Code for Fadista et al.: "Comprehensive genome-wide association study of different forms of hernia identifies more than 80 associated loci"

FIGURES

Figure 2 / Supplementary Figure 2

Figure 2 was generated with adjusted P-values < 0.01 from each of the 7 analyzed hernia groups using the kpPlotManhattan function from the karyoploteR R package: https://bernatgel.github.io/karyoploter_tutorial/.
The underlying GWAS summary stats have been deposited at the Danish National Biobank: https://www.danishnationalbiobank.com/gwas.
The plots in Supplementary Figure 2 were also done with the kpPlotManhattan function from the karyoploteR R package (R version 3.6.1 with karyoploteR_1.16.0).

Figure 3

R code to generate Figure 3 (R version 4.0.3 with UpSetR_1.4.0).
The upper legend plot was inserted afterwards.

```
#########################################################################
library(UpSetR)
Inguinal <- read.table("Directory/INGups.txt", header=F)
Umbilical <- read.table("Directory /UMBups.txt", header=F)
Femoral <- read.table("Directory /FEMups.txt", header=F)
Ventral <- read.table("Directory/VENTRups.txt", header=F)
Diaphragmatic <- read.table("Directory/DIAups.txt", header=F)
colnames(Inguinal) <- "Inguinal"
colnames(Umbilical) <- "Umbilical"
colnames(Femoral) <- "Femoral"
colnames(Ventral) <- "Ventral"
colnames(Diaphragmatic) <- "Diaphragmatic"
listInput <- list(Inguinal = as.character(Inguinal$Inguinal),
Diaphragmatic=as.character(Diaphragmatic$Diaphragmatic), Umbilical=as.character(Umbilical$Umbilical),
Femoral=as.character(Femoral$Femoral), Ventral=as.character(Ventral$Ventral))
upset(fromList(listInput), mainbar.y.label = "Number of loci", sets.x.label = "Total number of loci involved",
text.scale = c(1.5, 1.5, 1.5, 1.5, 1.5),
main.bar.color =
c("#000000","#000000","#000000","#000000","#E69F00","#E69F00","#E69F00","#E69F00","#E69F00","#0072B2"
,"#0072B2","#0072B2","#0072B2","#D55E00","#CC79A7"))
#########################################################################
```

Related files: input files in ***UpSet_data.zip***.

Figure 4 / Supplementary Figure 3

DEPICT plots were generated from the configuration and input files:

DEPICTFig4_tissue_plot.R	- R script to generate Fig 4
DEPICTFig4a_inputtissue_plotING.txt	- dataset for Fig 4a
DEPICTFig4b_inputtissue_plotANY.txt	- dataset for Fig 4b
DEPICTSupplFig3a.cfg	- configuration file for Supplementary Figure 3a
DEPICTSupplFig3b.cfg	- configuration file for Supplementary Figure 3b
DEPICTSupplFig3a_network_table	- dataset for Supplementary Figure 3a
DEPICTSupplFig3b_genesetID_GO0048598_network_table.txt	- dataset for Supplementary Figure 3b

Figure 5
The plot was generated in the GARFIELD run described below. The underlying data from Supplementary Data 6 are provided in the Source Data.

Figure 6
The genetic correlation plot is based on the corrplot function used here: GitHub - mkanai/ldsc-corrplot-rg: corrplot of LDSC genetic correlation results
The underlying data are provided in the Source Data.
R code to generate Figure 6 (R version 3.6.1 with corrplot_0.85).

```
##########################################################################
module load tools
module load gcc
module load intel/perflibs
module load R/3.6.1
Rscript plot_corrplot_rg_v2.R input_example/input_rg_hernias.txt input_example/traitlist_v2.txt
##########################################################################
```

Related files: R script ***plot_corrplot_rg_final.R***, input files ***input_rg_hernias.txt*** and ***traitlist_v2.txt***.

Supplementary Figure 1
Quantile-quantile plots were generated with the R code provided in ***QQplot_inguinal.R*** (R version 3.2.0).

ANALYSES

GWAS scans

We ran SAIGE (GitHub - weizhouUMICH/SAIGE) with sex, yob and PCA1 to PCA6 generated by flashPCA v2.0 (GitHub - gabraham/flashpca) for the British ancestry individuals.

Command for the Inguinal hernia GWAS (all the other GWAS have similar commands, and the sex-specific analysis have sex removed from the covariates):

```
#########################################################################
qsub -W group_list=ssi_gen1 -A ssi_gen1 -l nodes=1:ppn=28,mem=100gb,walltime=99:00:00
fit_nullModel_ING.r.flashPCA2.r
qsub -W group_list=ssi_gen1 -A ssi_gen1 -l nodes=1:ppn=28,mem=100gb,walltime=99:00:00:00 spa_chr1-
22.r.ING_flashPCA2.bash
#########################################################################
```

Related files: ***fit_nullModel_ING.r.flashPCA2.r*** and ***spa_chr1.r.ING_flashPCA2.r***.

GCTA-COJO

We ran GCTA-COJO v.1.26.0 with the following command:

```
#########################################################################
qsub -W group_list=ssi_gen1 -A ssi_gen1 -l nodes=1:ppn=28,mem=100gb,walltime=99:00:00:00
cojo_slct_MAFge05padj.p1e-5.bash
#########################################################################
```

Related file: ***cojo_slct_MAFge05padj.p1e-5.bash***.

Meta-analysis in METAL

METAL (version 2011.03.25) was run with the configuration provided in ***METALmeta.txt***

MultiPhen

MultiPhen (version 2.0.2) was run with the configuration provided in the R script ***MultiPhen_phenos.R***.

FUMA / MAGMA

FUMA / MAGMA analyses were run with FUMA (v 1.3.6) via the web on June 23 and 24, 2020, and the specifications and results are available in the public results section with IDs 424 to 430 (https://fuma.ctglab.nl/browse, author Frank Geller, titles UK Biobank followed by the respective hernia group).

DEPICT analysis

DEPICT (version 1 rel194) was run with the configuration provided in ***DEPICTrunING.cfg***.

GARFIELD

GARFIELD (v2) was run with the configuration provided in ***GARFIELD_ukbING.txt*** and the R script ***GARFIELD-plot2thresh.R***.

Gene Network

We generated Gene Network (version 2.0, accession date 12/15/2020, https://www.genenetwork.nl/) results for the HPO term inguinal hernia for the 192 genes studied in the DEPICT inguinal hernia gene prioritization.

Heritability

Heritability was estimated for the five hernia types by applying LD score regression, HESS and LDAK to the UK Biobank discovery GWAS scans. Heritability was transformed to the liability scale with GEAR (https://sourceforge.net/p/gbchen/wiki/Hong%20Lee's%20Transformation%20for%20Heritability/).
LD score regression heritability of each hernia GWAS and respective genetic correlations with other disease/traits were done in the LD hub website: http://ldsc.broadinstitute.org/

HESS v0.5.4-beta code using Inguinal hernia as an example:

```
######################################################################
for chrom in $(seq 22)
do
   python /services/tools/hess/0.5.4-beta/hess.py \
      --local-hsqg INGallMAFge05pSEadj_toLDhub.txt.to_HESS.txt \
      --chrom $chrom \
      --bfile 1kg_eur_1pct/1kg_eur_1pct_chr${chrom} \
      --partition ldetect-data/fourier_ls-chr${chrom}.bed \
      --out step1_ING
done

python /services/tools/hess/0.5.4-beta/hess.py --prefix step1_ING --out step2_ING
python /services/tools/hess/0.5.4-beta/hess.py --prefix step1_ING --reinflate-lambda-gc 1.1175 --out
step2_ING_reinflate-lambda-gc
######################################################################
```

LDAK v5.1 code:

```
######################################################################
for i in *to_LDAK.txt; do ldak --sum-hers $i.snpher --summary $i --tagfile bld.ldak.hapmap.gbr.tagging --cutoff
0.01 --check-sums NO; done
######################################################################
```

Mendelian randomization

Mendelian randomization analyses were done in R version 4.0.3 using packages MendelianRandomization_0.5.0 and MRPRESSO_1.0. Random-effects inverse-variance weighted method (IVW), simple median (weighted median with simple median weighting) and MR-Egger analyses (from the MendelianRandomization R package) were performed with default settings. The mr_presso function (from the MRPRESSO R package) was performed with the settings “OUTLIERtest = TRUE, DISTORTIONtest = TRUE, data = SummStats, NbDistribution = 1000, SignifThreshold = 0.05” .