

Transcriptome-Wide Association Study Pipeline (TWAS-pipeline)

INSTALLATIONS

--- TWAS ---

The following packages by the developers

Package	URLs
TWAS	http://sashagusev.github.io/TWAS/
weight files	https://data.broadinstitute.org/alkesgroup/TWAS/
z-score clean program	https://data.broadinstitute.org/alkesgroup/TWAS/ETC/CLEAN_ZSCORES.tar.bz2

are required and be unpacked. In addition, lists of genes in the three populations are made through the following scripts,

```
TWAS=/genetics/bin/TWAS
cd $TWAS
for pop in MET NTR YFS
do
  ls WEIGHTS_$1 | sed 's\\/\\"g' > $pop.lst
done
```

--- **TWAS-pipeline** ---. The pipeline is installed as follows,

```
git clone https://github.com/jinghuazhao/TWAS-pipeline
```

On our system, TWAS.sh and TWAS_get_weights.sh for TWAS and twas.sh, twas2.sh, twas2-collect.sh and twas2-1.sh for TWAS-pipeline have symbolic links under /genetics/bin and available from the \$PATH environment. A [Stata](#) equivalent has been developed by Dr Jian'an Luan.

To accommodate the suggestion of p value in accordance with the Z-score in the output, pnorm.c is included which can be compiled as follows,

```
gcc pnorm.c -lm -o pnorm
```

and a call pnorm z_score yields a p value with more decimal places.

--- **GNU Parallel** ---. Further information is available from [here](#).

RUNNING THE PIPELINE

Suppose you have a file containing GWAS summary statistics, you can run the pipeline as follows,

```
twas.sh input_file
```

where the `input_file` is in tab-delimited format containing `SNP_name`, `SNP_pos`, `Ref_allele`, `Alt_allele`, `Beta` and `SE`. The output will be contained in `<input_file>.imp`.

This assumes that `ssh` can access nodes in a clusters freely and in case this has not been done, a single node mode is more appropriate,

```
twas-single.sh input_file
```

TWAS using GTEx

This is achieved with `gtex.sh` and `gtex.subs` using weights from the GTEx project. File `GTEx_WEIGHTS.bim.gz` was created by `GTEx_WEIGHTS.sh` in accordance with reference `.bim` files used by TWAS and `GTEx_WEIGHTS.lst` was created to facilitate the imputation.

Additional topics are available from the wiki,

- [BUILDING REFERENCE PANEL](#)
- [AN EXPOSITION WITH GIANT DATA](#)
- [EPIGENOMEWIDE ASSOCIATION](#)
- [FUSION pipeline](#)

ACKNOWLEDGEMENTS

The work is possible with an EWAS project within the MRC Epidemiology Unit, for which colleagues and collaborators have contributed.

REFERENCES

Gusev A, et al. (2016). Integrative approaches for large-scale transcriptome-wide association studies. *Nature Genetics*, 48, 245-252