mTADA

This notebook descibes steps used to jointly analyze two traits by mTADA .

I. Introduction

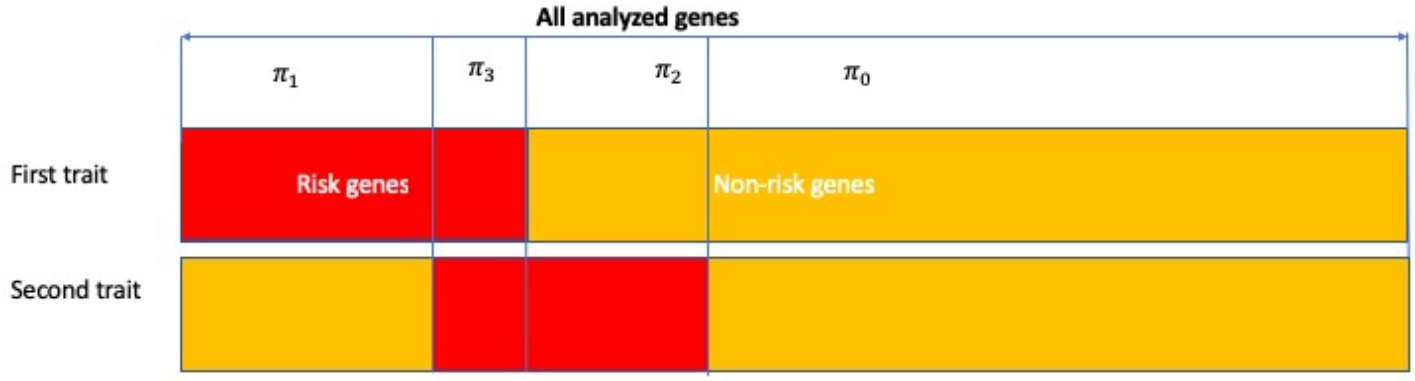
mTADA jointly analyze de novo mutations (DNMs) of two traits to 1) estimate the gene-level genetic overlap of the two traits; 2) report shared and specific risk genes; and 3) identify additional risk genes for each analyzed trait.

The method requires genetic parameters from single-trait analyses (the third and fourth columns in Table 1 below). Users can obtain single-trait parameters from extTADA/TADA methods.

Table 1. mTADA model for one variant category at the i^{th} gene.

Hypothesis	Proportion	First trait	Second trait
H_0	π_0	$x_{i1} \sim Poisson(2N_1\mu_i)$	$x_{i2} \sim Poisson(2N_2\mu_i)$
H_1	π_1	$x_{i1} \sim Poisson(2N_1\gamma_1\mu_i)$; $\gamma_1 \sim Gamma(\bar{\gamma}_1\beta_1, \beta_1)$	$x_{i2} \sim Poisson(2N_2\mu_i)$
H_2	π_2	$x_{i1} \sim Poisson(2N_1\mu_i)$	$x_{i2} \sim Poisson(2N_2\gamma_2\mu_i)$; $\gamma_2 \sim Gamma(\bar{\gamma}_2\beta_2, \beta_2)$
H_3	π_3	$x_{i1} \sim Poisson(2N_1\gamma_1\mu_i)$; $\gamma_1 \sim Gamma(\bar{\gamma}_1\beta_1, \beta_1)$	$x_{i2} \sim Poisson(2N_2\gamma_2\mu_i)$; $\gamma_2 \sim Gamma(\bar{\gamma}_2\beta_2, \beta_2)$

Figure 1. mTADA framework.



Data for reproducible analyses

Data used in the main manuscript are inside the folder data (data):

1. FullDataSet_DenovoMutations_for_mTADA.txt (data/FullDataSet_DenovoMutations_for_mTADA.txt): all gene-level de novo mutations. These DNMs are used in the main manuscript.
2. SingleTrait_Parameters.txt (data/SingleTrait_Parameters.txt): all single-trait parameters. We used `extTADA` to estimate these parameters from the DNMs above.

   Note: Users can re-run all these single-trait analyses by following an example here: https://github.com/hoangtn/extTADA (https://github.com/hoangtn/extTADA).

II. Requirements

`mTADA` is written in `R`. Other `R` packages are required to run `mTADA`:

- `rstan`: https://mc-stan.org/rstan/ (https://mc-stan.org/rstan/).
- `locfit`: https://cran.r-project.org/web/packages/locfit/index.html (https://cran.r-project.org/web/packages/locfit/index.html).

Software versions were used in our analyses: `R` version 3.5.2, `locfit` version 1.5-9.1, and `rstan` version 2.18.2.

III. An example: joint analysis of DD and EE DNMs

Only one function `mTADA` (in the **Run `mTADA`** section) is used to obtain results. Therefore, users can go directly to the **Run `mTADA`** section to run `mTADA`. However, some additional steps are described here.

Load the source codes

```
dataDir <- "./data/"
source("script/mTADA.R")
```

```
## locfit 1.5-9.1    2013-03-22
```

Read the data and single-trait parameters

```
## De novo data
data <- read.table(paste0(dataDir, "FullDataSet_DenovoMutations_for_mTADA.txt"), header
 = TRUE, as.is = TRUE)
## Single-trait parameters
sPar <- read.table(paste0(dataDir, "SingleTrait_Parameters.txt"), as.is = TRUE, header =
TRUE)

trait1 = "DD"
trait2 = "EE"
##Take a quick look at the single-trait parameters of DD and EE
sPar[grep(trait1, sPar[, 1]), ] ##Trait 1
```

```
##                 Parameter EstimatedValue
## 8                DD_pi[1]     0.02936283
## 9  DD_hyperGammaMeanDN[1]    22.31762802
## 10 DD_hyperGammaMeanDN[2]    86.03966530
## 11      DD_hyperBetaDN[1]     0.82594514
## 12      DD_hyperBetaDN[2]     0.80689775
```

```
sPar[grep(trait2, sPar[, 1]), ] ##Trait 2
```

```
##                 Parameter EstimatedValue
## 18               EE_pi[1]     0.01548789
## 19 EE_hyperGammaMeanDN[1]    51.08181282
## 20 EE_hyperGammaMeanDN[2]    65.15189031
## 21      EE_hyperBetaDN[1]     0.80906448
## 22      EE_hyperBetaDN[2]     0.80774192
```

Set parameters for two traits

As described above, `mTADA` needs single-trait parameters:

- the number of trios: *ntrio*;
- the mean and disperson parameters of relative risks: $bargamma\_j$ and β_j (j=1, 2);
- the proportion of risk genes: π_1^S and π_2^S.

All these parameters are shown above.

```
### Trait-1 INFORMATION
ntrio1 = 4293 #family numbers
p1 = 0.02936283 #The proportion of risk genes, this is p1S
meanGamma1 = c(22.31762802,  86.03966530) #Mean Gamma of two categories
beta1 = c(0.82594514, 0.80689775) #Beta values inside the distribution RR ~ Gamma(meanRR
*beta, beta)
dataT1 <- data[, paste0(c("dn_damaging_", "dn_lof_"), trait1)] #De novo data
muDataT1 <- data[, c("mut_damaging", "mut_lof")] #Mutation data of the first trait
########################################
### Trait-2 INFORMATION
ntrio2 = 356
p2 = 0.01548789 #This is p2S
meanGamma2 = c(51.08181282, 65.15189031)
beta2 = c(0.80906448, 0.80774192)
dataT2 <- data[, paste0(c("dn_damaging_", "dn_lof_"), trait2)]
muDataT2 <- muDataT1
```

Run `mTADA`

In this example, we only use a small number of iterations and two MCMC chains. However, users can change these parameters to obtain more reliable results.

```
nIteration = 2000 #This should be higher to obtain better results.
nChain = 2 #The number of MCMC chains

##########MAIN ANALYSIS
mTADAresults <- mTADA(geneName = data[, 1],
    #######Trait-1 information
                  ntrio1 = ntrio1, # Trio number of Trait 1
                  p1 = p1, #Risk-gene proportion of Trait 1
                  dataDN1 = data.frame(dataT1), #De novo data of Trait 1
                  mutRate1 = data.frame(muDataT1), # Mutation rates of Trait 1
                  hyperGammaMeanDN1 = c(meanGamma1), # Mean relative risks of Trait 1
                  hyperBetaDN01 = beta1, #NULL, #array(c(1, 1)),
    #######Trait-2 information
                  ntrio2 = ntrio2, # Trio number of Trait 2
                  p2 = p2, #Risk-gene proportion of Trait 2
                  dataDN2 = data.frame(dataT2), # De novo data of Trait 2
                  mutRate2 = data.frame(muDataT2), # Mutation rates of Trait 2
                  hyperGammaMeanDN2 = c(meanGamma2), # Mean relative risks of Trait 2
                  hyperBetaDN02 = beta2, #NULL, #array(c(1, 1)),
    ####Other parameters
                  nIteration = nIteration,
                  useMCMC = TRUE, #If FALSE, it will use the 'Variational Bayes' approac
h.
                  nChain = nChain
                      )
```

```
## No information for core numbers (nCore); therefore, nCore = nChain: 2 core(s) is/are
used

## Loading required package: ggplot2

## Loading required package: StanHeaders

## rstan (Version 2.18.2, GitRev: 2e1f913d3ca3)

## For execution on a local, multicore CPU with excess RAM we recommend calling
## options(mc.cores = parallel::detectCores()).
## To avoid recompilation of unchanged Stan programs, we recommend calling
## rstan_options(auto_write = TRUE)

## ==================
## Building the model
## ================

##
## =======Use MCMC==========

## recompiling to avoid crashing R session

## ====
## Only pi, alpha and hyper parameters are estimated in this step
## The method does not calculate HPDs for hyper betas, just their medians
## ===
```

Get results

`mTADA` 's output includes:

1. `data` : main gene-level results (posterior probabilities for the four models as described in the main manuscript: PP0, PP1, PP2 and PP3).
2. `probModel` : a vector of $\pi_j, (j = 0..3)$ in Table 1.
3. `pars` : the estimated value and credible interval of π_3 (described as p12 in the our code).
4. `mcmcData` : MCMC sampling results for π_3.

The most important information is from `data` . **Users can use this information to obtain top prioritized genes for downstream analyses (e.g., top shared/specific genes, top genes for each trait)**. However, we will also take a quick look at all these information.

Results for downstream analyses (gene-level posteior probabilities (PPs) of four models)

We demonstrate how to choose top proritized genes from `mTADA` 's results using a PP threshold of 0.8. These genes can be shared genes, specific genes; or genes for single traits.

```
fData <- mTADAresults$data ## Full analysis results of the two-trait analysis.
head(fData)
```

```
##   geneName dn_damaging_DD dn_lof_DD dn_damaging_EE dn_lof_EE        NO
## 1     A1BG              0         0              0         0 0.9783601
## 2 A1BG-AS1              0         0              0         0 0.9646035
## 3     A1CF              0         0              0         0 0.9892745
## 4      A2M              0         0              1         0 0.7687196
## 5  A2M-AS1              0         0              0         0 0.9636099
## 6    A2ML1              0         0              0         0 0.9918769
##           BOTH        FIRST      SECOND
## 1 0.0027968521 0.0103170918 0.008525977
## 2 0.0059043959 0.0206076714 0.008884411
## 3 0.0006301115 0.0027151990 0.007380160
## 4 0.0024240791 0.0002620490 0.228594301
## 5 0.0061341390 0.0213601262 0.008895786
## 6 0.0002035984 0.0009286126 0.006990863
```

Genes with PP3 > 0.8 (Posterior probabilities of Model 3)

```
fData[fData$BOTH > 0.8, ]
```

```
##       geneName dn_damaging_DD dn_lof_DD dn_damaging_EE dn_lof_EE
## 2348   CACNA1A              5         0              2         0
## 3201      CHD2              0         6              0         1
## 6254    GABBR2              2         0              2         0
## 6265    GABRB3              2         0              2         0
## 6610     GNAO1              4         1              2         0
## 7165     HECW2              5         1              1         0
## 7426    HNRNPU              0         7              0         1
## 8283     KCNQ2              9         0              2         0
## 8284     KCNQ3              3         0              1         0
## 10146      MLL              1        26              1         0
## 12480     PHIP              1         2              0         1
## 14673    SCN2A              9         4              2         0
## 14681    SCN8A              6         0              2         0
## 16228   STXBP1              6         5              4         1
##                  NO      BOTH        FIRST       SECOND
## 2348  3.156368e-04 0.9931599 4.013926e-03 2.510560e-03
## 3201  4.668500e-10 0.9349822 6.501777e-02 2.158151e-10
## 6254  2.546173e-03 0.9507336 1.729651e-03 4.499059e-02
## 6265  9.338741e-04 0.9792444 1.614628e-03 1.820708e-02
## 6610  1.622213e-08 0.9983506 1.649042e-03 3.157130e-07
## 7165  1.954506e-06 0.8884849 1.115127e-01 5.006059e-07
## 7426  8.875660e-13 0.9343115 6.568851e-02 4.058226e-13
## 8283  3.288808e-13 0.9981550 1.845015e-03 5.719657e-12
## 8284  4.359755e-03 0.9104263 8.368933e-02 1.524650e-03
## 10146 1.495782e-48 0.8634529 1.365471e-01 3.040590e-49
## 12480 1.482913e-02 0.8877874 9.282421e-02 4.559283e-03
## 14673 3.156474e-18 0.9963123 3.687715e-03 2.741407e-17
## 14681 4.280269e-06 0.9958090 4.153687e-03 3.298729e-05
## 16228 7.756999e-24 1.0000000 1.016192e-08 2.453867e-17
```

Genes with PP1 > 0.8 (Posterior probabilities of Model 1)

```
fData[fData$FIRST > 0.8, ]
```

```
##       geneName dn_damaging_DD dn_lof_DD dn_damaging_EE dn_lof_EE
## 347       ADNP              1        19              0         0
## 681    ANKRD11              0        32              0         0
## 1000    ARID1A              1         2              0         0
## 1001    ARID1B              0        30              0         0
## 1002     ARID2              0         3              0         0
## 1153     ASXL1              0         4              0         0
## 1155     ASXL3              0        14              0         0
## 1317     AUTS2              0         4              0         0
## 1450    BCL11A              2         3              0         0
## 1630     BRPF1              0         4              0         0
## 2355   CACNA1E              2         2              0         0
## 2434    CAMTA1              1         2              0         0
## 3202      CHD3              3         1              0         0
## 3203      CHD4              5         1              0         0
## 3206      CHD7              2         2              0         0
## 3457      CLTC              2         3              0         0
## 3516     CNOT3              2         2              0         0
## 3599  COL4A3BP              4         0              0         0
## 3773    CREBBP              7         3              0         0
## 3876   CSNK2A1              4         0              0         0
## 3924      CTCF              5         0              0         0
## 3942    CTNNB1              0        11              0         0
## 4632    DNMT3A              4         1              0         0
## 4832    DYRK1A              4        14              0         0
## 4861      EBF3              2         3              0         0
## 4903    EEF1A2              3         0              0         0
## 4948    EFTUD2              3         2              0         0
## 4974     EHMT1              2         7              0         0
## 5157     EP300              3        12              0         0
## 6120     FOXP1              4         8              0         0
## 6121     FOXP2              1         2              0         0
## 6351   GATAD2B              0         7              0         0
## 6606     GNAI1              5         0              0         0
## 7330    HIVEP2              2         2              0         0
## 7333       HK1              3         1              0         0
## 8168    KANSL1              0         8              0         0
## 8177     KAT6A              0         8              0         0
## 8178     KAT6B              0         8              0         0
## 8211     KCNB1              2         1              0         0
## 8228     KCNH1              4         0              0         0
## 8336     KDM5B              0         3              0         0
## 9618     LZTR1              2         1              0         0
## 9727    MAP4K4              3         2              0         0
## 9821      MBD5              0         3              0         0
## 9906    MED13L              5        13              0         0
## 9935     MEF2C              4         4              0         0
## 10670    MYT1L              2         2              0         0
## 10978     NFIX              1         4              0         0
## 11282     NSD1              1         7              0         0
## 12004    PACS1              8         0              0         0
## 12831     POGZ              0         6              0         0
## 12994    PPM1D              0         5              0         0
```

```
## 13062  PPP2R5D             12         0               0          0
## 13250  PRPF40A              1         2               0          0
## 13538    PUF60              0         3               0          0
## 13540     PUM2              1         2               0          0
## 13541     PURA              3         7               0          0
## 13599   QRICH1              0         3               0          0
## 14605    SATB2              4         8               0          0
## 14894    SETD2              1         2               0          0
## 14897    SETD5              2        14               0          0
## 15010   SHANK3              0         3               0          0
## 15074    SIN3A              1         3               0          0
## 15133  SLC12A2              2         1               0          0
## 15440   SLC6A1              6         2               0          0
## 15546  SMARCA2              9         0               0          0
## 15752      SON              0         3               0          0
## 15985    SRCAP              1         4               0          0
## 16337  SYNGAP1              0        13               0          0
## 16537  TBL1XR1              2         4               0          0
## 16578    TCF12              1         2               0          0
## 16581    TCF20              0         5               0          0
## 16587     TCF4              4         9               0          0
## 17284    TNPO3              1         2               0          0
## 17548   TRIP12              2         3               0          0
## 18337    WDR26              1         2               0          0
## 18420    WHSC1              0         3               0          0
##                  NO       BOTH     FIRST       SECOND
## 347   4.076700e-37 0.19465193 0.8053481 3.167503e-39
## 681   2.288871e-60 0.13400221 0.8659978 1.138544e-62
## 1000  8.444503e-02 0.11265787 0.8025160 3.810791e-04
## 1001  1.698387e-56 0.14147299 0.8585270 8.996828e-59
## 1002  2.188395e-03 0.16914194 0.8286553 1.435940e-05
## 1153  1.840748e-05 0.16713313 0.8328483 1.187474e-07
## 1155  2.518451e-25 0.19412114 0.8058789 1.950158e-27
## 1317  1.131522e-05 0.17891246 0.8210761 7.925989e-08
## 1450  7.443686e-07 0.18498008 0.8150192 5.430983e-09
## 1630  7.088960e-05 0.12826197 0.8716668 3.353229e-07
## 2355  4.889546e-02 0.08598278 0.8649655 1.562480e-04
## 2434  1.009580e-02 0.16477452 0.8250649 6.481503e-05
## 3202  5.950790e-02 0.10715368 0.8330924 2.460491e-04
## 3203  5.507747e-04 0.08451237 0.9149352 1.635449e-06
## 3206  4.681431e-02 0.09757541 0.8554386 1.716577e-04
## 3457  6.312271e-05 0.11373702 0.8861996 2.604289e-07
## 3516  1.530866e-04 0.17182201 0.8280239 1.021189e-06
## 3599  1.570226e-03 0.17954423 0.8188745 1.106750e-05
## 3773  1.295155e-10 0.09018929 0.9098107 4.127231e-13
## 3876  8.939816e-04 0.19122750 0.8078717 6.802519e-06
## 3924  3.486621e-05 0.18720809 0.8127568 2.581678e-07
## 3942  1.537751e-19 0.17648890 0.8235111 1.059418e-21
## 4632  3.842403e-05 0.16607543 0.8338859 2.459999e-07
## 4832  5.179249e-31 0.18200362 0.8179964 3.704492e-33
## 4861  8.597727e-07 0.18381289 0.8161862 6.224487e-09
## 4903  1.657449e-02 0.18034688 0.8029590 1.196710e-04
## 4948  2.497223e-05 0.14442457 0.8555503 1.355146e-07
## 4974  2.133419e-13 0.14195132 0.8580487 1.134585e-15
```

```
## 5157  4.059543e-23 0.10747500 0.8925250 1.571439e-25
## 6120  9.986252e-19 0.17037605 0.8296239 6.592696e-21
## 6121  5.419903e-03 0.17079259 0.8237514 3.612415e-05
## 6351  4.185648e-12 0.19940945 0.8005905 3.351439e-14
## 6606  1.518612e-05 0.19831115 0.8016735 1.207618e-07
## 7330  1.633915e-03 0.13646603 0.8618917 8.316382e-06
## 7333  2.798275e-03 0.13933118 0.8578559 1.461025e-05
## 8168  1.944443e-13 0.17756475 0.8224352 1.349533e-15
## 8177  2.067784e-12 0.14564487 0.8543551 1.133170e-14
## 8178  9.984733e-13 0.15292481 0.8470752 5.794630e-15
## 8211  8.645342e-03 0.17169806 0.8195984 5.822101e-05
## 8228  2.397887e-03 0.16493385 0.8326530 1.526890e-05
## 8336  3.002908e-02 0.11887309 0.8509630 1.348491e-04
## 9618  2.088935e-02 0.15756325 0.8214186 1.288097e-04
## 9727  2.175722e-04 0.12260477 0.8771767 9.775905e-07
## 9821  3.826780e-04 0.19855968 0.8010546 3.049268e-06
## 9906  1.520409e-28 0.11989470 0.8801053 6.658233e-31
## 9935  2.498053e-11 0.17545536 0.8245446 1.708784e-13
## 10670 5.462293e-04 0.15094353 0.8485071 3.123685e-06
## 10978 2.417674e-07 0.17716742 0.8228323 1.673414e-09
## 11282 2.430649e-11 0.13265511 0.8673449 1.195054e-13
## 12004 5.405960e-09 0.16906919 0.8309308 3.535946e-11
## 12831 1.674672e-09 0.18664209 0.8133579 1.235353e-11
## 12994 5.305667e-08 0.18842472 0.8115752 3.959883e-10
## 13062 5.245261e-15 0.16915721 0.8308428 3.432986e-17
## 13250 8.661032e-03 0.15901633 0.8322694 5.319620e-05
## 13538 2.903560e-04 0.19099780 0.8087096 2.204448e-06
## 13540 8.164386e-03 0.15626495 0.8355216 4.908634e-05
## 13541 2.495618e-16 0.19213465 0.8078654 1.907999e-18
## 13599 3.047342e-04 0.19867545 0.8010174 2.429722e-06
## 14605 1.812297e-19 0.19537655 0.8046235 1.414628e-21
## 14894 4.838585e-02 0.14535955 0.8059741 2.805267e-04
## 14897 1.790489e-27 0.16390034 0.8360997 1.128305e-29
## 15010 5.826150e-04 0.19892791 0.8004848 4.654333e-06
## 15074 2.368229e-04 0.14355836 0.8562035 1.276464e-06
## 15133 5.030627e-02 0.14061877 0.8087938 2.811647e-04
## 15440 2.192661e-10 0.18073311 0.8192669 1.554952e-12
## 15546 1.411983e-08 0.10979924 0.8902007 5.598529e-11
## 15752 3.825791e-03 0.16164559 0.8345048 2.382262e-05
## 15985 3.757334e-05 0.12272212 0.8772401 1.689730e-07
## 16337 1.013209e-22 0.14737786 0.8526221 5.629995e-25
## 16537 5.960269e-09 0.19714085 0.8028591 4.704748e-11
## 16578 3.097313e-03 0.17215594 0.8247260 2.078407e-05
## 16581 1.276101e-07 0.18552553 0.8144743 9.344249e-10
## 16587 1.133537e-20 0.16373717 0.8362628 7.134659e-23
## 17284 6.721918e-03 0.16853741 0.8246965 4.415995e-05
## 17548 4.269484e-05 0.13434232 0.8656148 2.130085e-07
## 18337 1.975758e-03 0.18114678 0.8168634 1.408472e-05
## 18420 3.972860e-03 0.14586602 0.8501392 2.191293e-05
```

Genes with PP2 > 0.8 (Posterior probabilities of Model 2)

```
fData[fData$SECOND > 0.8, ]
```

```
##       geneName dn_damaging_DD dn_lof_DD dn_damaging_EE dn_lof_EE
## 14671    SCN1A              2         0              4         4
##                NO      BOTH         FIRST    SECOND
## 14671 2.00889e-12 0.1159578 8.470647e-15 0.8840422
```

Use mTADA's results for single-trait analyses.

We can obtain single-trait results by summing PP1 and PP3 (Trait 1) or PP2 and PP3 (Trait 2).

Trait 1

```
fData[, 'pTrait1'] <- fData[, 'BOTH'] + fData[, 'FIRST']
fData1 <- fData[fData$pTrait1 > 0.8, ]
head(fData1[, c(1:5, 10)])
```

```
##      geneName dn_damaging_DD dn_lof_DD dn_damaging_EE dn_lof_EE   pTrait1
## 347      ADNP              1        19              0         0 1.0000000
## 447     AHDC1              0         8              0         0 1.0000000
## 681   ANKRD11              0        32              0         0 1.0000000
## 1000   ARID1A              1         2              0         0 0.9151739
## 1001   ARID1B              0        30              0         0 1.0000000
## 1002    ARID2              0         3              0         0 0.9977972
```

Trait 2

```
fData[, 'pTrait2'] <- fData[, 'BOTH'] + fData[, 'SECOND']
fData2 <- fData[fData$pTrait2 > 0.8, ]
head(fData2[, c(1:5, 11)])
```

```
##      geneName dn_damaging_DD dn_lof_DD dn_damaging_EE dn_lof_EE   pTrait2
## 2348  CACNA1A              5         0              2         0 0.9956704
## 3201     CHD2              0         6              0         1 0.9349822
## 6254   GABBR2              2         0              2         0 0.9957242
## 6265   GABRB3              2         0              2         0 0.9974515
## 6610    GNAO1              4         1              2         0 0.9983509
## 7165    HECW2              5         1              1         0 0.8884854
```

Other information

Some additional information can be obtained from mTADA's results.

```
pCI <- mTADAresults$pars ## Genetic parameters
piValue <- mTADAresults$probModel ## Posterior probabilities of genes for four models
mcmcResult <- mTADAresults$mcmcData ##MCMC results
```

The proportions of risk genes

piValue is a vector of π values. In the result below, pNO, pFIRST, pSECOND, and pBOTH are π_0, π_1, π_2 and π_3 respectively in **Table 1**.

```
piValue
```

```
##         pNO      pFIRST     pSECOND       pBOTH
## 0.961721614 0.022790496 0.008915556 0.006572334
```

Estimated information of π_3.

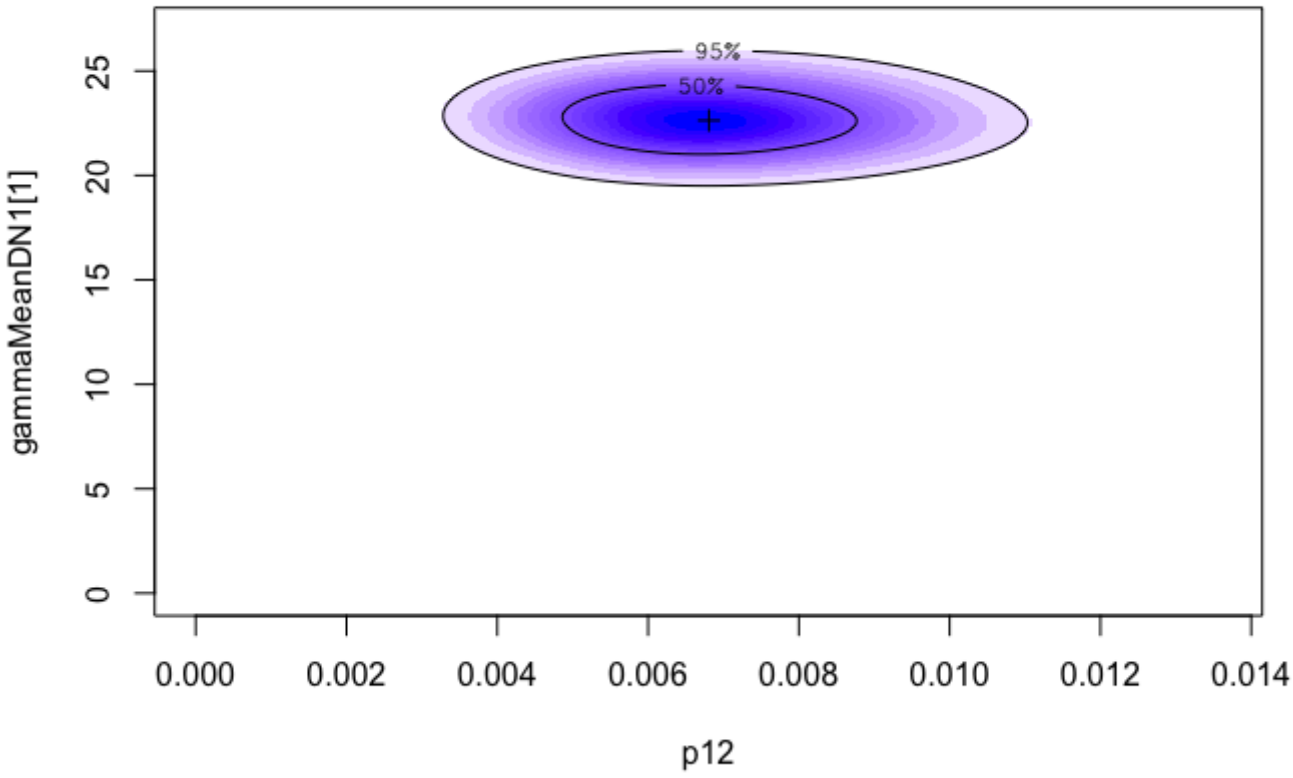
Credible-interval information is from ***pCI***.

```
pCI ## Mode: estimated values; CI: credible interval with low (l) and upper (u) values
```

```
##                          Mode          lCI         uCI
## p12                0.006572334  0.003861267  0.01016222
## gammaMeanDN1[1] 22.628526092 20.062524125 25.39720292
```

To check the convergent information of π_3, we can visualize MCMC results.

```
## p12 is pi3 in the model
plotParHeatmap1(mcmcResult = mcmcResult, pars = c('p12', 'gammaMeanDN1[1]'))
```



Citation

mTADA : a framework for identifying risk genes from de novo mutations in multiple traits. Hoang T. Nguyen, Amanda Dobbyn, Ruth C. Brown, Brien P. Riley, Joseph Buxbaum, Dalila Pinto, Shaun M Purcell, Patrick F Sullivan, Xin He, Eli A. Stahl.