CAP (Cholesterol And Pharmacogenetics) Simvastatin Study Data Summary

Genotype Data: Illumina HumanHap 300K beadchip or Illumina HumanHap 610K-Quad beadchip

Genotypes at 317,503 SNPs are provided for 305 Caucasian individuals (self-reporting at least 3 Caucasian grandparents)

Genotypes at 620,901 positions are provided for 282 additional Caucasians self-reporting at least 3 Caucasian grandparents (Note: some of these positions were assayed for copy number only and are not SNPs, so those genotypes are set to missing.)

PLINK binary (.bed, .bim, and .fam) files including the data for all 587 genotyped individuals are provided.

- ***CAP300and610K.bed***

  Binary file containing all of the genotypes. Can be converted to various human-readable formats using PLINK: http://pngu.mgh.harvard.edu/~purcell/plink/data.shtml#bed

- ***CAP300and610K.bim***

  Extended map file containing the following 6 columns:

  chromosome # - 1-26
  rs# or snp identifier
  Genetic distance (morgans) – set to 0 for all
  Base-pair position (bp units) – on hg18
  Allele 1 name
  Allele 2 name

  Chromosome codes:

X = X chromosome	-> 23
Y = Y chromosome	-> 24
XY = Pseudo-autosomal region of X	-> 25
MT = Mitochondrial	-> 26

- ***CAP300and610K.fam***

  Pedigree information file containing the following 6 columns:

  Family ID – same as Ceders ID from phenotype file
  Individual ID – set to 1 for everyone
  Paternal ID – set to 0 for everyone
  Maternal ID – set to 0 for everyone
  Sex – male = 1, female = 2
  Phenotype – set to 1 for everyone

  Individuals who were genotyped on the 610K platform are listed first, followed by those genotyped on the 300K platform.

Phenotype Data: A variety of covariate and phenotype data for the 587 self-reported Caucasians

- ***587CAPphenotypeColumns.txt***

  Describes the contents of the 60 columns of 587CAPphenotypeData.txt

- ***587CAPphenotypeData.txt***

  Contains clinical covariate information (sex, race, age, BMI, smoking status), cellular covariate information (simvastatin exposure data, cell count, RNA hybridization batch, and array slide batch) for the expression array study described below, genotype array platform, and a variety of quantitative phenotypes measured in collected blood samples (Tg, TC, LDLC, HDLC, CRP, ApoAI, ApoB, ApoCIII, LDL subfractions, IDL subfractions, etc.). Phenotype measurements were taken on blood samples from the study subjects both before and after simvastatin was administered.

Expression Array Data: Expression profiles of 480 paired lymphoblastoid cell lines (simvastatin or sham buffer treated, 24 hours) generated using the Illumina Ref8v3 beadchip. All 480 individuals were self-reported Caucasians.

- ***B480CAPexpressionN.txt***

  Baseline (sham buffer treated) expression values adjusted for experimental traits (simvastatin exposure batch, array slide batch, RNA hybridization batch, cell growth rate) and clinical traits of the donors (age, BMI, smoking status, gender). Expression values are provided for the 12951 probes that were expressed in the LCLs as determined by GenomeStudio ($p<0.05$).

- ***T480CAPexpressionN.txt***

  Treatment (simvastatin treated) expression values adjusted for experimental traits (simvastatin exposure batch, array slide batch, RNA hybridization batch, cell growth rate) and clinical traits of the donors (age, BMI, smoking status, gender). Expression values are provided for the 12951 probes that were expressed in the LCLs as determined by GenomeStudio ($p<0.05$).

- ***12951_annotations.txt***

  Annotations for the 12951 probes that were expressed in the LCLs as determined by GenomeStudio ($p<0.05$)

Additionally, raw expression datasets that are not adjusted for covariates and gene-based expression datasets are available upon request.

Relevant Publications:

- *GWAS meta-analysis:*
  - Barber, M.J., Mangravite, L.M., Hyde, C.L., Chasman, D.I., Smith, J.D., McCarty, C.A., Li, X., Wilke, R.A., Rieder, M.J., Williams, P.T., Ridker, P.M., Chatterjee A., Rotter, J.I., Nickerson, D.A., Stephens, M. and Krauss, R.M. (2010). Genome-wide association of lipid-lowering response to statins in combined study populations. PLoS ONE, 5: e9763. PMID: 20339536, PMCID: PMC2842298

- *Clinical populations:*
    - Simon, J.A., Lin, F., Hulley, S.B., Blanche, P.J., Waters, D., Shiboski, S., Rotter, J.I., Nickerson, D.A., Yang, H., Saad, M., & Krauss, R.M. (2006). Phenotypic predictors of response to simvastatin therapy among African Americans and Caucasians: the Cholesterol and Pharmacogenetics (CAP) Study. Am J. Cardiology, 97, 843-850. PMCID: 16516587
- *Use of lymphoblastoid cell lines:*
    - Medina, M.W., Gao, F., Ruan, W., Rotter, J.I., & Krauss, R.M (2008). Alternative splicing of HMGCR is associated with plasma LDL cholesterol response to simvastatin. Circulation, 118, 355-362. PMCID: 18559695
    - Mangravite, L.M., Medina, M.W., Cui, J., Pressman, S., Smith, J.D., Rieder, M.J., Guo, X., Nickerson, D.A., Rotter, J.I., & Krauss, R.M. (2010). Combined influence of LDLR and HMGCR sequence variation on lipid-lowering response to simvastatin. Arterioscler. Thromb. Vasc. Biol., 30, 1485-92. PMID: 20413733, PMCID: PMC2909117