# SCALLOP consortium analysis plan for INF panel proteins

***Adapted from SCALLOP/CVD1 analysis plan, last updated 7/12/2018***

Timeline for completing cohort-specific analyses and uploading the results for this project:



## 1. Overview

The SCAndinavian coLLaboration for Olink plasma Protein genetics (SCALLOP) consortium, https://www.olink.com/scallop/, is a collaborative framework for discovery and follow-up of genetic associations with proteins on the Olink Proteomics platform. A meta-analysis has been conducted on Olink CVD1 panel data from participating cohorts; consequent requests were sent and contributions made on the Olink INF panel. This document follows closely the SCALLOP/CVD1 analysis plan for the analysis, and in particular highlights relevant information required to facilitate the meta-analysis.

As with the CVD1 meta-analysis, the tasks will involve

* 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

## 2. Data and analysis

### Proteins

The Olink INFlammation panel of 92 proteins, e.g, https://github.com/jinghuazhao/INF/blob/master/doc/olink.inf.panel.annot.tsv.

### 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, e.g., via invnormal function,
* invnormal <- function(x) qnorm((rank(x,na.last="keep")-0.5)/sum(!is.na(x)))
* 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 will be merged at meta-analysis stage

### Software

It is preferable to use software which account for genotype uncertainty, such as SNPTEST, QUICKTEST, and BOLT-LMM.

## 3. Descriptive statistics

A [Google sheet](https://tinyurl.com/y76f5mv5) has been set up for filling up the information online; in order to do so please contact us via email to add you in.

<https://tinyurl.com/ycf5vkhn>

Alternatively, please fill out the spreadsheet as with SCALLOP/CVD1 with naming convention:

* STUDY.descriptives.DATE.xls
* Where STUDY is a short (14 characters or less) identifier for the population studied, which is the same for all files provided by your study.
* DATE is the date on which the file was prepared, in the format “DDMMYYYY”.

## 4. File formats for GWAS results

### SNP table for GWAS results

Please include the following columns. Missing values are coded as “NA”.

|  |  |  |
| --- | --- | --- |
| No | Variable name | Description of variable |
| 1 | SNPID | CHR:POS\_A1\_A2 (such that A1-10. The results will be replicated in independent cohorts. |

## 6. Uploading of results

See the CVD1 analysis plan.

## 7. 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).

## Appendix

**SLURM script for qctool 2.0.1**

This is called with sbatch qctool.sb, where qctool.sb contains the following lines:

#!/bin/bash --login  
# 6-12-2018 JHZ  
  
#SBATCH -J qctool  
#SBATCH -o qctool.log  
#SBATCH -p long  
#SBATCH -t 4-0:0  
#SBATCH --export ALL  
#SBATCH --nodes=1  
#SBATCH --ntasks-per-node=1  
#SBATCH --cpus-per-task=8  
  
export DIR=/scratch/bp406/data\_sets/interval\_subset\_olink/genotype\_files/unrelated\_4994\_pihat\_0.1875\_autosomal\_typed\_only  
export INTERVAL=$DIR/interval\_olink\_subset\_unrelated\_4994\_pihat\_0.1875\_autosomal\_typed\_only  
ln -sf $INTERVAL.bgen INTERVAL.bgen  
ln -sf $INTERVAL.sample INTERVAL.sample  
  
# to obtain SNP-specific statistics as in .bgen and .sample format with qctool, tested with qctool 2.0.1  
  
qctool -g INTERVAL.bgen -s INTERVAL.sample -snp-stats -osnp INTERVAL.snp-stats -sample-stats -osample INTERVAL.sample-stats  
  
# Note in particular: the # option allows for chromosome-specific analysis; the -strand option will enable results in positive strand.