Supplementary information

Large-scale plasma proteomics comparisons through genetics and disease associations

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1 Supplementary Notes

2 SN1. Comparison of CV from repeated samples and control samples

Both the Olink and SomaScan platforms include repeated measurements of control samples for quality
 control purposes. Prior research using CV of such control samples as a measure of precision has
 demonstrated lower CV for assays on a previous version of the SomaScan platform (1.2K) than on the
 Olink Explore 1536 platform¹⁻³. We observe similar results in our data: on control samples, the CV of
 SomaScan assays is on average smaller than the CV of Olink assays (Supplementary Table ST6)¹.

8 SN2. Comparison of batch effects between Olink in UK Biobank and SomaScan in Iceland

9 Both Olink and SomaScan use repeated measurements of control samples, specific to the platform, for 10 quality control purposes. Computing the variation in the measurements of the control samples using either pairs of measurements from the same plate or pairs from different plates allows us to evaluate 11 12 to what extent the variation is inherent to the assay itself and to what extent due to variability between 13 plates, and how those variations relate to the total variation of the assay. We evaluated the variation 14 in measurement of control samples in the Icelandic data set (measured by SomaLogic) and the UKB 15 data set (measured by Olink) using the MAD to estimate the standard deviation, calculating the variance as $\sigma^2 = (1.4825 * MAD)^2$. Assuming that the variance on the control samples inherent in the 16 assay σ_a^2 and the variance due to batch effect σ_p^2 are not correlated, we can decompose the total 17 variance of the control sample measurements as $\sigma_M^2 = \sigma_p^2 + \sigma_a^2$. 18

19 In order to determine the impact of the plate effect on measurement results, the plate effect must be 20 considered in relation to the total variance of the assay, σ^2 . We can then evaluate how much of the 21 total variance is due to the variability inherent in the assay (σ_a^2/σ^2) and how much due to batch effects 22 $(\frac{\sigma_M^2 - \sigma_a^2}{\sigma^2})$.

We can estimate σ_a^2 by using the difference between the two control samples measured on each plate, while we can estimate σ_M^2 by considering the control samples without regards to plate, and σ^2 from all values for the assay in question.

The fraction of assay variance explained by the variability inherent in the assay was 0.23 on the Olink platform and 0.10 on the SomaScan platform, while the fraction of variance explained by batch effects was 0.06 on Olink and 0.02 on SomaScan (Supplementary Figure SF9).

The discrepancy between the assay precision evaluated using the CV of duplicate measurements of samples and the variation of measurements of control samples may be in part due to the use of different control samples between the platforms.

32 SN3. Inter-class correlation:

33 The median correlation of the different assays for the two measurements of the same sample was 34 lower for the Olink platform than the SomaScan platform (Spearman r=0.78 vs 0.99, respectively, 35 Mann-Whitney $p=6.6 \times 10^{-130}$). Both platforms emphasize the relative quantification within each assay, 36 and neither of the platforms makes a claim towards the comparability of inter-class measurements. In 37 fact, the normalization process for the Olink data shifts the median measurement for each assay to 0, 38 and the difference between the levels of any two proteins on the Olink assay are therefore purely due 39 to the position of the individual sample within the distribution of the assay. Conversely, for the 40 SomaScan platform, the levels measured by two different assays can have vastly different medians, to 41 the extent that the variation within each assay is dominated by the difference in medians. This ensures 42 that for such SomaScan assays, any two measurements done with the assay with the higher median 43 will always be higher than any two measurements done with the other, leading to stronger inter-class 44 correlation between them. When adjusting for differences in data processing by shifting the median 45 for each assay on each platform to 0, the median correlation remained lower for Olink than for 46 SomaScan, although the difference was smaller (Spearman r=0.78 vs 0.83, respectively, Mann-Whitney 47 $p=6.4 \times 10^{-7}$; Supplementary Figure SF5).

48 SN4. The impact of SomaScan SMP normalization

As a normalization step, SomaScan scales each sample to conform to a reference population. This is done by calculating a scaling factor for each assay relative to a reference sample, averaging this scaling factor over all assays in the same dilution group, and applying the resulting scaling factor to all assays in the dilution group. While this can serve to reduce variation between samples, this may not always be desirable, as this has the effect of potentially removing large-scale variation in protein levels, affecting multiple proteins. Some studies therefore forego this normalization⁴. Here, we briefly note how the SMP normalization affects the present analysis.

56 SMP normalization reduces the median CV of the SomaScan assays (SMP: 9.9%, no SMP: 16.2%, 57 Wilcoxon signed-rank $p < 10^{-300}$).

The SMP normalization significantly reduces the median correlation between matching assays from the SomaScan and Olink platforms (SMP: r=0.33, no SMP: r=0.39, Mann-Whitney $p=1\times10^{-11}$), as well as the median correlation between random pairs of assays from the different platforms (SMP: -r=-0.01, no SMP: r=0.08, Mann-Whitney $p < 1\times10^{-300}$). SMP normalization also had a large effect on median within-platform correlation (SMP: -0.08, no SMP: 0.42, Mann-Whitney $p < 1\times10^{-300}$).

Using non-normalized data, the levels of 79% of SomaScan assays associated with age and 58% associated with sex (Supplementary Table ST14). The SomaScan normalization factors were associated with age and sex and affected the association with the normalized data accordingly (Supplementary Table ST14). The correlations between age and sex effects were less consistent between Olink and SomaScan (Spearman correlation=0.53 for age and 0.57 for sex).

68 In Iceland, we found 355,938 protein-phenotype associations ($p < 1.0 \times 10^{-5}$) in the non-normalized 69 SomaScan data (Supplementary Table ST16) compared to 218,503 associations for the SMP-70 normalized SomaScan data. Of these, 173,912 were significant for both normalization methods; 49% 71 and 80% of the associations for the non-normalized and normalized data, respectively. However, 18% 72 of the protein phenotype associations that were significant for both normalization methods had a 73 discordant direction of effects. The direction of association was more likely to be concordant between 74 non-normalized and normalized levels for positive associations (94%) than negative ones (78%). The 75 discordant associations were mostly with phenotypes that are likely to associate with overall protein 76 concentration, e.g., body mass index, blood cell counts, and markers of inflammation, liver function, 77 and kidney function.

- We identified 1,889 and 16,778 sentinel *cis* and *trans* pQTLs using the non-normalized SomaScan data,
 respectively, and 2,120 and 22,616 sentinel *cis* and *trans* pQTLS using the SMP normalized data (Table
 1). Most non-normalized sentinel *cis* and *trans* pQTLs corresponded (r²>0.8) to a sentinel normalized
 pQTL: 89% and 74%, respectively (Supplementary Tables ST19 and ST20).
- In Iceland, we performed 164 billion tests (4,907 assays × 33.5 million variants), detecting 18,667 and
 24,736 sentinel pQTLs for the non-normalized and normalized analyses, respectively, corresponding to
 estimated false discovery rates of 1.6% and 1.2%.
- Using non-normalized SomaScan data we found 38 pQTLs associating with more than 50 proteins. compared with 35 using the SMP-normalized data. The pleiotropic SomaScan pQTLs each had at least 27 protein associations for either normalization method, indicating that the normalization does not create or remove pleiotropic pQTLs. However, the pattern of association was substantially altered by normalization for some pleiotropic variants. For example, the del12 variant in *ASGR1* went from affecting 556 proteins positively and no proteins negatively in the non-normalized data, to affecting 288 proteins positively and 331 proteins negatively in the normalized data.
- We identified 1,889 and 16,778 sentinel *cis* and *trans* pQTLs using the non-normalized SomaScan data, respectively, and 2,120 and 22,616 sentinel *cis* and *trans* pQTLs using the normalized data (Table 1). The normalization suggested by SomaLogic leads to the detection of more pQTLs. However, this normalization correlates associates with many processes that affect the levels of multiple proteins.

96 This is reflected by discordant correlations between protein levels and phenotypes related to BMI, 97 inflammation, blood cell counts, and kidney and liver function and by the drastic effects of 98 normalization on pleiotropic variants like the ASGR1 variant which associates with higher levels of 99 many proteins in non-normalized data. Notably, the normalization decreases the correlation between 100 Olink and SomaScan assays, probably because it is adjusting out some of the biological variability as 101 previously described. However, the power to detect protein associations with sequence variants and 102 phenotypes that are not pleiotropic tends to increase following normalization.

103 SN5. Between-platform correlation of protein levels for shared targets

104 As the Olink NPX normalization leads to the mean level of each protein being 0 across the data set, 105 there is no correlation on median protein levels between platforms, and neither can the variation in 106 protein level IQR be explained by the intensity on the Olink platform. However, the protein level IQR 107 was correlated between the two platforms (Spearman correlation 0.12, $p=1.70\times10^{-8}$), and on both 108 platforms, higher IQR was correlated with better correspondence with the matching assay (Spearman correlation for Olink assay IQR 0.28, p=4.84×10⁻³⁹; for SomaScan assay IQR 0.52, p=1.57×10⁻¹⁴⁴, 109 110 Supplementary Figure SF2). This indicates that if either of a pair of assays has a low variation in levels, 111 the correlation with the corresponding assay tends to be low.

112 Olink's data processing shifts the mean of the measurements for each protein to 0. Therefore, the 113 comparison of the correlation of assay intensity with the correlation between the assays is not 114 informative.

115 SN6. Between-platform ranking of assays by correlation of levels

To assess whether the matching assays on the two platforms are measuring the same proteins, we compared the levels of all pairs of targeted proteins between platforms. For each assay, we ranked the assays on the other platform by their correlation with the given assay (Supplementary Figure SF3). For Olink Explore assays, the matching SomaScan assay (with the highest correlation, if more than one was matching) ranked in the top 1% of all assays in 874 of 1,864 cases. Conversely, for SomaScan assays, the matching Olink Explore assay (with the highest correlation, if more than one was matching) ranked in the top 1% of all assays in 968 of 1,994 cases.

123 SN7. Association of ADM with heart failure

124 In addition to BNP, we noted an association with levels of protein encoded by the Adrenomedullin 125 gene (*ADM*) which encodes pro-adrenomedullin which is cleaved into two peptides, ADM 126 (adrenomedullin) and PAMP (proadrenomedullin N-terminal 20 peptide). Two assays on SomaScan 127 (7922-5 and 14115-34) target protein products encoded by *ADM* and the correlation between them is 128 low (r=-0.12). A protein product encoded by ADM is also targeted on the Olink platform. One of the 129 SomaScan assays correlates positively with the Olink assay (7922-5; r=0.42) whereas the other does 130 not (14115-34; r=-0.24). Furthermore, both the Olink assay and the positively correlated SomaScan 131 assay (7922-5) have a cis pQTL, while the negatively correlated SomaScan assay (14115-34) does not. 132 Both the Olink assay and the positively correlated SomaScan assay (7922-5) associate with heart 133 failure. Levels of products encoded by ADM have a strong association with heart failure on Olink 134 $(OR=1.85 \text{ per SD}, p=6.69 \times 10^{-72})$, but a weaker association on the SomaScan 7922-5 assay (OR=1.23 per)SD, $p=2.69\times10^{-19}$). This is consistent with reports of elevated circulating ADM in heart failure⁵. In 135 contrast, the negatively correlated SomaScan assay (14115-34) is negatively associated with heart 136 137 failure (OR=0.81 per SD, $p=2.49\times10^{-23}$). This underlines the need for detailed characterization of the 138 proteoforms measured.

139 SN8. Our pQTL analyses using Olink in UK Biobank

140 In the UKB-BI Olink data, for 19% of the 26,926 sentinel pQTL associations, a secondary variant in the 141 same region associated with the same protein based on conditional analysis (8,640 secondary 142 associations in *cis* and 5,592 in *trans*). Combined, we found a total of 41,158 sentinel and secondary 143 pQTL associations.

- Most Olink sentinel *cis* pQTL associations had secondary pQTL associations (1,702 of 2,102; 81%), in contrast to only 3,340 (13%) of the 24,824 sentinel *trans* pQTL associations.
- Of the Olink pQTLs, 6,530 (73%) associated with the level of a single protein, 2,154 (24%) with levels of two to nine proteins, and 320 (4%) with levels of ten or more proteins. We refer to pQTLs that were associated with levels of fewer than ten proteins as *specific* and the rest as *nonspecific*. Specific variants were associated with 2,416 (82%) of the Olink assays.
- 150 Of the 2,931 Olink assays for which GWAS analysis was performed, 3% had only *cis* pQTLs, 18% had 151 only *trans* pQTLs and 68% had both *cis* and *trans* pQTLs. Furthermore, 10% had no pQTLs, whereas 9%
- had a single pQTL and 82% had two or more pQTLs.

153 SN9. Subsampling and accounting for the different number of variants tested

We performed a power analysis showing that reducing the sample size in the UK Biobank to be equal to the sample size in Iceland (n=35,892) would be expected to result in the detection of 3% fewer sentinel *cis* pQTL and 34% fewer *trans* pQTL associations: if the sample size in UKB were 35,892, for the overall set of assays, we would expect to detect 2,021 of the sentinel *cis* associations (96% of the 2,102 detected in the full set of individuals), and 16,399 of the sentinel *trans* associations (66% of the 24,824). When restricting to assays measuring proteins targeted by both platforms, we would expect to detect 1,423 of the sentinel *cis* associations (97% of 1,468), and 12,315 of the sentinel *trans* associations (66% of 18,578). The majority of the comparisons between platforms that we have performed on pQTL focused on *cis* pQTLs. Using a smaller set (36K) in UK-BI using Olink would therefore not impact our conclusions since the fraction of assays with *cis* pQTLs in UKB on the overlapping set would go from 80% to 78% with Olink instead of 60% with SomaScan.

165 In Iceland, we performed 164 billion tests (4,907 assays × 33.5 million variants), detecting 24,736 166 sentinel pQTLs, corresponding to an estimated false discovery rate of 1.2%. For the UKB-BI data set, 167 taking into account 169 billion tests (2,931 assays × 57.7 million variants), detecting 26,926 sentinel 168 pQTL associations corresponds to an estimated false discovery rate of 1.2%.

169 Correcting for the number of variants tested in UKB (57.7 million) would result in a multiple testing

170 correction threshold in UKB of 8.7×10⁻¹⁰ instead of 1.8×10⁻⁹. A total of 153 (1%) of the *cis* pQTLs have

- 171 significance between those two thresholds and 1,608 (5%) of the *trans* pQTLs. This does not affect the
- 172 conclusions of the comparison between the platforms.

173 SN10. Replication of UKB-BI pQTLs in Icelandic Olink data

174 We tested the sentinel pQTLs we discovered using the UKB-BI data set for association using Olink data 175 from 1,514 Icelanders and found 74% and 19% of the cis and trans pQTL associations to be nominally 176 significant (p < 0.05) and with consistent directions (Supplementary Table ST35). In comparison, a 177 power analysis resulted in expected proportions of replicated associations of 85% and 35% for cis and 178 trans pQTL associations, respectively. The ratio between expected and observed replication was 0.87 179 and 0.54 for cis and trans pQTLs, respectively, and while the power analysis represents a best-case 180 scenario, the replication rate may also be impacted by differences in population and sample handling 181 and processing (Supplementary Table ST13).

182 SN11. Cis pQTLs in high LD with a PAV and not cis eQTL

183 In general, a *cis* pQTL would be expected to be equally likely to correlate with increased levels of a protein as decreased. Therefore, the average effect of *cis* pQTLs would be expected to be close to zero. 184 185 However, if the pQTL is due to epitope effects, the alternate allele would be more likely to associate 186 with decreased levels of the protein as measured by the assay. As we have previously observed for 187 SomaScan, the effect of the alternative allele of *cis* pQTLs not in high LD with a PAV is on average close 188 to zero⁴. However, when a PAV is in high LD with a *cis* pQTL, we observe a negative effect for the 189 alternative allele and the negative effect tends to be even stronger when no *cis* eQTL is in high LD. 190 When the PAV in high LD is annotated as high impact (stop gained, frameshift, splice donor or 191 acceptor), the negative effect is consistent with expected nonsense-mediated decay, in particular when supported by *cis* eQTL. However, when the PAV in high LD is annotated as moderate impact
(missense, inframe indel, or splice region), the negative effect we observe for the alternative allele is
consistent with epitope effect.

195 SN12. pQTL replication between the Olink and SomaScan platforms

Replication of pQTLs detected using SomaScan has been attempted using Olink Target for a limited set
of proteins (n=90 and 163)⁶. In those studies, 65% (81% for *cis* and 52% for *trans*) and 67% (93% for *cis*and 64% for *trans*) of pQTLs identified in the Interval and deCODE studies replicated, respectively^{4,6,7}.
Reciprocally, 64% (75% for *cis* and 61% for *trans*) of the pQTLs identified using Olink Target were
replicated using SomaScan (n=163 proteins)^{4,6}. A recent study involved a larger number of proteins
targeted by both platforms (n=871) but was limited by the low number of participants measured using
Olink Target (n=485)⁸.

203 In addition to the correspondence of pQTLs, for comparison with previous work in the field, we 204 checked the replication of pQTLs detected on each of the platforms on the other platform^{7,8}. Of the 205 pQTLs we identified using Olink UKB-BI, we nominally (p < 0.05) replicated 70% of sentinel *cis* pQTLs 206 and 54% of sentinel trans pQTLs in the Icelandic SomaScan data (Supplementary Table ST30). 207 Conversely, we replicated 84% of sentinel cis pQTLs and 54% of sentinel trans pQTLs detected using 208 SomaScan data in the UKB-BI Olink data (Supplementary Table ST37). Thus, the replication rate using 209 Olink for cis pQTLs detected using SomaScan was somewhat higher than the replication rate using 210 SomaScan for *cis* pQTLs detected using Olink.

211 When attempting to replicate sentinel Olink pQTLs in UKB-BI using Icelandic SomaScan data, the 212 correlation between effect estimates was similar for cis pQTLs (r=0.51; 95% CI: 0.47-0.55) and trans pQTLs (r=0.48; 95% CI: 0.47-0.49) (Extended Data Figure EF7a, b). However, the correlation between 213 214 effects was substantially higher for cis pQTLs not in high LD with a PAV (r=0.63; 95% CI: 0.58-0.66) than 215 for cis pQTLs in high LD with a PAV (r=0.42; 95% CI: 0.33-0.50) (Extended Data Figure EF7c). For pQTLs 216 detected using SomaScan, the correlation with effect estimates using Olink was somewhat higher for 217 cis pQTLs (r=0.48; 95% CI: 0.43-0.53) than for trans pQTLs (r=0.41; 95% CI: 0.39-0.42) (Extended Data 218 Figure EF7d, e). As in the other direction of replication, the correlation was substantially higher for cis 219 pQTLs not in high LD with a PAV (r=0.74; 95% CI: 0.70-0.77) than for *cis* pQTLs in high LD with a PAV 220 (r=0.31; 95% CI: 0.21-0.40) (Extended Data Figure EF7f).

Assays targeting proteins with *cis* pQTLs that did not replicate between platforms had lower correlation between measured protein levels than assays for proteins with replicating *cis* pQTLs (Extended Data Figure EF7 a, b, d, e; Supplementary Tables ST30, ST31, and ST6). For *cis* pQTLs detected using the SomaScan v4 platform and replicated on the Olink Explore platform, this is based on 894 replicating and 164 non-replicating pQTLs, while for *cis* pQTLs detected using the Olink Explore platform and
 replicated using the SomaScan v4 platform, this is based on 871 replicating and 375 non-replicating
 pQTLs.

To investigate if the observed difference in replication between the cohorts might be caused by differences in LD structure, we computed for both cohorts the r2 in the source population between each reported sentinel pQTL variant and the variants in the credible sets for the pQTL, and compared the r2 for variants in high LD (r2 > 0.8) with their r2 in the replication cohort.

- Of the sentinel pQTLs detected in the Icelandic data set, 1,527 out of 9,611 variants (16%) did not map to the UKB-BI data set, while of the sentinel pQTLs detected in the UKB-BI data set, 3,864 out of 13,641 variants (28%) did not map to the Icelandic data set. In both cases, rare variants (MAF < 1%) were less likely to map than others, with 444 out of 1,421 (31%) variants detected in Iceland and 616 out of 1,074 (57%) variants detected in UKB-BI failing to map to UKB-BI and Iceland, respectively.
- 237 Of the variants in high LD with the reported sentinel variant in the Icelandic cohort (r2 > 0.8), 92% were 238 also in high LD in the UKB-BI cohort, while 89% of the sentinel variants in the UKB-BI cohort were also 239 in high LD in the Icelandic cohort. A further 5% and 8% of the variants in high LD with the sentinel 240 reported pQTLs from the Icelandic and UKB-BI data, respectively, had r2 between 0.6 and 0.8. Thus, 241 for both cohorts, 97% of the variants in high LD with the sentinel reported pQTL had r2 > 0.6 in the 242 replication cohort (Supplementary Figure SF7, Supplementary Tables ST32-ST34). It is therefore 243 unlikely that the difference in replication rate between the platforms is because of difference in LD 244 structure between the cohorts.

245 SN13. Replication of trans pQTLs conditional on cis pQTLs

For pQTLs detected in UKB-BI, subdividing signals into proteins having *cis* pQTLs on neither, only one, or both platforms resulted in 3%, 2%, and 13%, respectively, of signals having a sentinel corresponding *trans* pQTL in the Icelandic SomaScan data. Similarly, for pQTLs detected in the Icelandic SomaScan data, subdividing into proteins having *cis* pQTLs on neither, only one, or both platforms resulted in 3%, 4%, and 25%, respectively, of signals having a sentinel corresponding *trans* pQTL in the UKB-BI Olink data (Supplementary Table ST35).

252 SN14. Variants associating with a large number of proteins

The two variants associating with the largest number of proteins based on SomaScan but not on Olink are close to *CFH* and *SKIV2L*. The two variants associating with the largest number of proteins on Olink but not on SomaScan are close to *SLC22A4* and *GP6*. The variant at *GP6* is in high LD with a missense

variant (Pro219Ser) in *GP6*, it is an eQTL and a pQTL for GP6, and associates with platelet volume⁹ and

aggregation¹⁰. GP6 is the primary glycoprotein receptor that mediates collagen responses in platelets involved in thrombus formation and the difference in the associations between the platforms may reflect differences in plasma sample preparation and handling^{4,11,12}, as prolonged storage of blood samples may lead to platelet activation and subsequent secretion of proteins into plasma^{11,13}.

261 SN15. Concurrence between GWAS catalog LD with pQTL and credible set.

For sentinel pQTLs in the Olink UKB-BI data, there were 669,045 pairs where variants in high LD associated with levels of a particular protein and a phenotype in the GWAS catalog; 4,439 pairs in *cis* and 664,606 pairs in *trans*. Of those, 2,409 (54%) of the *cis* pairs and 529,604 (79%) of the *trans* pairs also have the GWAS catalog variant included in the credible set of the pQTL association.

For sentinel pQTLs in the Icelandic SomaScan data, there were 300,067 pairs where variants in high LD associated with levels of a particular protein and a phenotype in the GWAS catalog; 3,360 pairs in *cis* and 296,707 pairs in *trans*. Of those, 1,597 (48%) of the *cis* pairs and 196,836 (66%) of the *trans* pairs also had the GWAS catalog variant included in the credible set of the pQTL association.

270 SN16. Proteins targeted by both platforms, same *cis* pQTL for both platforms

The protein encoded by SULT2A1 (bile salt sulfotransferase) is targeted by both Olink and SomaScan 271 272 platforms and the *cis* pQTL from both platforms, rs212100 ($p=2.2\times10^{-410}$; effect=-0.38 SD) and chr19:47871693 (non-normalized *p*=2.5×10⁻⁹⁰; effect=-0.21 SD, normalized *p*=6.5×10⁻¹²²; effect=-0.25 273 274 SD), are in high LD (r^2 =1; MAF=16%). SULT2A1 levels are correlated between the platforms (r=0.48). 275 We and others have reported association of the minor allele of rs212100 with less gallstone risk¹⁴ and lower plasma levels of SULT2A1 using the SomaScan v4 platform^{4,15}. The results here using the Olink 276 277 Explore platform in UKB confer an independent replication. These variants are reported to be in high 278 LD with the sentinel SULT2A1 eQTL (Lung and Liver effect on RNA=-0.90 SD), but not with any PAV.

Similarly, we had reported relationship between a CHRDL2 *cis* pQTL and a colorectal cancer risk variant using SomaScan, implicating *CHRDL2* at the locus as the gene through which the effect is likely mediated in the absence of any associated eQTL or PAV⁴. Consistent with these results, the sentinel *cis* pQTL (rs11236228; MAF=4%) for CHRDL2 in Olink is in high LD (r^2 =1) with the disease-associated variant (rs4944940) with a similar effect (p=2.9×10⁻³⁷⁴; effect=-0.68 SD) to the one observed on SomaScan (effect=-0.62SD), thus providing an independent replication.

285 SN17. Comparison of pQTLs for IL34

The sentinel *cis* pQTL on Olink for IL34 is a stop-gained variant in *IL34* (rs4985556), located in the last exon (position 213 of 243 amino acids) and associates with greater Alzheimer's disease (AD) risk (OR=1.08, $p=2\times10^{-8}$)¹⁶. The stop-gained variant associates with lower IL34 levels ($p=1.3\times10^{-3260}$; effect=-1.09 SD; MAF=12%) which is consistent with the predicted loss of function. No *cis* pQTLs were detected for IL34 on SomaScan, and the correlation between the levels of IL34 measured on the two platforms is low (r=0.04). IL34 promotes microglial proliferation and clearance of soluble amyloid- β (A β) and as such confers neuroprotection against the neurotoxicity of A β . It has been proposed that the stopgained variant associating with less IL34 could increase AD risk by reducing the neuroprotective properties of IL34¹⁶.

295 SN18. Proteins targeted by both platforms, different *cis* pQTL detected by the platforms

296 In some instances, *cis* pQTLs for a given protein are detected on both platforms but they have little 297 correlation and only one of them correlates with a disease-associated variants. In the case of the CD58 298 (Lymphocyte function-associated antigen 3) protein we observed *cis* pQTLs on both the Olink Explore 299 and SomaScan v4 platforms, however, the cis pQTLs were different. The sentinel cis pQTL on Olink 300 Explore (rs10801908, MAF=12%) and SomaScan v4 (rs61789227; MAF=2.1%) have very different minor 301 allele frequencies and are in low LD (r²=0.04) (Extended Data Figure EF8). However, a secondary cis 302 pQTL for CD58 on SomaScan v4 (rank 2, rs10754443; MAF=11%; effect=-0.10 SD, $p=3\times10^{-16}$) is in high 303 LD (r^2 =0.81) with the sentinel *cis* pQTL on Olink Explore. None of the *cis* pQTLs on the two platforms associate with a PAV. The correlation between the levels of CD58 measured on the two platforms was 304 low (r=0.02). The sentinel *cis* pQTL (rs10801908) for CD58 on Olink Explore (*p*=2.2×10⁻¹⁴⁷, effect=-0.26 305 SD) is reported to associate with 25% less risk of multiple sclerosis (MS)^{17,18}. The minor allele of this 306 307 variant associated with lower CD58 levels on Olink Explore and less MS risk. The glycoprotein CD58, 308 also known as lymphocyte-function antigen 3 (LFA-3), is a costimulatory receptor distributed on a 309 broad range of human tissues including cells of the immune system, making it relevant for autoimmune 310 diseases, including MS¹⁹. Based on these results both platforms are likely targeting CD58 and the discrepancies observed could result from the two platforms targeting different CD58 isoforms, or 311 312 multimeric versus monomeric forms.

313 SN19. Proteins targeted by either SomaScan or Olink

Olink Explore 3072 targets 2,923 proteins, of which 1,098 are not targeted by SomaScan v4, including ITGA11. The minor allele of Val433Met in *ITGA11* (rs2306022; MAF=9%) is the sentinel *cis* pQTL for ITGA11 (p=3.3×10⁻⁶²¹⁷, effect=-0.37SD) and is reported to confer risk of Dupuytren contracture (OR=1.27, PP=0.99) and uterine fibroids (OR=1.12, PP=1.00)^{20,21} (Supplementary Figure SF8). The fact that the variant which associates with ITGA11 levels is a PAV, and not a *cis* eQTL, raises the concern that the observed reduction in ITGA11 may be the result of an epitope effect. Validation of this thus needs to be performed using an alternative method. Of the 4,719 proteins targeted on SomaScan v4, a total of 2,891 are not targeted on Olink Explore 3072. We have previously reported on instances of *cis* pQTLs on SomaScan for proteins that are not targeted by Olink and their relationship with disease-associated variants including GREM1 and colorectal cancer, ASIP and melanoma, and STAT3 and multiple sclerosis⁴ (Supplementary Figure SF8).

325 SN20. Proportion of assays with *cis* pQTLs on the Olink and SomaScan platforms

326 A greater fraction of the Olink Expansion set of assays targets intracellular and less abundant proteins 327 (undiluted) than of the 1536 set. Both these characteristics are associated with lower fraction of assays 328 having a *cis* pQTL within each set of assays. Consequently, we observe a lower fraction of proteins with 329 *cis* pQTLs for proteins targeted in the Expansion set of assays than by the initial 1536 set (56% vs 85%). 330 Similarly, proteins targeted on a previous generation of the SomaScan platform (SomaScan 1.2K, Supplementary Table ST2) are more likely to have a pQTL in our data than proteins targeted on the 331 332 SomaScan v4 platform and not the older version (40% vs 56%). Analyzing only the proteins targeted by 333 both platforms, and considering separately the 1,109 and 739 proteins included in the 1536 and 334 Expansion sets, the fraction of proteins with *cis* pQTLs was in both cases greater on Olink than on 335 SomaScan (87% vs. 67% for 1536 and 67% vs. 51% for Expansion).

336

338 Supplementary tables

	Olink	Olink		SomaScan	
	Explore	Explore	Olink	(non-	SomaScan
-	3072	1536	Expansion	normalized)	(normalized)
n_samples	1474	1474	1474	229	227
median cv	16.5334	13.9926	19.1373	16.2204	9.8715
q1	12.1503	10.9256	14.1360	13.5926	7.2613
mean	16.5334	13.9926	19.1373	16.2204	9.8715
q3	22.9726	20.2436	24.3455	20.8062	15.2698
iqr	10.8223	9.3180	10.2095	7.2137	8.0085
median overlap					
CV	14.9084	13.2008	18.5044	15.2557	9.5442
q1 overlap	11.5143	10.6146	13.4038	12.7109	7.2322
mean overlap	14.9084	13.2008	18.5044	15.2557	9.5442
q3 overlap	21.8905	18.6046	24.2382	19.5903	14.4378
iqr overlap	10.3762	7.9899	10.8344	6.8794	7.2056

341 Supplementary Table ST3: Distribution of CV for Olink and SomaScan assays

Quantile	0.1	0.25	0.5	0.75	0.9
Intra-assay					
SomaScan	0.02	0.03	0.03	0.04	0.06
(1.2K)					
SomaScan (all)	0.02	0.02	0.03	0.04	0.06
Olink (v1)	0.03	0.03	0.05	0.07	0.11
Olink (all)	0.03	0.04	0.06	0.11	0.17
Inter-assay					
SomaScan	0.04	0.05	0.06	0.08	0.12
(1.2K)					
SomaScan (all)	0.04	0.04	0.05	0.07	0.11
Olink (v1)	0.09	0.12	0.16	0.24	0.36
Olink (all)	0.10	0.14	0.20	0.31	0.50

Supplementary Table ST4: Assay CV, replicating the results of Katz *et al.*¹, showing higher precision of

assays on the SomaScan platform. Comparing the assay CV directly does not take into account differentscales of the platforms.

	Olink vs somascan (non-	Olink vs somascan	SomaScan normalized vs non-
-	normalized)	(normalized)	normalized
median_corr	0.3883	0.3255	0.737
min_corr	-0.2865	-0.3548	-0.377
max_corr	0.9356	0.9098	1
q1_corr	0.1124	0.0325	0.556
q3_corr	0.6254	0.5843	0.8651
iqr_corr	0.513	0.5518	0.3091
baseline_corr	0.0777	-0.0055	nan
q1_baseline_corr	0.0112	-0.0634	nan
q3_baseline_corr	0.2142	0.0611	nan

351 platforms using normalized (smp) and non-normalized (pc0) data.

³⁵⁰ Supplementary Table ST5: Median Spearman correlation between assays on the Olink and SomaScan

	Olink dilution						
SomaScan dilution		1:1	1:10	1:100	1:1000	1:100000	total
	1:5	1050	300	107	27	4	1488
	1:200	119	110	116	60	17	422
	1:20000	3	4	11	36	59	113
	total	1172	414	234	123	80	2023

Supplementary Table ST7: Assay dilution groups for the Olink and SomaScan platforms.

			SomaScan d	ilution		
			1:5	1:200	1:20000	all
		count	1050	119	3	1172
		median normalized corr	0.157	0.273	0.105	0.161
		median non-normalized				
	1:1	corr	0.240	0.301	0.197	0.243
		count	300	110	4	414
		median normalized corr	0.437	0.614	0.223	0.479
		median non-normalized				
	1:10	corr	0.487	0.629	0.267	0.516
		count	107	116	11	234
		median normalized corr	0.335	0.594	0.480	0.516
		median non-normalized				
	1:100	corr	0.382	0.615	0.494	0.540
		count	27	60	36	123
		median normalized corr	0.165	0.544	0.576	0.511
		median non-normalized				
	1:1000	corr	0.334	0.603	0.562	0.545
		Count	4	17	59	80
	1.100000	Median normalized corr	0.138	0.359	0.451	0.426
	1.100000	Median non-normalized				
		corr	0.169	0.428	0.520	0.495
		count	1488	422	113	2023
		median normalized corr	0.208	0.528	0.483	0.325
Olink		median non-normalized				
dilution	all	corr	0.297	0.569	0.520	0.388

359 platforms by dilution group

Supplementary Table ST8: Median correlation between matching assays on the Olink and SomaScan

	dilution		median	count	median cv
platform	group	count	CV	(matching)	(matching)
	1:1	1961	19.75546	1091	18.50443
	1:10	524	13.22939	384	12.81051
	1:100	257	11.23674	211	11.03967
	1:1000	127	11.60512	113	11.60512
olink	1:100000	72	11.11745	63	11.09153
	1:5	4013	9.993957	1462	9.892588
somascan_non-	1:200	791	8.973037	419	8.045246
normalized	1:20000	157	10.46488	113	10.27222
	1:5	4013	16.79949	1462	16.17287
	1:200	791	13.58756	419	12.42079
somascan_normalized	1:20000	157	14.79755	113	14.37824

Supplementary Table ST9: CV by dilution group for all assays on each platform and for the set of 363 matching assays.

	All proteins	SomaScan v4	SomaScan	Olink Explore	Olink
	according to		1.2k	3072	Explore
	HPA				1536
Intracellular	12159 (63%)	2425 (49%)	338 (30%)	1414 (46%)	562 (36%)
Membrane	5384 (28%)	1434 (29%)	336 (30%)	891 (29%)	532 (34%)
Secreted	1644 (9%)	1064 (22%)	443 (40%)	751 (24%)	463 (29%)

- **Supplementary Table ST10:** The difference in protein location (according to Human Protein Atlas; HPA)
- 368 between SomaScan and Olink.

		cis	no <i>cis</i>
	both below LOD	185	498
	one below LOD	94	83
50% of values	neither below LOD	1823	260

Supplementary Table ST11: Number of proteins with *cis* pQTL detected or not detected on Olink

depending on if the median of the NPX values was below the limit of detection on the validation sets

of samples from healthy individuals (n=24) and diseased individuals (n=48).

	UKB-BI	Iceland 36k	UVS	HERA
Country	UK	Iceland	Iceland	Iceland
Count	50104	36195	17560	18635
Donor age mean	57.9	56.3	58.4	54.4
Donor age std	8.1	16.9	17.1	16.5
BMI mean	27.3	27.3	26.5	28.2
BMI std	4.7	5	4.6	5.4
Sex proportion (female)	0.54	0.57	0.57	0.57
Bias	healthy	diseased	diseased	diseased
Sample age (years) mean*	13	10.2	16.7	4.2
Sample age (years) std	2.4	7.4	1.2	5.4
Plasma handling protocol	stand 30min, centrifuge, ship to processing center, aliquot	stand 30min, centrifuge, aliquot	stand 30min, centrifuge, aliquot	stand 30min, centrifuge, aliquot
Storage temperature	-80°C	-80°C	-80°C	-80°C
Freeze-thaw cycles	0	0	0	0
Delayed sample handling**	TRUE	FALSE	FALSE	FALSE

Supplementary Table ST13: Differences in the UKB-BI and Icelandic cohorts and study characteristics.
 Age is in years and the unit of BMI is kg/m². *assuming all SomaScan measurements performed in 2019
 and all Olink measurements in 2022. **UKB samples were kept at 4°C until they were shipped to
 processing center for aliquoting, preferably within 24h¹². Icelandic samples were aliquoted
 immediately following centrifuging.

r2 range	uk_to_is	is_to_uk
0.0-0.2	0.6%	1.6%
0.2-0.4	0.5%	0.5%
0.4-0.6	1.9%	1.1%
0.6-0.8	7.6%	5.2%
0.8-1.0	89.3%	91.7%

Supplementary Table ST34: LD between pQTL variants and credible set variants in UKB-BI and Iceland.
For each pQTL we compute the LD in the source cohort between the pQTL and each variant in the

credible set. For variants in high LD in the source cohort, the table shows the LD of the variants in the replication cohort. For both directions, 97% of the variant pairs had $r^2 > 0.6$.

392 Supplementary Figures



393

Supplementary Figure SF1: Top row: Comparison of assay CVs on the Olink and SomaScan platforms
 computed using random samples (left) and duplicate measurements of samples (right). Bottom row:
 Comparison of assay CVs computed using random samples and duplicate measurements of samples
 on the Olink (left) and SomaScan (right) platforms.

Correlation of assay IQR with inter-platform correlation

Correlation of assay IQR with inter-platform correlation





400 Supplementary Figure SF2: Relationship between assay IQR and inter-platform correlation. Assay IQR

401 is correlated with inter-platform correlation, with higher assay IQR associating with higher inter-

402 platform correlation.



Highest vs matching correlation coefficient - Olink vs. SomaScan normalized





Supplementary Figure SF3: Top: Histogram of the rank of the matching assay compared to all possible
 pairs. For an assay on a given platform, the matching assay on the other platform is among the highest ranked assays on that platform in a majority of cases.

Bottom: The difference between the highest correlation coefficient for an assay and the correlation coefficient for the matched assay. The histogram shows the distribution of the differences in correlation coefficient between the matching assay and the assay with the strongest correlation. The right-hand plot shows the distribution of the correlation coefficients. For assays on the diagonal, the matching assay is the assay showing the highest correlation in protein levels. For the majority of assays, the difference between the strongest correlation and the correlation with the matching assay is small.



Supplementary Figure SF4: Correlation of CV to percentage of measurements below limit of detection

417 for Olink assays. The Spearman correlation is 0.69, $p < 10^{-300}$.



421

420 Supplementary Figure SF5: Histogram of intra-class correlation coefficients for Olink (UKB) and

422 Shifting the values for each assay on the SomaScan platform to have a mean of 0, as is done for the

SomaScan (Iceland 36K) data sets. The correlation is computed for the paired samples in each data set.

423 Olink assays, greatly impacts the median correlation.



Supplementary Figure SF6: The fraction of assays with a *cis* pQTL compared to the percentage of
 measurements above LOD, increments of 5%. The area of the dots represents the number of assays in
 each bin.



432 **Supplementary Figure SF7:** Histogram showing the r² in the replication cohort between pairs of a 433 sentinel pQTL and a credible set variant from the source cohort having r² > 0.8 in the source cohort. 434 For pQTLs detected in both data sets, 97% of the pairs have r² > 0.6, with r² > 0.8 in about 90% of cases 435 (Supplementary Table ST34).





Supplementary Figure SF8: Left: Association at *ITGA11* locus between variants and ITGA11 levels
 measured using Olink Explore, and Dupuytren's disease. All r² are shown to the same variant.

442 Right: Association at *STAT3* locus between variants and STAT3 levels measured using SomaScan v4

443 (top) and multiple sclerosis risk (bottom). All r² are shown to the same variant.

444 *p*-values were based on a two-sided likelihood ratio test and not adjusted for multiple comparisons.





Supplementary Figure SF9: Fraction of total variance of the assay inherent in the assay itself (left) and

448 due to plate effect (right). Estimated using control samples from both platforms.

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Index of supplementary tables

ST2: Assays on the Olink platform

oid: Internal Olink ID of assay
uniprot: UniProt ID of the protein targeted by the assay
target_full_name: Name of the protein targeted by the assay according to Olink
gene_name: Name of the gene encoding the protein targeted by the assay
dilution: Dilution group of the assay (1:n)
cv: CV of repeated measurements of the same sample
rand_cv: CV of randomly chosen pairs of samples from the assay
rand_cv_iceland_1k: rand_cv on the Icelandic 1K data set

ST3: Assays on the SomaScan platform

seqid: Internal SomaScan ID of the assay uniprot: UniProt ID of the protein targeted by the assay target_name: Name of the protein targeted by the assay according to SomaLogic target_full_name: Full name of the protein targeted by the assay according to SomaLogic gene_name: Name of the gene encoding the protein targeted by the assay dilution: Dilution group of the assay (1:n) nonnorm_cv: CV of repeated measurements of the same sample, non-SMP normalized nonnorm_rand_cv: CV of randomly chosen pairs of samples from the assay, non-SMP normalized norm_cv: CV of repeated measurements of the same sample, SMP normalized norm_rand_cv: CV of randomly chosen pairs of samples from the assay, non-SMP normalized norm_rand_cv: CV of randomly chosen pairs of samples from the assay, SMP normalized norm_rand_cv: CV of randomly chosen pairs of samples from the assay, SMP normalized norm_rand_cv: CV of randomly chosen pairs of samples from the assay, SMP normalized norm_rand_cv: CV of randomly chosen pairs of samples from the assay, SMP normalized norm_rand_cv: CV of randomly chosen pairs of samples from the assay, SMP normalized norm_rand_cv: CV of randomly chosen pairs of samples from the assay, SMP normalized norm_rand_cv: CV of randomly chosen pairs of samples from the assay, SMP normalized nand_cv_iceland_1k: norm_rand_cv on the Icelandic 1K data set, SMP normalized on 1.2k: Was the protein included on the SomaScan 1.2k platform?

ST6: Correlation between assays on the Olink and SomaScan platforms

seqid: Internal SomaScan ID of the SomaScan assay
oid: Internal Olink ID of the Olink assay
uniprot: UniProt ID of the target protein
target: Name of the target protein
target_name: Full name of the target protein
gene_name: Name of the gene encoding the protein targeted by the assays
olink_nonnorm_corr: Spearman correlation between protein levels measured with Olink and non-
SMP normalized SomaScan assay
<pre>olink_nonnorm_pval: Significance of olink_nonnorm_corr</pre>
olink_smpnorm_corr: Spearman correlation between protein levels measured with Olink and SMP
normalized SomaScan assay
<pre>olink_smpnorm_pval: Significance of olink_smpnorm_corr</pre>
nonnorm_smpnorm_corr: Spearman correlation between protein levels measured with SMP
normalized and non-SMP normalized SomaScan assay
nonnorm_smpnorm_pval: Significance of nonnorm_smpnorm_corr
olink_panelset: Inclusion of assay on Olink Explore 1536 (1) or Olink Expansion (2)

- smp_quantile_in_olink: Quantile of correlation of the corresponding assay among all SomaScan assays to the relevant Olink assay (SMP normalized)
- *nonnorm_quantil_in_olink:* Quantile of correlation of the corresponding assay among all SomaScan assays to the relvant Olink assay (non-SMP normalized)
- nonnorm_quantile_in_somascan: Quantile of correlation of the corresponding assay among all Olink assays to the relevant SomaScan assay (non-SMP normalized)

ST11: Median correlation of assays by tissue of preferential expression

- *tissue:* Tissue of preferential expression (according to Human Protein Atlas)
- *median_correlation:* Median of correlation coefficients for proteins preferentially expressed in the tissue
- *mean_correlation:* Mean of correlation coefficients for proteins preferentially expressed in the tissue
- *n_assay_pairs:* Number of assay pairs targeting proteins preferentially expressed in the tissue
- *n_proteins:* Number of unique proteins targeted by both platforms and preferentially expressed in the tissue

ST13: Correlations of protein levels measured on Olink with subject age, sex, and sample age in the UKB data sets

oid: Internal Olink ID of the assay uniprot: UniProt ID of the targeted protein gene_name: Name of the gene encoding the protein beta age bi: Beta of subject age in the British-Irish ancestry group pval_age_bi: Significance of beta_age_bi beta_age_af: Beta of subject age in the African ancestry group pval age af: Significance of beta age af beta_age_sa: Beta of subject age in the South-Asian ancestry group *pval age sa:* Significance of beta age sa beta sex bi: Beta of subject sex in the British-Irish ancestry group pval sex bi: Significance of beta sex bi beta_sex_af: Beta of subject sex in the African ancestry group pval sex af: Significance of beta sex af *beta_sex_sa:* Beta of subject sex in the South-Asian ancestry group pval sex sa: Significance of beta sex sa *beta_sample_age:* Beta of sample age, all ancestry groups pval_sample_age: Significance of beta_sample_age

ST14: Correlations of protein levels measured on SomaScan with subject age, sex, and sample age in the Iceland data set

seqid: Internal SomaScan ID of the assay
gene_name: Name of the gene encoding the protein targeted by the assay

beta age no normalization: Beta of subject age (non-SMP normalized) beta age SMP normalization: Beta of subject age (SMP normalized) pval age no normalization: Significance of beta age no normalization pval age SMP normalization: Significance of beta age SMP normalization beta sex no normalization: Beta of subject sex (non-SMP normalized) beta sex SMP normalization: Beta of subject sex (SMP normalized) pval sex no normalization: Significance of beta sex no normalization pval sex SMP normalization: Significance of beta sex SMP normalized) pval sex SMP normalization: Significance of beta sex SMP normalization pval sex SMP normalization: Significance of beta sex SMP normalization beta sample age no normalization: Beta of sample age (non-SMP normalized) pval sample age no normalization adjusted for site: Beta of sample age (non-SMP normalization beta sample site (UVS or HERA) pval sample age no normalization adjusted for site: Significance of beta sample age no normalization adjusted for site: Significance of beta sample age no normalization adjusted for site: Significance of beta sample age no

ST15: Significant associations between protein levels on Olink and phenotypes in the UKB data set

oid: Internal Olink ID for the assay *uniprot:* The UniProt ID of the protein targeted by the assay gene_name: The name of the gene encoding the protein targeted by the assay *icd10:* ICD10 code of the phenotype phenotype: Name of the phenotype OR_BI: Odds ratio in the BI ancestry group pval_BI: Significance of OR_BI *nbi:* Number of affected individuals in the BI ancestry group OR_AF: Odds ratio in the AF ancestry group pval AF: Significance of OR AF *naf:* Number of affected individuals in the AF ancestry group OR SA: Odds ratio in the SA ancestry group pval SA: Significance of OR SA nsa: Number of affected individuals in the SA ancestry group beta BI: Beta of the association in the BI ancestry group *beta* AF: Beta of the association in the AF ancestry group beta SA: Beta of the association in the SA ancestry group

ST16: Significant associations between protein levels on SomaScan and phenotypes in the Iceland data set

seqid: Internal SomaLogic ID of the assay
gene_name: Name of the gene encoding the protein targeted by the assay
beta no normalization: Beta of the association (non-SMP normalized)
pval no normalization: Significance of beta no normalization
beta SMP normalization: Beta of the association (SMP normalized)
pval SMP normalization: Significance of beta SMP normalization
Phenotype: Name of the phenotype

ListType: Quantitative or case-control phenotype *ncases:* Number of cases (case-control phenotypes) *ncontrols:* Number of controls (case-control phenotypes) *nmeasured:* Number of measurements (quantitative phenotypes)

ST17: Significant associations of protein levels to IBD, both Olink (UKB-BI) and SomaScan (Iceland)

oid: Internal Olink assay ID OR olink: Odds ratio for the association on the Olink platform *pval* olink: Significance of the association on the Olink platform rank olink: Rank of the association on the Olink platform segid: Internal SomaLogic assay ID uniprot: UniProt ID of the target protein *Gene name:* The name of the gene encoding the target protein TargetFullName: Full name of the targeted protein OR_somascan: Odds ratio for the association on the SomaScan platform pval somascan: Significance of the association on the SomaScan platform rank somascan: Rank of the association on the Olink platform correlation: Correlation between protein levels measured using the assays targeted by: Indicator of which platforms target the protein (olink only, somascan only or olink somascan) *cis_pqtl_olink:* Indicator if the protein has a *cis* pQTL on the Olink platform cis pqtl somascan: Indicator if the protein has a cis pQTL on the SomaScan platform

ST18: pQTLs detected on the SomaScan platform in the Iceland data set using SMP normalized data

locusID global: Global identifier of the pQTL (set of variants with $r^2 \ge 0.80$) locusID prot: Protein-specific indicator of sentinel pQTL association gene prot: Name of the gene encoding the protein *chr prot:* Chromosome of the gene encoding the protein strand prot: Strand of the gene encoding the protein TSS prot: Transcription start site of the gene encoding the protein shortname prot: Name of the targeted protein *longname prot:* Full name of the targeted protein UniProt: UniProt ID of the targeted protein variant: RS name of the variant associating with the protein LD class size: Number of variants in high LD (r2 > 0.8) with the variant LD class: Variants in high LD ($r_2 > 0.8$) with the variant *chr var:* Chromosome of the variant pos var: Position of the variant region start: Start of the region containing the sentinel variant region end: End of the region containing the sentinel variant Amin: Minor allele of the variant Amaj: Major allele of the variant

Info: Imputation info of the variant

MAF PC: Minor allele frequency (%)

cis trans: Is the pQTL cis or trans for the protein

distTSS: Distance between variant and transcription start site

closest genes: List of genes close to the variant

- *cis eqtl coding genes:* List of genes that harbor a protein-altering (coding) or eQTL variant in high LD with pQTL variant
- *beta adj:* Effect (in standard deviations; SD) on protein levels; adjusted for variants of higher rank in the step-wise conditional analysis (if any)

beta unadj: Marginal/unadjusted effect (in SD) on protein levels

- *mLog10pval adj:* Negative base-10 logarithm corresponding to beta adj, e.g. a value of 12 means that the p-value is 10^{-12}
- *mLog10pval unadj:* Negative base-10 logarithm corresponding to beta unadj, e.g. a value of 12 means that the p-value is 10^{-12}

rank locus: Rank in step-wise conditional analysis, where sentinel variants have rank=1 and secondary variants rank 2, 3, and so on

count locus: Number of significant variants in step-wise conditional analysis

count cis eQLT same gene: For cis pQTL associations, the number of cis-eQTL in high LD for the gene encoding the protein with affected leves (NA for trans pQTL associations)

- prop same direction cis eqtl same gene: For cis pQTL associations, the proportion of cis-eQTL in high LD that have the same direction of effect for the pQTL and the eQTL for the gene encoding the protein with affected levels (NA for trans pQTL associations);
- *count cis eQTL different gene:* For cis pQTL associations, the number of cis-eQTL in high LD for genes other than the gene encoding the protein with affected leves (NA for trans pQTL associations).
- any coding same gene: For cis-pQTL associations, «Y» if there are protein altering variants (PAV) in high LD with the pQTL variant for the gene encoding the affected protein, «N» otherwise (NA for trans pQTL associations).
- any coding diff gene: For cis-pQTL associations, «Y» if there are PAV in high LD with the pQTL variant for other genes than the gene encoding the affected protein, «N» otherwise (NA for trans pQTL associations).
- *Rank Proteins per pQTL:* Ranks (in terms of significance of the sentinel pQTL association) of the associated proteins per pQTL.

Count Proteins per pQTL: Count of the associated proteins per pQTL

Rank pQTL per protein: Rank of the pQTL among all pQTL associated with protein

Count pQTL per protein: Number of pQTLs associated with protein

Reported: «Y» if pQTL association is previously reported (for same protein and any variant in high LD), «N» otherwise.

Reported rsid: RSid of the variant reported (if any)

Reported p: P-value of the reported association

Reported PMID: PMID of the reporting article

Reported r2: r2 between the reported variant and the pQTL

SeqId: Internal SomaLogic ID of the assay

r2 joint pQTL: Variance explained (r2) by the effect in a joint model for all variants at the locus

Effect in joint model: Effect estimate in a joint model for all variants at the locus *P-value joint model:* Significance of the effect for the joint model

ST19: pQTLs detected on the SomaScan platform in the Iceland data using non-normalized data

See S10

ST20: pQTLs detected on the Olink platform in the UKB-BI data set

Chrom: Chromosome of the variant

Pos: Position of the variant

OlinkID: Internal Olink ID of the assay

Affected Protein Gene Name: Name of the gene encoding the associated protein

pQTL ID: Global identifier of the pQTL

Region ID prot: Protein-specific indicator of sentinel pQTL association.

CisOrTrans: Indicator if the pQTL association is cis or trans

marker: The variant associating with the protein levels

rsName: RS name of the variant

MAF PC: Minor allele frequency of the variant (%)

Info: Imputation info of the variant

Amin: Minor allele of the variant

Amaj: Major allele of the variant

Log10 pval gc cor unadj: Significance of the association without adjusting for other signals at the locus. Negative log10 of the p-value.

Log10 pval gc cor adj: Significance of the association, adjusted for higher-rank signals at the locus. Negative log10 of the p-value.

Effect Amin unadj: Effect of the minor allele of the variant without adjusting for other signals at the locus.

Effect Amin adj: Effect of the minor allele of the variant, adjusted for higher-rank signals at the locus.

Rank Within Locus: Rank in step-wise conditional analysis, where sentinel variants have rank=1 and secondary variants rank 2, 3, and so on.

Number Within Locus: Number of significant variants in step-wise conditional analysis.

Sentinel Marker: The variant at the locus with the most significant association with the protein

Affected Protein Gene chrom: Chromosome of the gene encoding the protein

Affected Protein Gene chromstart: Start of the gene

Affected Protein Gene chromend: End of the gene

strand: Strand of the gene

TopAtLocus: Indicator if the pQTL is the sentinel signal at the locus

Affected Protein Gene TSS: Transcription start site for the gene

SameChrom: Indicator if the gene and variant are on the same chromosome

distanceTSSvariant: Distance between transcription start site and variant

rank proteins per pQTL: rank (in terms of significance of the sentinel pQTL association) of the associated proteins per pQTL.

count proteins per pQTL: Count of the associated proteins per pQTL.

rank pQTL per protein: Rank of the pQTL among all pQTL associated with protein. *count pQTL per protein:* Number of pQTL associated with protein.

r2 sentinel: r2 between the variant and the sentinel variant at the locus

cis eQTL genes: Genes that harbor an eQTL variant in high LD with pQTL variant

PAV genes: Genes that harbor a protein-altering (coding) variant in high LD with pQTL variant *UniProt:* UniProt ID of the protein

- *cis eQTL same gene:* For cis-pQTL associations, «Y» if there are cis-eQTL in high LD with the pQTL variant for other genes than the gene encoding the affected protein, «N» otherwise (NA for trans pQTL associations)
- *PAV same gene:* For cis-pQTL associations, «Y» if there are protein altering variants (PAV) in high LD with the pQTL variant for other genes than the gene encoding the affected protein, «N» otherwise (NA for trans pQTL associations),

Olink version: Version of the Olink platform (Explore or Expansion)

protein on soma: Indicator if the protein is also targeted by the SomaScan platform r2 Joint PQTL: Variance explained (r2) by the effect in a joint model for all variants at the locus Coef joint: Effect of the model in a joint model of all independent variants at the locus Pval joint: Significance of the variant in a joint model of all independent variants at the locus

ST21: pQTLs detected on the Olink platform in the UKB-AF data set

Chrom: Chromosome of the variant Pos: Position of the variant marker: The variant associating with the protein levels OlinkID: The internal Olink ID of the assay *mloq10pval:* Significance of the association between the variant and the protein levels. Negative log10 of the p-value. *Effect:* The effect of the variant on the protein levels. rsName: The RS name of the variant MAF PC: Minor allele frequency of the variant (%) Info: Imputation info of the variant Amin: Minor allele of the variant Amaj: Major allele of the variant close genes: Genes close to the variant prot_gene: The gene encoding the protein targeted by the assay prot Chrom: Chromosome of the gene encoding the protein targeted by the assay prot_TSS: Transcription start site of the gene encoding the protein targeted by the assay cis trans: Indicator if the pQTL is cis or trans for the protein *Olink set:* Indicator to which set of Olink panels the assay belongs any_PAV_same_gene: For cis-pQTL associations, «Y» if there are protein altering variants (PAV) in high LD with the pQTL variant for other genes than the gene encoding the affected protein, «N» otherwise (NA for trans pQTL associations)

ST22: pQTLs detected on the Olink platform in the UKB-SA data set

See S13

ST23: Percentage of measurements below the LOD from each assay on the Olink platform the UKB data

oid: Internal Olink ID of assay *perc.below.lod:* Percentage of values of assay below limit of detection

ST24: Comparison between pQTLs detected on Olink in the UKB-AF and UKB-BI data sets

Chrom: Chromosome of the variant Pos AFR: Position of the variant in the UKB-AF data set Pos EUR: Position of the variant in the UKB-BI data set marker AFR: Name of the variant in the UKB-AF data set OlinkID: Internal Olink ID of the assay *mloq10pval AFR:* Significance of the association in the UKB-AF data set. Negative log10 of p-value. Effect AFR: Effect of the association in the UKB-AF data set. rsName_ARF: RS name of the variant in the UKB-AF data set MAF PC AFR XAF: Minor allele frequency of the variant in the UKB-AF data set Info AFR: Imputation info in the UKB-AF data set Amin AFR: Minor allele in the UKB-AF data set Amaj AFR: Major allele in the UKB-AF data set close genes AFR: Genes that are close to the variant in the UKB-AF data set *prot_gene:* Name of the gene encoding the targeted protein prot Chrom: Chromosome of the gene encoding the targeted protein prot_TSS: Transcription start site of the gene encoding the targeted protein cis_trans: Indicator if the pQTL is cis or trans for the protein *Olink set:* Indicator if the assay is in the 1536 or Expansion set of assays MAF flip: Indicator if the minor alleles in the UKB-AF and UKB-BI data sets are different MAF_PC_AFR_XBI: Minor allele frequency of the pQTL discovered in the UKB-AF data set in the **UKB-BI** imputation MAF_AFR_div_XAF_XBI: Ratio MAF_PC_AFR_XAF/MAF_PC_AFR_XBI distance: Distance between pQTL detected in UKB-AF data-set and pQTL detected in UKB-BI data set marker EUR: Name of the variant in the UKB-BI data set *mlog10pval_EUR:* Significance of the association in the UKB-BI data set. Negative log10 of p-value. *Effect* EUR: Effect of the association in the UKB-BI data set rsName EUR: RS name of the marker in the UKB-BI data set MAF PC EUR: Minor allele frequency of the marker in the UKB-BI data set Info EUR: Imputation info in the UKB-BI data set Amin EUR: Minor allele in the UKB-BI data set Amaj EUR: Minor allele in the UKB-BI data set r2 XAF: r2 between the variant in the UKB-AF data set and the UKB-BI data set, calculated in the UKB-AF data set r2_XBI: r2 between the variant in the UKB-AF data set and the UKB-BI data set, calculated in the UKB-BI data set

Idclass_AFR_marker: The LD class of the variant in the UKB-AF data set *Idclass_AFR_size:* Size of the LD class of the variant in the UKB-AF data set *Idclass_AFR_rsname:* RS names of the variants in the LD class in the UKB-AF data set *Idclass_EUR_marker:* The LD class of the variant in the UKB-BI data set *Idclass_EUR_size:* Size of the LD class of the variant in the UKB-BI data set *Idclass_EUR_rsname:* RS names of the variants in the LD class in the UKB-BI data set *Idclass_EUR_rsname:* RS names of the variants in the LD class in the UKB-BI data set *size_Idclass_overlap:* Number of variants common to the UKB-AF and UKB-BI LD classes *rsname_Idclass_overlap:* RS names of the variants common to the UKB-AF and UKB-BI LD classes

ST25: Comparison between pQTLs detected on Olink in the UKB-SA and UKB-BI data sets

See S17

ST26: Proportion of proteins with cis pQTLs depending on dilution, subcellular location and overlap between platforms

Platform: Proteomics platform (SomaScan or Olink)
Value Type: Protein dilution, subcellular location or overlap
Value: Value to classify by
Proportion of proteins with cis-pQTL: Proportion of proteins with cis pQTL
Number of proteins in group: Total number of proteins in the group

ST27: Comparison of results for each protein targeted by at least one of the platforms

UniProt: UniProt ID of the target protein OlinkID: Internal Olink ID of the targeted protein SegId: Internal SomaLogic ID of the targeted protein Gene: Name of the gene encoding the targeted protein olink smp corr: Spearman correlation between the Olink and SomaScan assays (SMP normalization) *olink smp pval:* Significance of olink smp corr Targeted Olink: Indicator if the protein is targeted by the Olink Explore 3072 platform Targeted Soma: Indicator if the protein is targeted by the SomaScan v4 platform cis pQTL olink: Indicator if the protein has a cis pQTL in the UKB-BI Olink data PAV olink: Indicator if the protein has a pQTL in high LD with a PAV in the UKB-BI Olink data eQTL olink: Indicator if the protein has a pQTL in high LD with a cis eQTL in the UKB-BI Olink data Dilution olink: Dilution group on the Olink platform cis pQTL soma: Indicator if the protein has a cis pQTL in the Icelandic SomaScan data PAV soma: Indicator if the protein has a pQTL in high LD with a PAV in the Icelandic SomaScan data eQTL soma: Indicator if the protein has a pQTL in high LD with a cis eQTL in the Icelandic SomaScan data Dilution soma: Dilution group on the SomaScan platform *location:* Subcellular location of the protein RNA tissue specificity: RNA tissue specificity of the protein RNA tissue specific nTPM: RNA tissue specific normalized transcript expression values Olink set: Olink assay set (1536 or Expansion)

N platforms tested: Number of platforms (SomaScan or Olink) targeting the protein *N platforms with cis pQTL:* Number of platforms on which a cis pQTL was detected for the protein *cis pQTL on both and high correlation (>0.5):* Indicator if the protein has a cis pQTL on both

platforms and the correlation between levels is high

r2 top cis pQTL: r2 between the top cis pQTLs on each platform

confidence tier: Indicates the level of confidence. Tier 1: cis pQTL on both platforms, high correlation of levels. Tier 2: cis pQTL on at least one platform. Tier 3: cis pQTL on neither platform.

ST28: Correspondence of pQTLs between the Olink (UKB-BI) and SomaScan (Iceland) platforms

Chrom: Chromosome of the Olink and SomaScan pQTLs

OLINK_Pos: Position of the Olink pQTL

r2_UK: r² between Olink and SomaScan pQTL, based on UKB imputation

dist_UK_IS: Distance between Olink and SomaScan pQTL

OLINK_OlinkID: Internal Olink assay ID

OLINK_UniProt: UniProt ID of protein

OLINK_gene_prot: Gene symbol of gene encoding protein

OLINK_pQTL_ID: Global identifier of the Olink pQTL

OLINK_cis_trans: Indicator if the pQTL association is cis or trans

OLINK_rsName: RS name of the Olink pQTL

OLINK_MAF_PC: Minor allele frequency of the Olink pQTL (%)

OLINK_close_genes: Closest genes to the Olink pQTL

OLINK_mLog10pval_unadj: Significance of the Olink pQTL association without adjusting for other signals at the locus. Negative log10 of the p-value.

OLINK_mLog10pval_adj: Significance of the Olink pQTL association, adjusted for higher-rank signals at the locus. Negative log10 of the p-value.

OLINK_beta_unadj: Effect of the minor allele of the Olink pQTL variant without adjusting for other signals at the locus.

OLINK_beta_adj: Effect of the minor allele of the Olink pQTL variant, adjusted for higher-rank signals at the locus.

OLINK_rank_locus: Rank in step-wise conditional analysis for Olink pQTL, where sentinel variants have rank=1 and secondary variants rank 2, 3, and so on

OLINK_count_locus: Number of significant variants in step-wise conditional analysis for Olink pQTL

- *OLINK_rank_proteins_per_pQTL:* For Olink pQTL: Rank (in terms of significance of the sentinel pQTL association) of the associated proteins per pQTL.
- OLINK_count_proteins_per_pQTL: For Olink pQTL: Count of the associated proteins per pQTL
- *OLINK_rank_pQTL_per_protein:* For Olink pQTL: Rank of the pQTL among all pQTL associated with protein.
- *OLINK_count_pQTL_per_protein:* For Olink pQTL: Number of pQTL associated with protein *SOMA Pos:* Position of the SomaScan pQTL

SOMA_locusID_global: Global identifier of the SomaScan pQTL

SOMA_SeqId: Internal SomaScan assay ID

- *SOMA_variant:* RS name of the SomaScan pQTL
- SOMA_MAF_PC: Minor allele frequency of the SomaScan pQTL (%)

SOMA_cis_trans: Indicator if the pQTL association is cis or trans

- SOMA_closest_genes: Closest genes to the Olink pQTL
- *SOMA_cis_eqtl_coding_genes:* List of genes that harbor a protein-altering (coding) or eQTL variant in high LD with pQTL variant
- SOMA_beta_unadj: Marginal/unadjusted effect (in SD) of SomaScan pQTL on protein levels
- *SOMA_beta_adj:* Effect (in standard deviations; SD) of SomaScan pQTL on protein levels; adjusted for variants of higher rank in the step-wise conditional analysis (if any)
- *SOMA_mLog10pval_unadj:* Negative base-10 logarithm corresponding to beta unadj, e.g. a value of 12 means that the p-value is 10⁻¹²
- SOMA_mLog10pval_adj: Negative base-10 logarithm corresponding to beta adj, e.g. a value of 12 means that the p-value is 10⁻¹²
- SOMA_rank_locus: Rank in step-wise conditional analysis for SomaScan pQTL, where sentinel variants have rank=1 and secondary variants rank 2, 3, and so on
- SOMA_count_locus: Number of significant variants in step-wise conditional analysis for Olink pQTL
- *SOMA_rank_proteins_per_pQTL:* For SomaScan pQTL: Rank (in terms of significance of the sentinel pQTL association) of the associated proteins per pQTL.
- SOMA_count_proteins_per_pQTL: For SomaScan pQTL: Count of the associated proteins per pQTL
- *SOMA_rank_pQTL_per_protein:* For SomaScan pQTL: Rank of the pQTL among all pQTL associated with protein.

SOMA_count_pQTL_per_protein: For SomaScan pQTL: Number of pQTL associated with protein

ST29: Pleiotropic trans pQTLs on the Olink (UKB-BI) and SomaScan (Iceland) platforms

Chrom: Chromosome of variant

Olink Pos (hg38): Position of associated variant on Olink

- Highly Pleiotropic Olink: Indicator if the variant is highly pleiotropic on Olink
- Highly Pleiotropic Soma SMP: Indicator if the variant is highly pleiotropic on SomaScan with SMP normalization
- *Highly Pleiotropic Soma PCO:* Indicator if the variant is highly pleiotropic on SomaScan without SMP normalization
- *r2 SMP Olink:* r2 between the corresponding variants in the Olink data and the SMP normalized SomaScan data
- distance SMP olink: Distance between the corresponding variants in the Olink data and the SMP normalized SomaScan data
- *r2 PC0 Olink:* r2 between the corresponding variants in the Olink data and the non-SMP normalized SomaScan data
- *distance PCO olink:* Distance between the corresponding variants in the Olink data and the non-SMP normalized SomaScan data

Olink nprot: Number of proteins associating with the variant in the Olink data

- Soma SMP nprot: Number of proteins associating with the variant in the SMP normalized SomaScan data
- Soma PCO nprot: Number of proteins associating with the variant in the non-SMP normalized SomaScan data

nprot SMP div nprot Olink: Soma SNP nprot / Olink nprot

nprot PCO div nprot Olink: Soma PCO nprot / Olink nprot

nprot SMP div nprot PCO: Soma SMP nprot / Soma PCO nprot

Olink Name: Name of associated variant in the Olink data

Olink rsName: RS name of the associated variant in the Olink data

Olink MAF PC: Minor allele frequency of the associated variant in the Olink data (%)

Olink close genes: Genes close to the associated variant in the Olink data

Soma SMP Pos: Position of the associated variant in the SomaScan data using SMP normalization *Soma SMP Name:* Name of the associated variant in the SomaScan data using SMP normalization

- Soma SMP rsName: RS name of the associated variant in the SomaScan data using SMP normalization
- Soma SMP MAF PC: Minor allele frequency of the associated variant in the SomaScan data using SMP normalization (%)
- Soma SMP close genes: Genes close to the associated variant in the SomaScan data using SMP normalization

Soma PCO Pos: Position of the associated variant in the non-SMP normalized SomaScan data *Soma PCO Name:* Name of the associated variant in the non-SMP normalized SomaScan data *Soma PCO rsName:* RS name of the associated variant in the non-SMP normalized SomaScan data *Soma PCO MAF PC:* Minor allele frequency of the associated variant in the non-SMP normalized

SomaScan data (%)

Soma PCO close genes: Genes close to the associated variant in the non-SMP normalized SomaScan data

ST30: Correspondence between pleiotropic trans pQTLs on the Olink (UKB-BI) and SomaScan (Iceland) platforms

Chrom: Chromosome of the variant Pos (hg38): Position of the variant rsName: RS name of the variant MAF (%): Minor allele frequency of the variant (%)

ST31: Cis pQTLs in high LD with disease-associated variants from the GWAS catalog

Chrom: Chromosome of the variant
Pos: Position of the variant
variant: Variant name
pQTL ID: ID of the pQTL (including platform)
Olink ID: Internal Olink ID of the assay
SeqId: Internal SomaLogic ID of the assay
gene prot: Name of the gene encoding the targeted protein
close genes: Genes close to the variant
source: Source of the pQTL (Olink data, SMP normalized SomaScan data, non-SMP normalized SomaScan data)
r2: r2 between the pQTL variant and the variant in the GWAS catalog
GWAS EFO: Experimental Factor Ontology reported in the GWAS catalog
GWAS P: Significance of the association reported in the GWAS catalog

GWAS PMID: PubMed ID of the article reporting the association in the GWAS catalog
GWAS PHENO: Phenotype reported in the GWAS catalog
GWAS PHENO TEXT: Information describing context of GWAS phenotype (e.g. females, smokers).
pQTL log10 p: Significance of the pQTL association. Negative log10 of p-value.
pQTL Effect amin: Effect of the minor allele of the pQTL
MAF PC: Minor allele frequency of the pQTL variant (%)
credible set: Indicator if the GWAS catalog variant is included in the credible set of variants for the pQTL

ST32: Trans pQTLs in high LD with disease-associated variants from the GWAS catalog

Chrom: Chromosome of the variant *pQTL ID:* ID of the pQTL (including platform) Olink ID: Internal ID of the Olink assay gene prot: Name of the gene encoding the protein N prot: Number of proteins associating with the variant GWAS EFO: Experimental Factor Ontology reported in the GWAS catalog N GWAS EFO: Number of EFOs reported in the GWAS catalog GWAS RSID: RS name of variants reported in the GWAS catalog MAF PC: Minor allele frequency of the pQTL variant (%) prop in credible set: Proportion of the GWAS catalog variants included in the credible set of variants for the pQTL source: Platform where the pQTL was detected gene at locus: Closest gene to pQTL variant linked protein(s): Proteins among the associated proteins ("gene prot") that are linked to "gene at locus" according to STRING database (see below) STRING score(s): STRING scores corresponding to linked proteins

ST33: Summary of the numbers of pQTLs associating with disease-associated variants from the GWAS catalog using LD and / or credible sets

Platform: Platform where the pQTL is detected
Entity: Objects being counted
Total count r2 only: Number of pairs of items where the associated variants are in high LD
Cis only count r2 only: Number of pairs of items involving only cis pQTL associations where the associated variants are in high LD
Trans only count r2 only: Number of pairs items involving only trans pQTL associations where the associated variants are in high LD
Cis and Trans count r2 only: Number of pairs items involving both cis and trans pQTL associations where the associated variants are in high LD
Cis and Trans count r2 only: Number of pairs items involving both cis and trans pQTL associations where the associated variants are in high LD
Total count r2 and credible set: Number of pairs of items where the associated variants are in high LD and the GWAS catalog variant is in the credible set for the pQTL associations where the associated variants are both in high LD and the GWAS catalog variant is in the credible set for the pQTL associations where the associated variants are both in high LD and the GWAS catalog variant is in the credible set for the pQTL associations where the associated variants are both in high LD and the GWAS catalog variant is in the credible set for the pQTL associations where the associated variants are both in high LD and the GWAS catalog variant is in the credible set for the pQTL associations where the associated variants are both in high LD and the GWAS catalog variant is in the credible set for the pQTL association.

- *Trans only count r2 and credible set:* Number of pairs of items involving only cis pQTL associations where the associated variants are both in high LD and the GWAS catalog variant is in the credible set for the pQTL association.
- *Cis and Trans count r2 and credible set:* Number of pairs items involving both cis and trans pQTL assocations where the associated variants are in high LD and the GWAS catalog variant is in the credible set for the pQTL association.

ST35: Replication of pQTLs detected in the Olink data (UKB-BI) in the Icelandic Olink data (n=1,514)

Chrom: Chromosome of variant *Pos:* Position of variant Name: Name of variant OlinkID: Internal Olink ID of assay Affected Protein Gene name: Name of the gene encoding the protein *pQTL ID:* ID of the pQTL cis_trans: Indicator if the pQTL is cis or trans for the protein rsName: RS name of the variant MAF PC: Minor allele frequency of the variant (%) Info: Imputation info of the variant Amin: Minor allele of the variant Amaj: Major allele of the variant close_genes: Genes close to the variant Log10 Pval UK: Significance of the pQTL in the UKB-BI data. Negative log10 of the p-value. *Effect_Amin_UK:* Effect of the minor allele in the UKB-BI data. Pval_Iceland: Significance of the pQTL in the Icelandic Olink data Effect Amin Iceland: Effect of the minor allele in the Icelandic Olink data Same Direction: Indicator if the direction of effect in the UKB-BI and Icelandic Olink data is concordant *Replicates:* Indicator if the UKB-BI association is replicated in the Icelandic Olink data (P<0.05)

ST36: Replication of pQTLs detected in the Olink data (UKB-BI) in the SomaScan data (Iceland)

Chrom: Chromosome of the variant Pos_IS: Position of the variant in the Icelandic data Name_IS: Name of the variant in the Icelandic data Pos_UK: Position of the variant in the UKB-BI data Name_UK: Name of the variant in the UKB-BI data pQTL_ID: pQTL ID in the UKB-BI data cis_trans: Indicator if the pQTL is cis or trans for the protein gene_prot: Name of the gene encoding the protein SeqId: Internal SomaLogic assay ID OlinkID: Internal Olink assay ID rsName: RS name of the variant close_genes: Genes close to the variant Amin: Minor allele of the variant Amaj: Major allele of the variant

Info_UK: Imputation info in the UKB-BI data set
MAF_PC_UK: Minor allele frequency of the variant in the UKB-BI data set (%)
Info_IS: Imputation info in the Icelandic data set
MAF_PC_IS: Minor allele frequency of the variant in the Icelandic data set (%)
P_UK: Significance of the association in the UKB-BI data set
Effect_Amin_UK: Effect of the minor allele in the UKB-BI data set
P_IS: Significance of the association in the Icelandic data set
Effect_Amin_IS: Effect of the minor allele in the Icelandic data set
Effect_Amin_IS: Effect of the minor allele in the Icelandic data set
Same_direction: Indicator if the direction of effect is concordant between the UKB-BI and Icelandic data sets
P_repl_nom: The replication in the Icelandic data set reaches Bonferroni-corrected significance

ST37: Replication of pQTLs detected in the SomaScan data (Iceland) in the Olink data (UKB-BI)

See S21

ST38: Correlation between pQTLs and credible set variants for pQTLs detected using Olink in the UKB-BI data set

Chrom: Chromosome of the variant Pos: Position of the variant *OlinkID:* The internal Olink ID of the assay Affected_Protein_Gene_name: Name of the gene encoding the associated protein *pQTL_ID:* Global identifier of the pQTL region ID prot: Protein-specific indicator of sentinel pQTL association CisOrTrans: Indicator if the pQTL association is cis or trans *Marker:* The variant associating with the protein levels rsName: RS name of the variant MAF_PC: Minor allele frequency of the variant (%) Info: Imputation info of the variant Amin: Minor allele of the variant Amaj: Major allele of the variant *close_genes:* Closest genes to the variant Log10_pval_gc_cor_unadj: Significance of the association without adjusting for other signals at the locus. Negative log10 of the p-value. Log10 pval qc cor adj: Significance of the association, adjusted for higher-rank signals at the locus. Negative log10 of the p-value. *Effect_Amin_unadj:* Effect of the minor allele of the variant without adjusting for other signals at the locus. *Effect_Amin_adj:* Effect of the minor allele of the variant, adjusted for higher-rank signals at the locus. *RankWithinLocus:* Rank in step-wise conditional analysis, where sentinel variants have rank=1 and secondary variants rank 2, 3, and so on

NumberWithinLocus: Number of significant variants in step-wise conditional analysis *SentinelMarker:* The variant at the locus with the most significant association with the protein *Affected Protein Gene chrom:* Chromosome of the gene encoding the protein

Affected Protein Gene chromstart: Start of the gene

Affected Protein Gene chromend: End of the gene

Strand: Strand of the gene

cis_eQTL_genes: Genes that harbor an eQTL variant in high LD with pQTL variant

PAV_genes: Genes that harbor a protein-altering (coding) variant in high LD with pQTL variant *UniProt:* UniProt ID of the protein

- r2cor_est: Estimated correlation between a) r² between the sentinel pQTL and other variants in the credible set, calculated in the UKB dataset and b) r² between the sentinel pQTL and other variants in the credible set, calculated in the Icelandic dataset
- *r2cor_l95:* Lower limit of 95% confidence interval corresponding to r2cor_est.
- *r2cor_u95:* Upper limit of 95% confidence interval corresponding to r2cor_est.
- *r2_IS_min:* Minimum r² between the sentinel pQTL and other variants in the credible set, calculated in the Icelandic dataset
- *r2_IS_median:* Median r² between the sentinel pQTL and other variants in the credible set, calculated in the Icelandic dataset
- *r2_IS_mean:* Mean r² between the sentinel pQTL and other variants in the credible set, calculated in the Icelandic dataset
- r2_IS_max: Maximum r² between the sentinel pQTL and other variants in the credible set, calculated in the Icelandic dataset
- *r2_UK_min:* Minimum r² between the sentinel pQTL and other variants in the credible set, calculated in the UKB dataset
- *r2_UK_median:* Median r² between the sentinel pQTL and other variants in the credible set, calculated in the UKB dataset
- *r2_UK_mean:* Mean r² between the sentinel pQTL and other variants in the credible set, calculated in the UKB dataset
- *r2_UK_max:* Maximum r² between the sentinel pQTL and other variants in the credible set, calculated in the UKB dataset
- n_r2 : Number of pairs of r² values used in the calculation of the estimated correlation in r2cor_est

ST39: Correlation between pQTLs and credible set variants for pQTLs detected using SomaScan in the Icelandic data set

Chrom: Chromosome of the variant Pos: Position of the variant Marker: The variant associating with the protein levels Seqld: The SomaLogic internal ID of the assay locusID_global: Global identifier of the pQTL locusID_prot: Protein-specific indicator of sentinel pQTL association gene_prot: Name of the gene encoding the associated protein chr_prot: Chromosome of the gene encoding the protein strand_prot: Strand of the gene TSS_prot: Start of the gene transcription site shortname prot: Name of the protein *longname prot:* Full name of the protein UniProt: UniProt ID of the protein Variant: RS name of the variant (if applicable) LD class size: Number of variants in high LD with the variant LD class: Variants in high LD with the variant region start region end Amin: Minor allele of the variant Amaj: Major allele of the variant Info: Imputation info of the variant MAF PC: Minor allele frequency of the variant (%) cis_trans: Indicator if the pQTL association is in cis or trans closest genes: Closest genes to the variant cis_eqtl_coding_genes: Genes that harbor an eQTL variant in high LD with pQTL variant beta adj: Effect of the minor allele of the variant, adjusted for higher-rank signals at the locus beta unadj: Effect of the minor allele of the variant without adjusting for other signals at the locus *mLog10pval_adj:* Significance of the association, adjusted for higher-rank signals at the locus. Negative log10 of the p-value

mLog10pval_unadj: Significance of the association without adjusting for other signals at the locus.

Negative log10 of the p-value

rank_locus

count_locus

count_cis_eQTL_same_gene

prop_same_direction_cis_eqtl_same_gene

count_cis_eQTL_diff_gene

any_coding_same_gene

any_coding_diff_gene

Rank_Proteins_per_Locus

Count_Proteins_per_Locus

Rank_Loci_per_Protein

Count_Loci_per_Protein

Reported

Reported_rsid

Reported_P

Reported_PMID

Reported_r2

r2cor_est: Estimated correlation between a) r² between the sentinel pQTL and other variants in the credible set, calculated in the UKB dataset and b) r² between the sentinel pQTL and other variants in the credible set, calculated in the Icelandic dataset

r2cor_l95: Lower limit of 95% confidence interval corresponding to r2cor_est.

r2cor_u95: Upper limit of 95% confidence interval corresponding to r2cor_est.

r2_IS_min: Minimum r² between the sentinel pQTL and other variants in the credible set, calculated in the Icelandic dataset

- *r2_IS_median:* Median r² between the sentinel pQTL and other variants in the credible set, calculated in the Icelandic dataset
- *r2_IS_mean:* Mean r² between the sentinel pQTL and other variants in the credible set, calculated in the Icelandic dataset
- *r2_IS_max:* Maximum r² between the sentinel pQTL and other variants in the credible set, calculated in the Icelandic dataset
- *r2_UK_min:* Minimum r² between the sentinel pQTL and other variants in the credible set, calculated in the UKB dataset
- *r2_UK_median:* Median r² between the sentinel pQTL and other variants in the credible set, calculated in the UKB dataset
- *r2_UK_mean:* Mean r² between the sentinel pQTL and other variants in the credible set, calculated in the UKB dataset
- *r2_UK_max:* Maximum r² between the sentinel pQTL and other variants in the credible set, calculated in the UKB dataset
- n_r2 : Number of pairs of r² values used in the calculation of the estimated correlation in r2cor_est