# Inflammation pQTLs – findings from the SCALLOP consortium

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## Abstract

BACKGROUND. METHODS. FINDINGS. INTERPRETATION.

## Introduction

We report pQTLs associated with OLINK/INF1 panel, using cohorts in the SCAndinavian coLLaboration for Olink plasma Protein genetics (SCALLOP) consortium, a collaborative framework for discovery and follow-up of genetic associations with proteins on the Olink Proteomics platform.

The objectives of the study are as follows

* Identification of pQTLs in SCALLOP discovery cohorts
* Study of pQTLs in replication cohorts
* Investigation of the mechanistic basis of identified cis- and trans-pQTL by functional annotation
* Examination of pQTL pleiotropic effects
* Evaluation over the causal role of INF proteins disease outcomes such as CHD and stroke
* Other downstream analysis

## Data and analysis

### Proteins

The Olink INFlammation panel of 92 proteins, e.g,

### SNPs

* 1000 genomes imputation, build 37 (hg19) positions.
* SNPs filtering on imputation quality at time of meta-analysis.
* Quality control on aspects such as SNP/sample call rates, gender mismatch, abnormal inbreeding coefficient, failed cryptic relatedness test, ancestry outlier, heterozygosity and Hardy-Weinberg equilibrium test.

### Association analysis

* Rank-based inverse normal transformation on the raw measurement of proteins including those below lower limit of detection.
* Multiple linear regression for all samples including sex, age, principal components and other cohort specific covariates.
* Additive genetic model
* For case-control data, cases and controls are analysed separately – results were merged at meta-analysis stage

Software which account for genotype uncertainty, such as SNPTEST were used but due to the relatively large number of proteins, results based on PLINK were also accepted, both amended with outputs from qctool –snp-stats.

## Meta-analysis

Meta-analysis will be performed centrally using the inverse-N weighted analysis of regression betas and standard errors, as implemented in the software METAL.

Genomic control and appropriate marker filters will be applied at this stage.

* **Marker exclusion filters**: we will apply imputation quality filters at the meta-analysis stage, so provide unfiltered results.
* **Genomic control (GC)**: genomic control will be applied at the meta-analysis stage (single GC), so GC-correction is not needed for each cohort.
* **Significance**: the Bonferroni threshold for the genome-wide analyses will be set at 5 x 10-10. The results will be replicated in independent cohorts.

## Contact information

For general questions about SCALLOP, please contact Anders Malarstig (anders.malarstig@ki.se). For technical issues about TRYGGVE, please contact Lasse Folkersen (lasfol@cbs.dtu.dk).

For questions regarding SCALLOP/INF, please contact Jing Hua Zhao (jhz22@medschl.cam.ac.uk) and James Peters ([jp549@medschl.cam.ac.uk](mailto:jp549@medschl.cam.ac.uk)).

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## References

Folkersen L, et al. (2017). Mapping of 79 loci for 83 plasma protein biomarkers in cardiovascular disease. PLoS Genetics 13(4), doi.org/10.1371/journal.pgen.1006706.

Kwan JSH, et al. (2014). Meta-analysis of genome-wide association studies identiﬁes two loci associated with circulating osteoprotegerin levels. Hum Mol Genet 23(24): 6684–669.

Sun BB, et al. (2018). Genomic atlas of the human plasma proteome. Nature 558: 73–79.

## Supplementary information

URL:

SCALLOP, <https://www.olink.com/scallop/>

OLINK/INF1 panel, <https://github.com/jinghuazhao/INF/blob/master/doc/olink.inf.panel.annot.tsv>.

METAL <https://github.com/statgen/METAL>

PLINK, <http://zzz.bwh.harvard.edu/plink>

Uniprot, [https://www.uniprot.org](https://www.uniprot.org/)