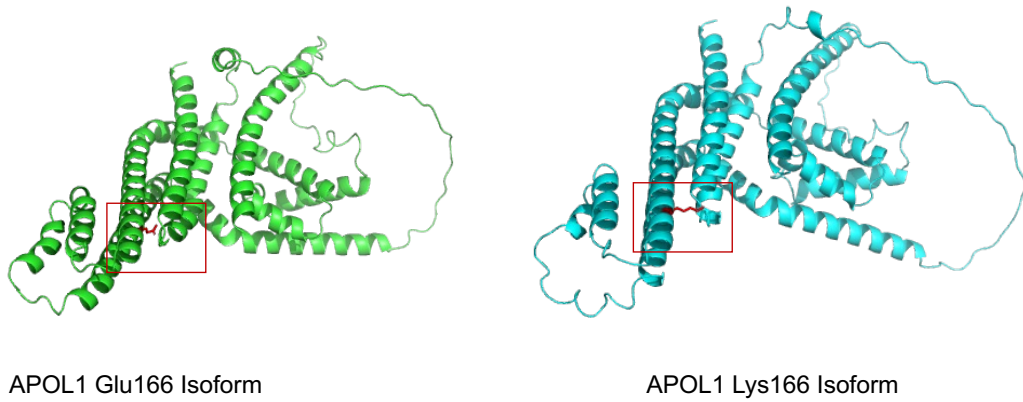


Supplementary Figure 36. Visual representation of predicted consequences of ACP1 platform-discordant PAV. Protein amino acid sequences were obtained from UniProt (<https://www.uniprot.org/>) and modeled in AlphaFold (<https://alphafoldserver.com/>).

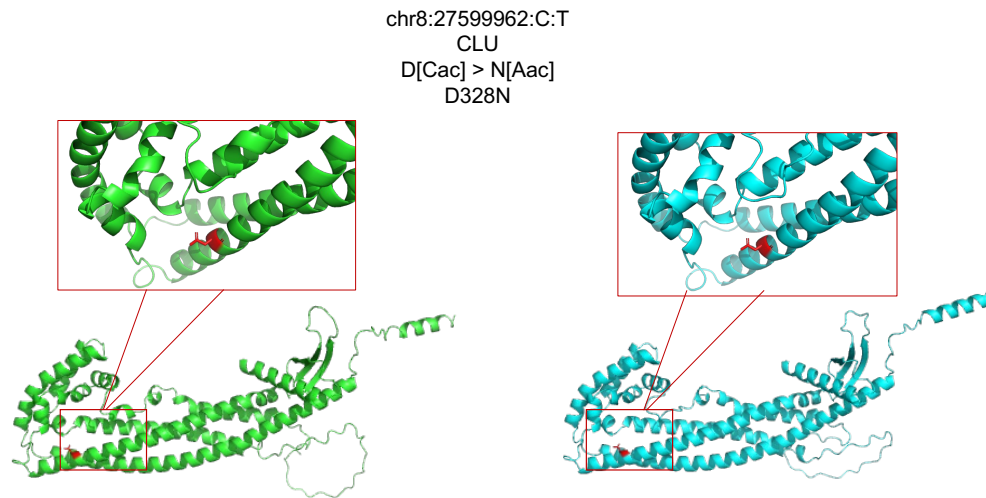


Supplementary Figure 37. Visual representation of predicted consequences of APOE platform-discordant PAV. Protein amino acid sequences were obtained from UniProt (<https://www.uniprot.org/>) and modeled in AlphaFold (<https://alphafoldserver.com/>).

chr22:36265284:G:A
APOL1
E[Gag] > K[Aag]
E166K

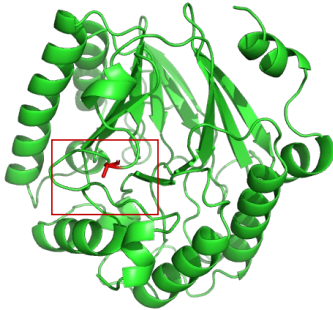


Supplementary Figure 38. Visual representation of predicted consequences of APOL1 platform-discordant PAV. Protein amino acid sequences were obtained from UniProt (<https://www.uniprot.org/>) and modeled in AlphaFold (<https://alphafoldserver.com/>).

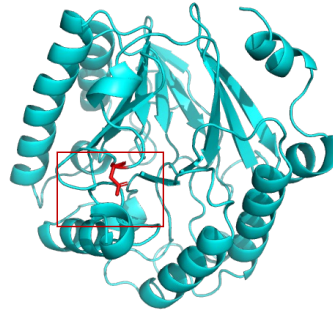


Supplementary Figure 39. Visual representation of predicted consequences of CLU platform-discordant PAV. Protein amino acid sequences were obtained from UniProt (<https://www.uniprot.org/>) and modeled in AlphaFold (<https://alphafoldserver.com/>).

chr16:12803721:G:T
CPPED1
A[gGc] > D[gTc]
A19V



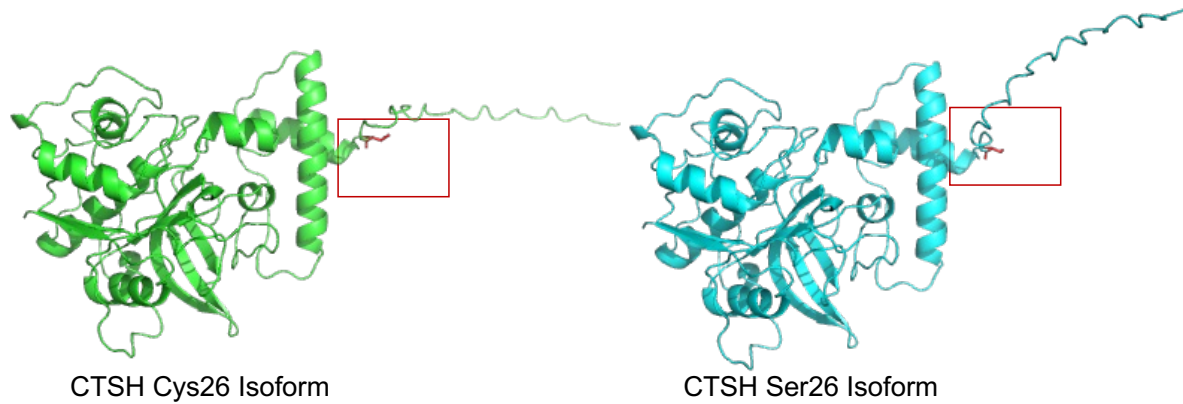
CPPED1 Ala19 Isoform



CPPED1 Asp19 Isoform

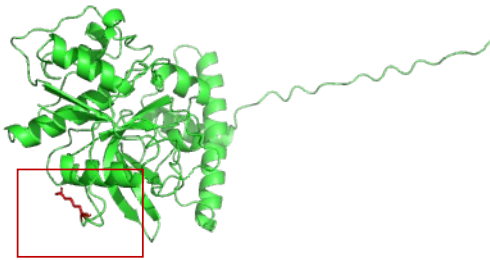
Supplementary Figure 40. Visual representation of predicted consequences of CPPED1 platform-discordant PAV. Protein amino acid sequences were obtained from UniProt (<https://www.uniprot.org/>) and modeled in AlphaFold (<https://alphafoldserver.com/>).

chr15:78944905:C:G
CTSH
C[tCc] > S[tGc]
C26S

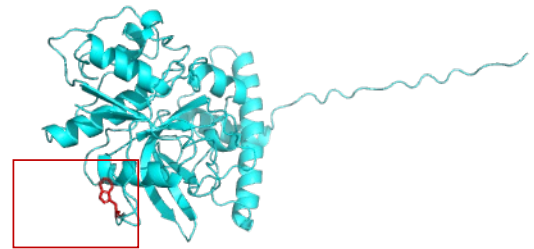


Supplementary Figure 41. Visual representation of predicted consequences of CTSH platform-discordant PAV. Protein amino acid sequences were obtained from UniProt (<https://www.uniprot.org/>) and modeled in AlphaFold (<https://alphafoldserver.com/>).

chr1:150755063:G:A
CTSS
R[Ggg] > W[Agg]
R113W

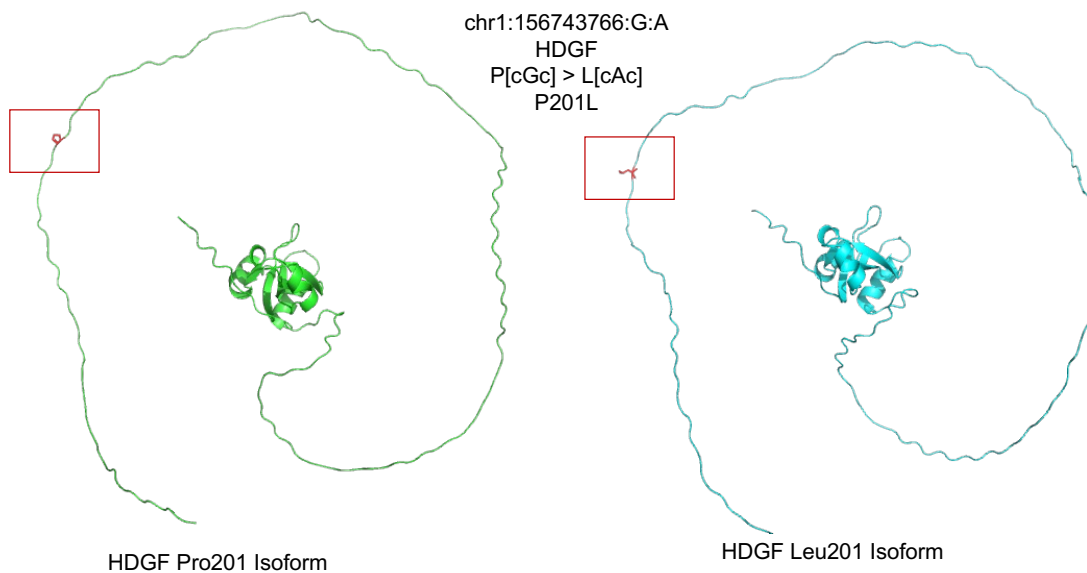


CTSS Arg113 Isoform



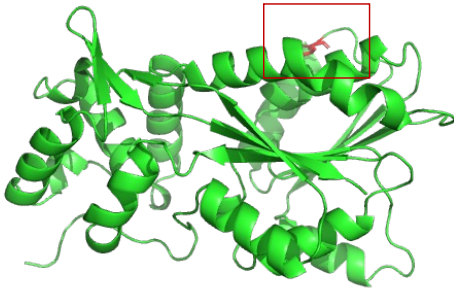
CTSS Trp113 Isoform

Supplementary Figure 42. Visual representation of predicted consequences of CTSS platform-discordant PAV. Protein amino acid sequences were obtained from UniProt (<https://www.uniprot.org/>) and modeled in AlphaFold (<https://alphafoldserver.com/>).

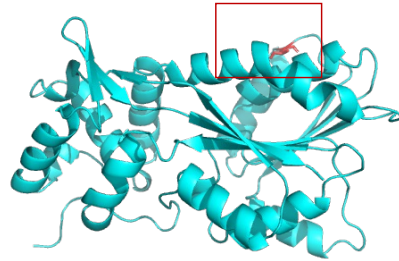


Supplementary Figure 43. Visual representation of predicted consequences of HDGF platform-discordant PAV. Protein amino acid sequences were obtained from UniProt (<https://www.uniprot.org/>) and modeled in AlphaFold (<https://alphafoldserver.com/>).

chr2:138002079:C:T
HNMT
T[aCa] > I[aTa]
T105I

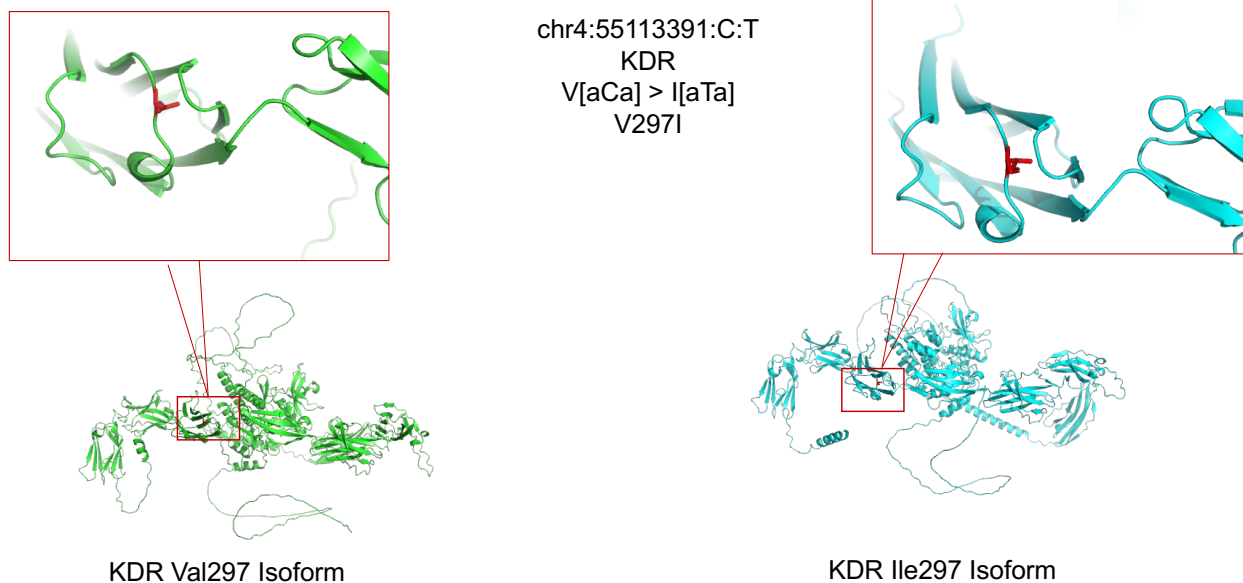


HNMT Thr105 Isoform



HNMT Ile105 Isoform

Supplementary Figure 44. Visual representation of predicted consequences of HNMT platform-discordant PAV. Protein amino acid sequences were obtained from UniProt (<https://www.uniprot.org/>) and modeled in AlphaFold (<https://alphafoldserver.com/>).

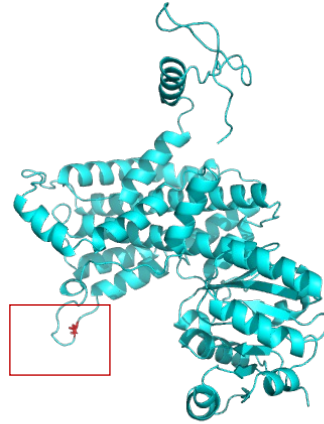


Supplementary Figure 45. Visual representation of predicted consequences of KDR platform-discordant PAV. Protein amino acid sequences were obtained from UniProt (<https://www.uniprot.org/>) and modeled in AlphaFold (<https://alphafoldserver.com/>).

chr1:10413143:G:A
PGD
D[Gat] > N[Aat]
D246N

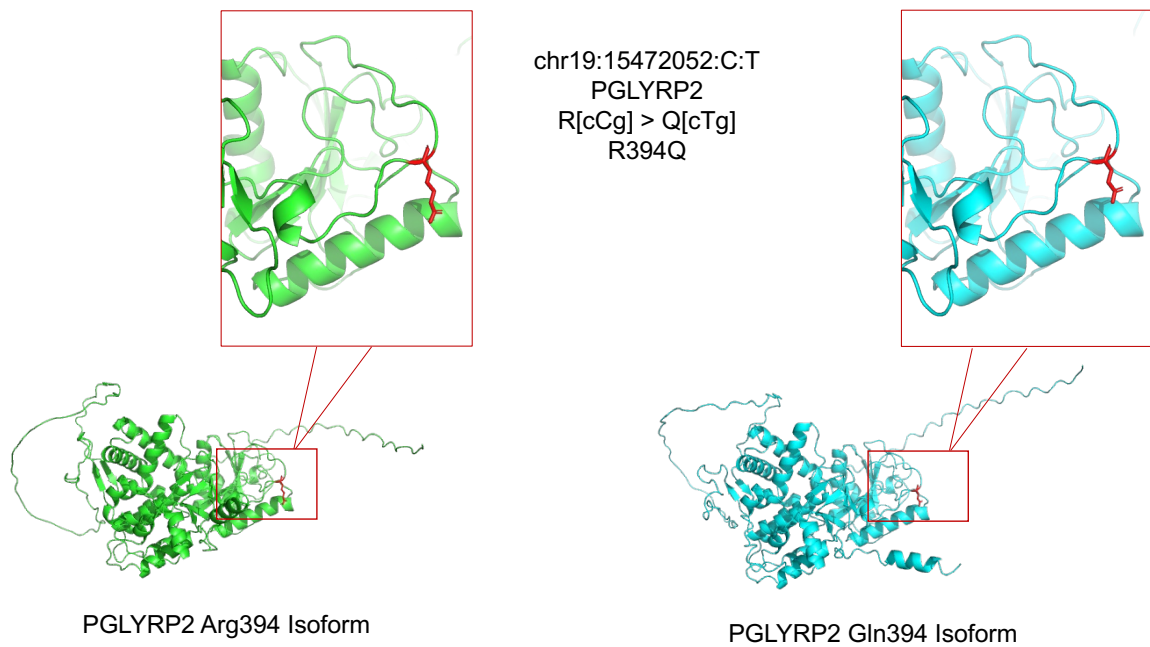


PGD Asp246 Isoform

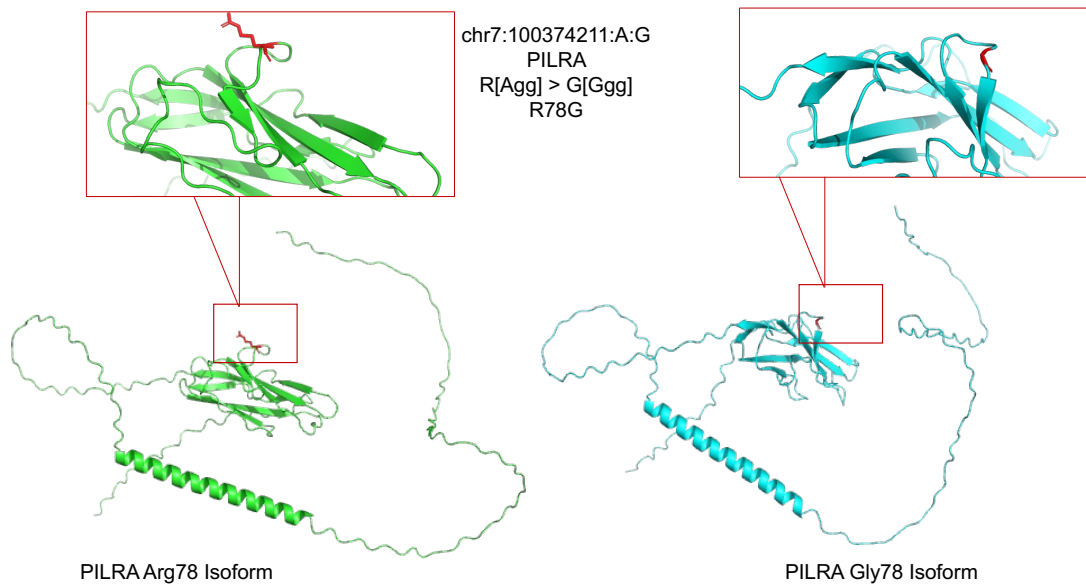


PGD Gln246 Isoform

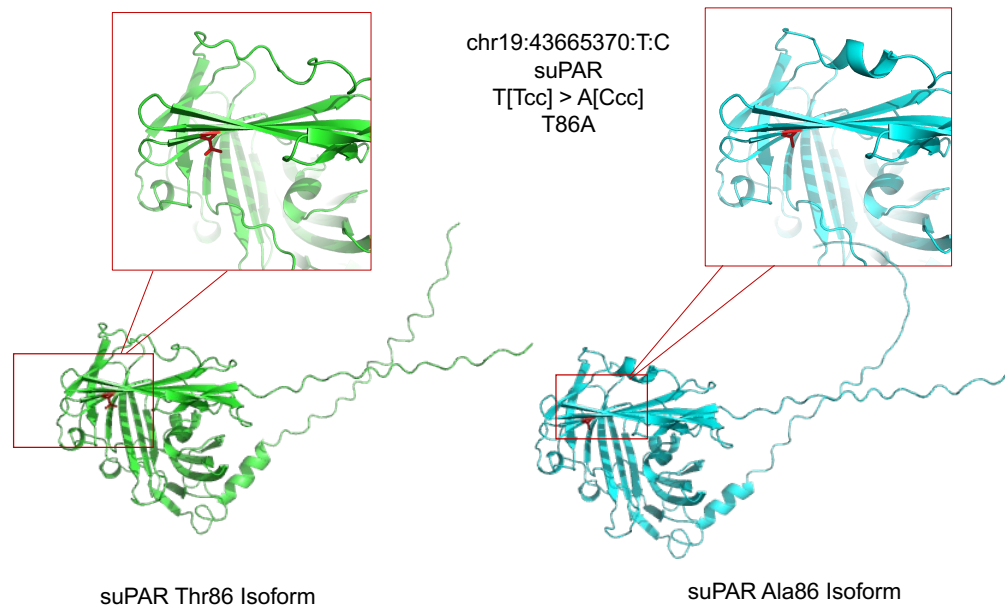
Supplementary Figure 46. Visual representation of predicted consequences of PGD platform-discordant PAV. Protein amino acid sequences were obtained from UniProt (<https://www.uniprot.org/>) and modeled in AlphaFold (<https://alphafoldserver.com/>).



Supplementary Figure 47. Visual representation of predicted consequences of PGLYRP2 platform-discordant PAV. Protein amino acid sequences were obtained from UniProt (<https://www.uniprot.org/>) and modeled in AlphaFold (<https://alphafoldserver.com/>).

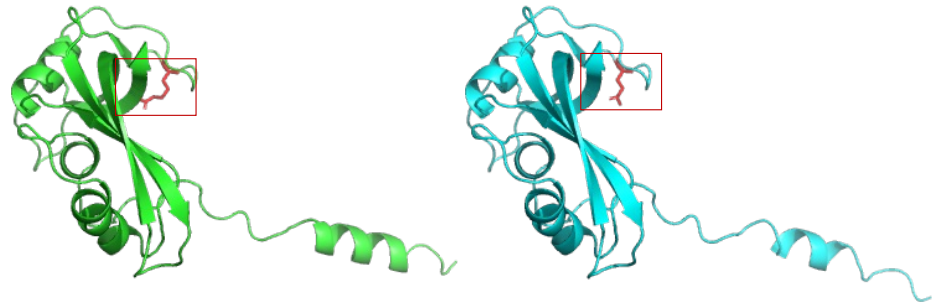


Supplementary Figure 48. Visual representation of predicted consequences of PILRA platform-discordant PAV. Protein amino acid sequences were obtained from UniProt (<https://www.uniprot.org/>) and modeled in AlphaFold (<https://alphafoldserver.com/>).



Supplementary Figure 49. Visual representation of predicted consequences of suPAR platform-discordant PAV on suPAR. Protein amino acid sequences were obtained from UniProt (<https://www.uniprot.org/>) and modeled in AlphaFold (<https://alphafoldserver.com/>).

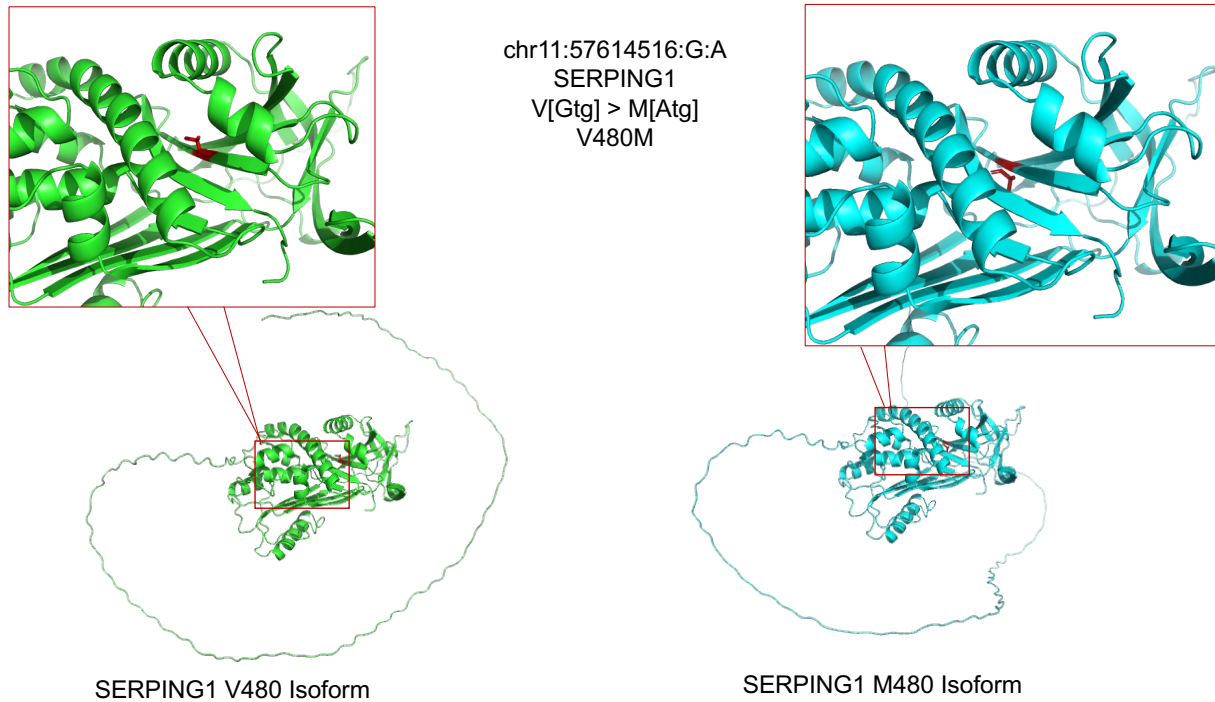
chr14:20781965:G:A
RNASE6
R[cGg] > Q[cAg]
R89Q



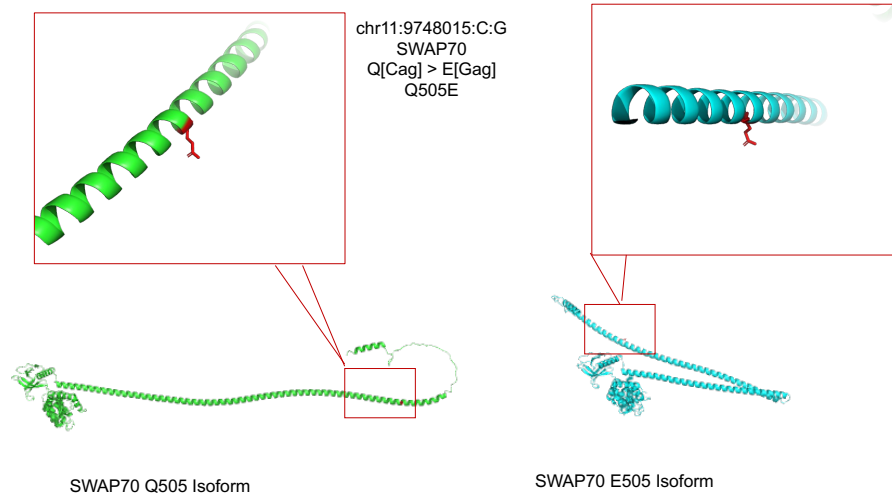
RNASE6 R89 Isoform

RNASE6 Q89 Isoform

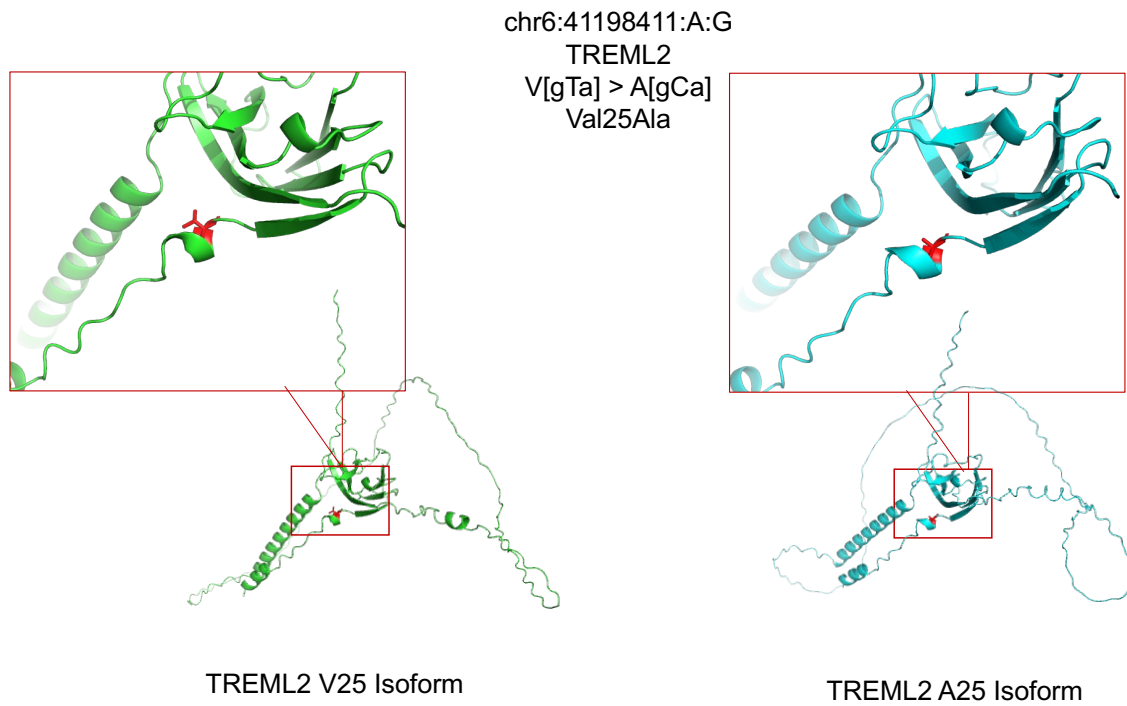
Supplementary Figure 50. Visual representation of predicted consequences of RNASE6 platform-discordant PAV. Protein amino acid sequences were obtained from UniProt (<https://www.uniprot.org/>) and modeled in AlphaFold (<https://alphafoldserver.com/>).



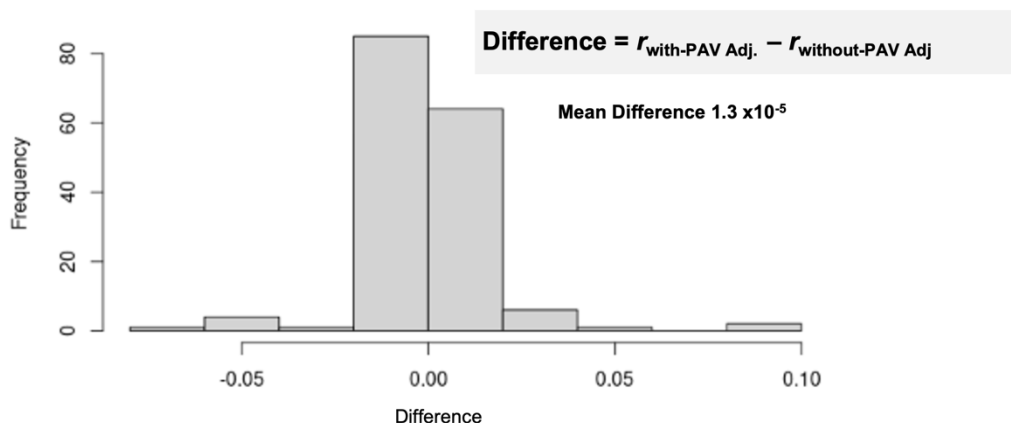
Supplementary Figure 51. Visual representation of predicted consequences of SERPING1 platform-discordant PAV. Protein amino acid sequences were obtained from UniProt (<https://www.uniprot.org/>) and modeled in AlphaFold (<https://alphafoldserver.com/>).



Supplementary Figure 52. Visual representation of predicted consequences of SWAP70 platform-discordant PAV. Protein amino acid sequences were obtained from UniProt (<https://www.uniprot.org/>) and modeled in AlphaFold (<https://alphafoldserver.com/>).



Supplementary Figure 53. Visual representation of predicted consequences of TREML2 platform-discordant PAV. Protein amino acid sequences were obtained from UniProt (<https://www.uniprot.org/>) and modeled in AlphaFold (<https://alphafoldserver.com/>).



Supplementary Figure 54. Histogram of differences in inter-platform Pearson's correlation estimates without and with adjustment for significant lead *trans*-pQTL ($p < 1 \times 10^{-11}$, genome-wide significant with further correction for 2,708 probe pairs) variants in SomaScan-specific pleiotropic regions (difference = correlation of PAV adjusted protein measure – correlation of protein measures without adjustment for PAV). Difference > 0 reflects improved correlation estimate. Source Data is available in Supplementary Data Table 28.

Supplementary References

1. UniProt Consortium. Uniprot: the universal protein knowledgebase in 2025. *Nucleic Acids Res.* (2024) doi:10.1093/nar/gkae1010.
2. Jumper, J. *et al.* Highly accurate protein structure prediction with AlphaFold. *Nature* 596, 583–589 (2021).
3. Schrödinger, L., & DeLano, W. *PyMOL*. (2020).