# Package 'BIGDAWG'

October 12, 2022

Type Package

Title Case-Control Analysis of Multi-Allelic Loci

Version 3.0.3

Date 2021-11-01

Author Derek Pappas <djpappas75@gmail.com>, Steve Mack <Steven.Mack@ucsf.edu>, Jill Hollenbach <Jill.Hollenbach@ucsf.edu>

Maintainer Steve Mack < Steven . Mack@ucsf . edu>

URL http://tools.immunogenomics.org/,
https://github.com/IgDAWG/BIGDAWG

BugReports https://github.com/IgDAWG/BIGDAWG/issues

**Description** Data sets and functions for chi-squared Hardy-Weinberg and case-control association tests of highly polymorphic genetic data [e.g., human leukocyte antigen (HLA) data]. Performs association tests at multiple levels of polymorphism (haplotype, locus and HLA aminoacids) as described in Pappas DJ, Marin W, Hollen-

bach JA, Mack SJ (2016) <doi:10.1016/j.humimm.2015.12.006>. Combines rare variants to a common class to account for sparse cells in tables as described by Hollenbach JA, Mack SJ, Thomson G, Gourraud PA (2012) <doi:10.1007/978-1-61779-842-9\_14>.

License GPL (>= 3)

**Depends** R (>= 3.5.0)

**Imports** XML, httr, haplo.stats, parallel

Suggests knitr, rmarkdown

VignetteBuilder knitr

RoxygenNote 7.1.2

**Encoding UTF-8** 

NeedsCompilation no

Repository CRAN

**Date/Publication** 2021-11-17 11:50:14 UTC

# R topics documented:

A	3
A.wrapper	4
AA.df.check	5
AA.df.cs	5
AAtable.builder	6
AlignmentFilter	6
AlignObj.Create	7
AlignObj.Update	7
Append.System	8
BIGDAWG	8
Build.Matrix	10
ouildHAPnames	10
ouildHAPsets	11
œi	11
cci.pval	12
cci.pval.list	13
Check.Cores	13
Check.Data	14
Check.Params	14
Check.Params.GLS	15
CheckAlleles	16
CheckHLA	17
CheckLoci	17
CheckRelease	18
CheckString.Allele	18
	19
Condense.EPL	19
Create.Null.Table	20
	20
	21
· · · · · · · · · · · · · · · · · · ·	21
DRB345.parser	22
Err.Log	22
EVSremoval	23
Exon.Filter	23
ExonPtnAlign.Create	24
ExonPtnList	24
Filler	25
	25
Format.Tab	26
getAllele.Count	26
getCS.Mat	27
	27
	28
	28
	29

A 3

Α	Amino Acid Analysis Function	
Index		46
	opanickolouse	
	UpdateRelease	45
	TableMaker	44
	Tab2GL.wrapper	44
	Tab2GL.Sub	43
	Tab2GL.Loci	42
	Stripper	42
	<b>-</b>	41
	RunChiSq	41
	rmABstrings	40 41
	prepData	40
	PreCheck	39
	PgrpFormat	39
	PgrpExtract	38
	MergeData_Output	38
	makeComb	37
	make2x2	37
	L.wrapper	36
	L	36
	HWE.wrapper	35
	HWE.ChiSq	35
	HWE	34
	HLA data	34
	H.MC.wrapper	33
	H.MC	32
	GLSconvert	32
	GL2Tab.wrapper	31
	GL2Tab.Loci	31
	getObsFreq	30 30
	getHap	29

# Description

This is the workhorse function for the amino acid analysis.

# Usage

```
A(Locus, loci.ColNames, genos, grp, Strict.Bin, ExonAlign, Cores)
```

A.wrapper

#### **Arguments**

Locus being analyzed.

loci.ColNames The column names of the loci being analyzed.

genos Genotype table.

grp Case/Control or Phenotype groupings.

Strict.Bin Logical specify if strict rare cell binning should be used in ChiSq test.

ExonAlign Exon protein alignment filtered for locus.

Cores Number of cores to use for analysis.

#### Note

This function is for internal BIGDAWG use only.

A.wrapper

Amino Acid Wrapper

#### **Description**

Wrapper function for amino acid analysis.

# Usage

```
A.wrapper(
loci,
loci.ColNames,
genos,
grp,
Exon,
EPL,
Cores,
Strict.Bin,
Output,
Verbose
)
```

#### **Arguments**

loci Loci being analyzed.

loci.ColNames The column names of the loci being analyzed.

genos Genotype table.

grp Case/Control or Phenotype groupings.

Exon Exon(s) for targeted analysis.

EPL Protein Alignment List.

AA.df.check 5

Cores Number of cores to use for analysis.

Strict.Bin Logical specify if strict rare cell binning should be used in ChiSq test

Output Data return carryover from main BIGDAWG function

Verbose Summary display carryover from main BIGDAWG function

#### Note

This function is for internal BIGDAWG use only.

AA.df.check Contingency Table Check

#### **Description**

Checks amino acid contingency table data frame to ensure required variation exists.

#### Usage

```
AA.df.check(x, Strict.Bin)
```

## Arguments

x contingency table.

Strict.Bin Logical specify if strict rare cell binning should be used in ChiSq test.

#### Note

This function is for internal BIGDAWG use only.

AA.df.cs Contingency Table Amino Acid ChiSq Testing

#### **Description**

Runs ChiSq test on amino acid contingency table data frames.

#### Usage

```
AA.df.cs(x, Strict.Bin)
```

#### **Arguments**

x contingency table.

Strict.Bin Logical specify if strict rare cell binning should be used in ChiSq test.

#### Note

6 AlignmentFilter

AAtable.builder

Amino Acid Contingency Table Build

#### **Description**

Build Contingency Tables for Amino Acid Analysis.

# Usage

```
AAtable.builder(x, y)
```

## **Arguments**

x Filtered alignment list element.

y Phenotype groupings.

#### Note

This function is for internal BIGDAWG use only.

 ${\tt AlignmentFilter}$ 

Alignment Filter

## **Description**

Filter Protein Exon Alignment File for Specific Alleles.

# Usage

```
AlignmentFilter(Align, Alleles, Locus)
```

# Arguments

Align Protein Alignment Object.

Alleles to be pulled.

Locus to be filtered against.

#### Note

AlignObj.Create 7

## **Description**

Create Object for Exon Protein Alignments.

## Usage

```
AlignObj.Create(Loci, Release, RefTab)
```

# Arguments

Loci to be bundled.

Release IMGT/HLA database release version.

RefTab Data of reference exons used for protein alignment creation.

#### Note

This function is for internal BIGDAWG use only.

AlignObj.Update	Updated Alignment Object Creator

# Description

Synthesize Object for Exon Protein Alignments.

# Usage

```
AlignObj.Update(Loci, Release, RefTab)
```

#### **Arguments**

Loci to be bundled.

Release IMGT/HLA database release version.

RefTab Data of reference exons used for protein alignment creation.

# Note

8 BIGDAWG

Append.System

Append Genetic System Locus Designation to Allele String

## **Description**

Adds genetic system (HLA/KIR) to each allele name

#### Usage

```
Append.System(x, df.name)
```

# **Arguments**

```
x Vector Column genotypes to appenddf.name String SystemLocus name for each allele.
```

#### Note

This function is for internal use only.

BIGDAWG

BIGDAWG Main Wrapper Function

#### **Description**

This is the main wrapper function for each analysis.

#### Usage

```
BIGDAWG(
 Data,
 HLA = TRUE,
 Run.Tests,
 Loci.Set,
 Exon,
  All.Pairwise = FALSE,
  Trim = FALSE,
 Res = 2,
 EVS.rm = FALSE,
 Missing = 2,
  Strict.Bin = FALSE,
  Cores.Lim = 1L,
  Results.Dir,
  Return = FALSE,
  Output = TRUE,
```

BIGDAWG 9

```
Merge.Output = FALSE,
Verbose = TRUE
)
```

#### **Arguments**

Data Name of the genotype data file.

HLA Logical Indicating whether data is HLA class I/II genotyping data only.

Run. Tests Specifics which tests to run.

Loci.Set Input list defining which loci to use for analyses (combinations permitted).

Exon Numeric Exon(s) for targeted amino acid analysis.

All.Pairwise Logical indicating whether all pairwise loci should be analyzed in haplotype

analysis.

Trim Logical indicating if HLA alleles should be trimmed to a set resolution.

Res Numeric setting what desired resolution to trim HLA alleles.

EVS.rm Logical indicating if expression variant suffixes should be removed.

Missing Numeric setting allowable missing data for running analysis (may use "ignore").

Strict.Bin Logical specify if strict rare cell binning should be used in ChiSq test.

Cores.Lim Integer setting the number of cores accessible to BIGDAWG (Windows limit is

1 core).

Results.Dir Optional, string of full path directory name for BIGDAWG output.

Return Logical Should analysis results be returned as list.

Output Logical Should analysis results be written to output directory.

Merge.Output Logical Should analysis results be merged into a single file for easy access.

Verbose Logical Should a summary of each analysis be displayed in console.

#### **Examples**

```
## Not run:
### The following examples use the synthetic data set bundled with BIGDAWG

# Haplotype analysis with no missing genotypes for two loci sets
# Significant haplotype association with phenotype
# BIGDAWG(Data="HLA_data", Run.Tests="H", Missing=0, Loci.Set=list(c("DRB1","DQB1")))

# Hardy-Weinberg and Locus analysis ignoring missing data
# Significant locus associations with phenotype at all but DQB1
# BIGDAWG(Data="HLA_data", Run.Tests="L", Missing="ignore")

# Hardy-Weinberg analysis trimming data to 2-Field resolution with no output to files (console only)
# Significant locus deviation at DQB1
BIGDAWG(Data="HLA_data", Run.Tests="HWE", Trim=TRUE, Res=2, Output=FALSE)

## End(Not run)
```

10 buildHAPnames

Build.Matrix

Build Output Matrix for GL2Tab Conversion

# Description

Initializes output matrix format for GL2Tab conversion

# Usage

```
Build.Matrix(System, Loci)
```

#### **Arguments**

System Character Genetic system HLA- or KIR

Loci The loci for header names

#### Note

This function is for internal use only.

buildHAPnames

Haplotype Name Builder

# Description

Builds table of names for HAPsets

#### Usage

```
buildHAPnames(Combn, loci)
```

# Arguments

Combination of loci to extraction from genos

loci Character vector of unique loci being analyzed.

# Note

buildHAPsets 11

buildHAPsets

Haplotype List Builder

#### **Description**

Builds table of haplotypes from combinations

#### Usage

```
buildHAPsets(Combn, genos, loci, loci.ColNames)
```

#### **Arguments**

Combin Combination of loci to extraction from genos

genos The genotype columns of the loci set being analyzed.

loci Character vector of unique loci being analyzed.

loci.ColNames Character vector of genos column names.

#### Note

This function is for internal BIGDAWG use only.

cci

Case-Control Odds ratio calculation and graphing

#### **Description**

cci function port epicale version 2.15.1.0 (Virasakdi Chongsuvivatwong, 2012)

#### Usage

```
cci(
   caseexp,
   controlex,
   casenonex,
   controlnonex,
   cctable = NULL,
   graph = TRUE,
   design = "cohort",
   main,
   xlab,
   ylab,
   xaxis,
   yaxis,
   alpha = 0.05,
```

12 cci.pval

```
fisher.or = FALSE,
  exact.ci.or = TRUE,
  decimal = 2
)
```

# Arguments

caseexp	Number of cases exposed
controlex	Number of controls exposed
casenonex	Number of cases not exosed
controlnonex	Number of controls not exposed
cctable	A 2-by-2 table. If specified, will supercede the outcome and exposure variables
graph	If TRUE (default), produces an odds ratio plot
design	Specification for graph; can be "case control", "case-control", "cohort" or "prospective"
main	main title of the graph
xlab	label on X axis
ylab	label on Y axis
xaxis	two categories of exposure in graph
yaxis	two categories of outcome in graph
alpha	level of significance
fisher.or	whether odds ratio should be computed by the exact method
exact.ci.or	whether confidence limite of the odds ratio should be computed by the exact method
decimal	number of decimal places displayed

# Note

This function is for internal BIGDAWG use only.

cci.pval Case Control Odds Ratio Calculation from Epicalc	
---	--

# Description

Calculates odds ratio and pvalues from 2x2 table

# Usage

```
cci.pval(x)
```

# Arguments

x List of 2x2 matrices for calculation, output of TableMaker.

cci.pval.list

# Note

This function is for internal BIGDAWG use only.

cci.pval.list

Case Control Odds Ratio Calculation from Epicalc list variation

## **Description**

Variation of the cci.pvalue function

## Usage

```
cci.pval.list(x)
```

## **Arguments**

Х

List of 2x2 matrices to apply the cci.pvalue function. List output of TableMaker.

#### Note

This function is for internal BIGDAWG use only.

Check.Cores

Check Cores Parameters

# Description

Check cores limitation for OS compatibility

## Usage

```
Check.Cores(Cores.Lim, Output)
```

# Arguments

Cores.Lim Integer How many cores can be used.

Output Logical Should analysis results be written to output directory.

14 Check.Params

Check.Data

Check Data Structure

# Description

Check data structure for successful conversion.

# Usage

```
Check.Data(Data, System, Convert)
```

# **Arguments**

Data String Type of output.

System Character Genetic system HLA or KIR

Convert String Direction for conversion.

#### Note

This function is for internal use only.

Check.Params

Check Input Parameters

# Description

Check input parameters for invalid entries.

# Usage

```
Check.Params(
    HLA,
    Loci.Set,
    Exon,
    All.Pairwise,
    Trim,
    Res,
    EVS.rm,
    Missing,
    Cores.Lim,
    Return,
    Output,
    Merge.Output,
    Verbose
)
```

Check.Params.GLS 15

#### **Arguments**

HLA Logical indicating whether data is HLA class I/II genotyping data only.

Loci.Set Input list defining which loci to use for analyses (combinations permitted).

Exon Numeric Exon(s) for targeted amino acid analysis.

All.Pairwise Logical indicating whether all pairwise loci should be analyzed in haplotype

analysis.

Trim Logical indicating if HLA alleles should be trimmed to a set resolution.

Res Numeric setting what desired resolution to trim HLA alleles.

EVS.rm Logical indicating if expression variant suffixes should be removed.

Missing Numeric setting allowable missing data for running analysis (may use "ignore").

Cores.Lim Integer setting the number of cores accessible to BIGDAWG (Windows limit is

1 core).

Return Logical Should analysis results be returned as list.

Output Logical Should analysis results be written to output directory.

Merge.Output Logical Should analysis results be merged into a single file for easy access.

Verbose Logical Should a summary of each analysis be displayed in console.

#### Note

This function is for internal use only.

Check .Params . GLS Check Input Parameters for GLS conversion

## Description

Check input parameters for invalid entries.

#### Usage

```
Check.Params.GLS(
   Convert,
   File.Output,
   System,
   HZY.Red,
   DRB345.Check,
   Cores.Lim
)
```

16 CheckAlleles

#### **Arguments**

Convert String Direction for conversion.

File.Output String Type of output.

System String Genetic system (HLA or KIR) of the data being converted

HZY.Red Logical Reduction of homozygote genotypes to single allele.

DRB345. Check Logical Check DR haplotypes for consistency and flag unusual haplotypes.

Cores.Lim Integer How many cores can be used.

#### Note

This function is for internal use only.

CheckAlleles HLA Allele Legitimacy Check for Amino Acid Analysis

# Description

Checks available alleles against data to ensure complete overlap.

# Usage

```
CheckAlleles(x, y)
```

#### **Arguments**

x Exon protein list alignment object.

y Genotypes from data file

#### Note

CheckHLA 17

CheckHLA

HLA Formatting Check for Amino Acid Analysis

# Description

Checks data to see if HLA data is properly formatted.

## Usage

```
CheckHLA(x)
```

## **Arguments**

Х

All columns of HLA genotyping data.

#### Note

This function is for internal BIGDAWG use only.

CheckLoci

HLA Loci Legitimacy Check for Amino Acid Analysis

# Description

Checks available loci against data to ensure complete overlap.

# Usage

```
CheckLoci(x, y)
```

## **Arguments**

x Loci available in exon protein list alignment object.

y Unique column names

## Note

18 CheckString.Allele

CheckRelease

Function to Check Release Versions

#### **Description**

This updates the protein alignment used in checking HLA loci and alleles as well as in the amino acid analysis.

#### Usage

```
CheckRelease(Package = T, Alignment = T, Output = F)
```

#### **Arguments**

Package Logical to check for BIGDAWG package versions

Alignment Logical to check the IMGT/HLA database version for the alignment bundled

with BIGDAWG.

Output Should any error be written to a file

#### Note

Requires active internet connection.

CheckString.Allele

GL String Allele Check

#### **Description**

GL String check for allele ambiguity formatting

#### Usage

```
CheckString.Allele(x)
```

#### **Arguments**

Х

GL String to check against

#### Note

CheckString.Locus 19

CheckString.Locus

GL String Locus Check

# Description

Check GL string for loci appearing in multiple gene fields.

#### Usage

```
CheckString.Locus(x, Loci)
```

## Arguments

x GL String to check against

Loci to check

#### Note

This function is for internal use only.

Condense.EPL

Condensing Exon Specific Alignments to Single Dataframe

# Description

Combines multiple Exon Specific Alignments into a single Alignment object

#### Usage

```
Condense.EPL(EPL.Exon)
```

# Arguments

EPL.Exon

Exon-Locus Specific Amino Acid Alignment.

## Note

Create.Null.Table

Create Empty Table

#### **Description**

Creates matrix of NA for no result tables.

# Usage

```
Create.Null.Table(Locus, Names, nr)
```

## **Arguments**

Locus being analyzed.

Names Column names for final matrix.

nr Number of rows.

#### Note

This function is for internal BIGDAWG use only.

 ${\tt DRB345.Check.Wrapper} \quad \textit{DRB345 haplotype zygosity wrapper}$ 

#### **Description**

Checks DR haplotypes for correct zygosity and flags unanticipated haplotypes

#### Usage

```
DRB345.Check.Wrapper(Genotype, Loci.DR)
```

# Arguments

Genotype Row of data set data frame following DRB345 parsing

Loci . DR DRBx Loci of interest to test for consistency

#### Note

DRB345.Check.Zygosity DRB345 haplotype zygosity checker single locus

# Description

Checks DR haplotypes for correct zygosity and flags unanticipated haplotypes for a single DRBx

#### Usage

```
DRB345.Check.Zygosity(Locus, Genotype)
```

#### **Arguments**

Locus of interest to test for consistency

Genotype Row of data set data frame following DRB345 parsing

#### Note

This function is for internal use only.

DRB345.Exp

DRB345 Expected

# Description

Checks DRB1 Genotype and Returns Expected DR345 Loci

#### Usage

```
DRB345.Exp(DRB1.Genotype)
```

# Arguments

```
DRB1.Genotype DRB1 Subject Genotypes
```

## Note

22 Err.Log

DRB345.parser

DRB345 Column Processing

#### **Description**

Separates DRB345 column pair into separate columns for each locus

# Usage

```
DRB345.parser(Tab)
```

## Arguments

Tab

Data frame of sampleIDs, phenotypes, and genotypes

#### Note

This function is for internal BIGDAWG use only.

Err.Log

Error Code Display and Logging

# Description

Displays error codes attributable to data formatting and Locus/Allele naming. Writes to log file.

# Usage

```
Err.Log(Output, x, y = NULL, z = NULL)
```

## **Arguments**

Output Logical indicating if Error logging should be written to a file.

x Log Code.

y Misc information relevant to error.

z Misc information relevant to error.

#### Note

EVSremoval 23

EVSremoval	Expression Variant Suffix Removal
------------	-----------------------------------

# Description

Removes expression variant suffixes from HLA alleles in the exon protein alignment object.

# Usage

```
EVSremoval(Locus, EPList)
```

# Arguments

Locus Locus to be filtered against.

EPList Exon Protein Alignment Object

#### Note

This function is for internal BIGDAWG use only.

Exon.Filter	Filter Exon Specific Alignment Sections

# Description

Filters the ExonPtnAlign object by locus and exon.

# Usage

```
Exon.Filter(Locus, Exon, EPL.Locus, RefExons, E.Ptn.Starts)
```

# **Arguments**

Locus being analyzed. Exon Exon being analyzed.

EPL.Locus ExonPtnAlign object filtered by Locus

RefExons Reference Exon Table
E.Ptn.Starts Exon Protein Overlay Map

#### Note

24 ExonPtnList

ExonPtnAlign.Create Protein Exon Alignment Formatter

# Description

Dynamically creates an alignmnet of Allele exons for Analysis.

# Usage

ExonPtnAlign.Create(Locus, RefTab)

# Arguments

Locus alignment to be formatted.

RefTab Reference exon protein information for alignment formatting.

#### Note

This function is for internal BIGDAWG use only.

ExonPtnList Exon protein alignments.

# Description

Alignment object for use in the amino acid analysis.

# Usage

ExonPtnList

#### **Format**

A list where each element is an alignment dataframe for a single locus.

Filler 25

Filler

Replace or Fill 00:00 allele strings

#### **Description**

Replaces or Fills absent allele strings.

# Usage

```
Filler(x, Locus = NULL, Type)
```

## Arguments

x Genotype

Locus Column to adjust.

Type String specifying whether to pad ('Fill') or leave blank ('Remove') absent calls

#### Note

This function is for internal use only.

Format.Allele

Ambiguous Alleles Locus Name Formatting

#### **Description**

Remove or Append Locus name from/to allele in an ambiguous allele string

# Usage

```
Format.Allele(x, Type)
```

# Arguments

x Allele String

Type String specifying whether to strip ('off') or append ('on') locus prefix

#### Note

26 getAllele.Count

Format.Tab

Tabular Data Locus Format Tool

#### **Description**

Correctly orders the expanded GL string

# Usage

```
Format.Tab(x, Order)
```

# Arguments

x Single row of converted GL string

Order Single row data frame for mapping converted GL strings

#### Note

This function is for internal use only.

getAllele.Count

Recompute number of alleles

# Description

Using Freq.Final, recompute number of alleles

#### Usage

```
getAllele.Count(x)
```

#### **Arguments**

Х

Locus specific contingency matrix getCS.Mat output.

## Note

getCS.Mat 27

# Description

Chi Square contingency matrix builder with rare cell binning

# Usage

```
getCS.Mat(Locus, genos.sub, Allele.Freq, Allele.Combn)
```

#### **Arguments**

Locus of interest.

genos. sub Genotypes for locus of interest.

Allele.Freq Allele frequencies.

Allele.Combn Allele combinations.

#### Note

This function is for internal BIGDAWG use only.

getCS.stat	Chi square test statistic

# Description

Calculate chi square test statistic

# Usage

```
getCS.stat(Locus, Freq.Final)
```

# Arguments

Locus of interest.

Freq.Final Contingency Matrix getCS.Mat output.

# Note

28 getFileName

GetField

HLA trimming function

# Description

Trim a properly formatted HLA allele to desired number of fields.

# Usage

```
GetField(x, Res)
```

# Arguments

x HLA allele.

Res Resolution desired.

#### Note

This function is for internal BIGDAWG use only.

getFileName

File Name Extraction

# Description

Function to extract file path.

# Usage

```
getFileName(x)
```

# Arguments

Х

File name.

## Note

GetFiles 29

GetFiles

File Fetcher

# Description

Download Protein Alignment and Accessory Files

# Usage

```
GetFiles(Loci)
```

# Arguments

Loci

HLA Loci to be fetched. Limited Loci available.

#### Note

This function is for internal BIGDAWG use only.

getHap

Haplotype Table Maker

# Description

Builds table of haplotypes

# Usage

```
getHap(SID, HaploEM)
```

# Arguments

SID Index number (i.e., row number) of sample ID from genotype matrix.

HaploEM Haplotype output object from haplo.stat::haplo.em function.

## Note

30 GL2Tab.Loci

getObsFreq

Observed Frequency

#### **Description**

Get observed frequency of genotypes

# Usage

```
getObsFreq(x, genos.locus)
```

## **Arguments**

x Single genotype.genos.locus Locus genotypes.

#### Note

This function is for internal BIGDAWG use only.

GL2Tab.Loci

Locus Ordering for GL2Tab

# Description

Orders Locus Calls

# Usage

```
GL2Tab.Loci(Locus, Genotype, System)
```

# Arguments

Locus to condense

Genotype Row of loci to condense

System Character Genetic system HLA or KIR

#### Note

GL2Tab.Sub

GL2Tab.Sub	Genotype List String Expander
------------	-------------------------------

# Description

Expands GL string into a table of adjacent loci

# Usage

```
GL2Tab.Sub(x, System)
```

#### **Arguments**

x Character GL string to expand

System Character Genetic system HLA or KIR

#### Note

This function is for internal use only.

GL2Tab.wrapper Genoty	pe List String to Tabular Data Conversion
-----------------------	---

# Description

Expands GL strings to columns of adjacent locus pairs.

# Usage

```
GL2Tab.wrapper(df, System, Strip.Prefix, Abs.Fill, Cores)
```

#### **Arguments**

df Data frame containing GL strings
System Character Genetic system HLA or KIR

Strip.Prefix Logical Should System/Locus prefixes be stripped from table data.

Abs.Fill Logical Should absent loci special designations be used.

Cores Integer How many cores can be used

#### Note

This function is for internal use only

32 H.MC

GLSconvert

Genotype List String Conversion

# Description

Main Workhorse wrapper for cross converting columnar table to GL string representaion.

# Usage

```
GLSconvert(
  Data,
  Convert,
  File.Output = "txt",
  System = "HLA",
  HZY.Red = FALSE,
  DRB345.Check = FALSE,
  Strip.Prefix = TRUE,
  Abs.Fill = FALSE,
  Cores.Lim = 1L
)
```

# Arguments

Data	String File name or R Data Frame.
Convert	String Direction for conversion.
File.Output	String Type of File.Output.
System	String Genetic system (HLA or KIR) of the data being converted
HZY.Red	Logical Reduction of homozygote genotypes to single allele.
DRB345.Check	Logical Check DR haplotypes for consistency and flag unusual haplotypes.
Strip.Prefix	Logical Should System/Locus prefixes be stripped from table data.
Abs.Fill	Logical Should absent loci special designations be used.
Cores.Lim	Integer How many cores can be used.

H.MC

Haplotype Analysis Function for Multicore

# Description

This is the workhorse function for the haplotype analysis.

# Usage

```
H.MC(genos.sub, grp, Strict.Bin, Verbose)
```

H.MC.wrapper 33

#### **Arguments**

genos.sub The genotype columns of the loci(locus) set being analyzed.

grp Case/Control or Phenotype groupings.

Strict.Bin Logical specify if strict rare cell binning should be used in ChiSq test

Verbose Summary display carryover from main BIGDAWG function

#### Note

This function is for internal BIGDAWG use only.

H.MC.wrapper

Haplotype Wrapper for Multicore

#### **Description**

Wrapper for main H function

#### Usage

```
H.MC.wrapper(
SID,
Tabsub,
loci,
loci.ColNames,
genos,
grp,
All.Pairwise,
Strict.Bin,
Output,
Verbose,
Cores
)
```

#### **Arguments**

SID Character vector of subject IDs.

Tabsub Data frame of genotype calls for set being analyzed.

loci Character vector of unique loci being analyzed.

loci.ColNames Character vector of genos column names.

genos The genotype columns of the loci set being analyzed.

grp Case/Control or Phenotype groupings.

All.Pairwise Haplotype argument carryover from main BIGDAWG function

Strict.Bin Logical specify if strict rare cell binning should be used in ChiSq test

Output Data return carryover from main BIGDAWG function

Verbose Summary display carryover from main BIGDAWG function

Cores Cores carryover from main BIGDAWG function

34 HWE

# Note

This function is for internal BIGDAWG use only.

HLA\_data

Example HLA Dataset

# Description

A synthetic dataset of HLA genotypes for using bigdawg.

# Usage

HLA\_data

#### **Format**

A data frame with 2000 rows and 14 variables

HWE

Hardy Weinbergy Equilibrium Function

# Description

This is the main function for the HWE analysis.

# Usage

HWE(Tab)

# Arguments

Tab

data frame of genotype files post processing.

#### Note

HWE.ChiSq 35

HWE.ChiSq Hardy Weinbergy Equilibrium Function
--

# Description

This is the workhorse function for each group analysis.

# Usage

```
HWE.ChiSq(genos.sub, loci, nloci)
```

# Arguments

genos.sub data frame of genotype files post processing.

loci list of loci.

nloci number of loci in list

#### Note

This function is for internal BIGDAWG use only.

HWE.wrapper	Hardy-Weinbery Wrapper

# Description

Wrapper for main HWE function

# Usage

```
HWE.wrapper(Tab, Output, Verbose)
```

#### **Arguments**

Tab Data frame of genotype files post processing.

Output Data return carryover from main BIGDAWG function

Verbose Summary display carryover from main BIGDAWG function

# Note

36 L.wrapper

Locus Analysis Function

#### **Description**

This is the workhorse function for the locus level analysis.

#### Usage

L

```
L(loci.ColNames, Locus, genos, grp, Strict.Bin)
```

## **Arguments**

loci.ColNames The column names of the loci being analyzed.

Locus being analyzed.

genos Genotype table

grp Case/Control or Phenotype groupings.

Strict.Bin Logical specify if strict rare cell binning should be used in ChiSq test

#### Note

This function is for internal BIGDAWG use only.

L.wrapper Locus Wrapper

## **Description**

Wrapper for main L function

#### Usage

```
L.wrapper(nloci, loci, loci.ColNames, genos, grp, Strict.Bin, Output, Verbose)
```

#### **Arguments**

nloci Number of loci being analyzed.

loci Loci being analyzed.

loci.ColNames The column names of the loci being analyzed.

genos Genotype table

grp Case/Control or Phenotype groupings.

Strict.Bin Logical specify if strict rare cell binning should be used in ChiSq test

Output Data return carryover from main BIGDAWG function

Verbose Summary display carryover from main BIGDAWG function

make2x2 37

#### Note

This function is for internal BIGDAWG use only.

make2x2

Creation of a 2x2 table using the indicated orientation.

#### **Description**

make2x2 function port epicalc version 2.15.1.0 (Virasakdi Chongsuvivatwong, 2012)

# Usage

```
make2x2(caseexp, controlex, casenonex, controlnonex)
```

# Arguments

caseexp Number of cases exposed
controlex Number of controls exposed
casenonex Number of cases not exosed
controlnonex Number of controls not exposed

#### Note

This function is for internal BIGDAWG use only.

makeComb

Genotype Combination Maker

# Description

Make data frame of possible genotype combinations

## Usage

makeComb(x)

## Arguments

Χ

Number of alleles.

#### Note

38 PgrpExtract

MergeData\_Output

Data Object Merge and Output

#### **Description**

Whole data set table construction of per haplotype for odds ratio, confidence intervals, and pvalues

# Usage

```
MergeData_Output(BD.out, Run, OutDir)
```

## **Arguments**

BD. out Output of analysis as list.

Run Tests that are to be run as defined by Run.Tests.

OutDir Output directory defined by Results.Dir or default.

#### Note

This function is for internal BIGDAWG use only.

PgrpExtract

HLA P group Finder

#### **Description**

Identify P group for a given allele if exists.

# Usage

```
PgrpExtract(x, y)
```

# Arguments

x Allele of interest.

y Formatted P groups.

#### Note

PgrpFormat 39

PgrpFormat	HLA P group File Formatter	

#### **Description**

Format the hla\_nom\_p.txt read table object for a specific locus.

#### Usage

```
PgrpFormat(x, Locus)
```

#### **Arguments**

x P group object from read.table command.

Locus to be filtered on.

#### Note

This function is for internal BIGDAWG use only.

PreCheck	Data Summary Function

# Description

Summary function for sample population within data file.

#### Usage

```
PreCheck(Tab, All.ColNames, rescall, HLA, Verbose, Output)
```

## Arguments

Tab Loci available in exon protein list alignment object.

All. ColNames Column names from genotype data.
rescall HLA resolution set for analysis.

HLA BIGDAWG argument passed to function

Verbose Summary display carryover from BIGDAWG function.

Output Data output carryover form BIGDAWG function

#### Note

40 rmABstrings

prepData

Prepare imported data

# Description

Prepare imported data for processing, checks, and analysis.

# Usage

```
prepData(Tab)
```

#### **Arguments**

Tab

Genotypes dataframe.

#### Note

This function is for internal BIGDAWG use only.

 ${\tt rmABstrings}$ 

Replace absent allele strings

# Description

Replaces allowable absent allele strings with ^ symbol.

#### Usage

```
rmABstrings(df)
```

# Arguments

df

Genotypes dataframe.

#### Note

RunChiSq 41

RunChiSq

Strict Chi-squared Contingency Table Test

# Description

Calculates chi-squared contingency table tests and bins all rare cells.

# Usage

RunChiSq(x)

#### **Arguments**

Χ

Contingency table.

#### Note

This function is for internal BIGDAWG use only.

 ${\tt RunChiSq\_c}$ 

Contextual Binning Chi-squared Contingency Table Test

# Description

Calculates chi-squared contingency table tests and bins rare cells at 20

#### Usage

```
RunChiSq_c(x)
```

# Arguments

Х

Contingency table.

#### Note

42 summaryGeno.2

Stripper

Removes System and Locus from Alleles

# Description

Removes the System and Locus designations for alleles calls in GL2Tab

## Usage

```
Stripper(x)
```

## **Arguments**

Χ

Allele

#### Note

This function is for internal use only.

summaryGeno.2

Haplotype missing Allele summary function

# Description

Summary function for identifying missing alleles in a matrix of genotypes.

# Usage

```
summaryGeno.2(geno, miss.val = 0)
```

# Arguments

geno

Matrix of genotypes.

miss.val

Vector of codes for allele missing values.

## Note

This function is for internal BIGDAWG use only and is ported from haplo.stats.

Tab2GL.Loci 43

Tab2GL.Loci	Locus Condenser for Tab2GL
-------------	----------------------------

# Description

Condenses alleles calls of a single locus string using "+"

# Usage

```
Tab2GL.Loci(Locus, Genotype, System, HZY.Red)
```

#### **Arguments**

Locus to condense

Genotype Row of loci to condense

System Character Genetic system HLA or KIR

HZY.Red Logical Should homozygote genotypes be a single allele for non-DRB345.

#### Note

This function is for internal use only.

Tab2GL . Sub	Genotype List String Condenser	
--------------	--------------------------------	--

# Description

Condenses column of loci into a GL string using "^"

#### Usage

```
Tab2GL.Sub(x, System, HZY.Red)
```

## **Arguments**

x Row of loci to condense

System Character Genetic system HLA or KIR

HZY.Red Logical Should homozygote genotypes be a single allele for non-DRB345.

#### Note

44 TableMaker

Tab2GL.wrapper	Genotype List String to Tabular Data Conversion
----------------	---

# Description

Expands GL strings to columns of adjacent locus pairs.

# Usage

```
Tab2GL.wrapper(df, System, HZY.Red, Abs.Fill, Cores)
```

# Arguments

df	Data frame containing GL strings
System	Character Genetic system HLA or KIR
HZY.Red	Logical Should homozygote genotypes be a single allele for non-DRB345.
Abs.Fill	Logical Should absent loci special designations be used
Cores	Integer How many cores can be used.

#### Note

This function is for internal use only.

|--|

# Description

Table construction of per haplotype for odds ratio, confidence intervals, and pvalues

# Usage

TableMaker(x)

## **Arguments**

x Contingency table with binned rare cells.

# Note

UpdateRelease 45

UpdateRelease	Update function for protein aligment upon new IMGT HLA data re- lease

# Description

This updates the protein alignment used in checking HLA loci and alleles as well as in the amino acid analysis.

# Usage

```
UpdateRelease(Force = F, Restore = F, Output = F)
```

# Arguments

Force Logical specifiying if update should be forced.

Restore Logical specifying if the original alignment file be restored.

Output Logical indicating if error reporting should be written to file.

# **Index**

* datasets	EVSremoval, 23
ExonPtnList, 24	Exon.Filter, 23
HLA_data, 34	ExonPtnAlign.Create, 24
	ExonPtnList, 24
A, 3	
A.wrapper, 4	Filler, 25
AA.df.check, 5	Format.Allele, 25
AA.df.cs, 5	Format.Tab, 26
AAtable.builder, 6	
AlignmentFilter, 6	getAllele.Count, 26
AlignObj.Create,7	getCS.Mat, 27
AlignObj.Update,7	getCS.stat, 27
Append.System, 8	GetField, 28
DICDAWC 0	getFileName, 28
BIGDAWG, 8	GetFiles, 29
Build.Matrix, 10	getHap, 29
buildHAPnames, 10	getObsFreq, 30
buildHAPsets, 11	GL2Tab.Loci, 30
cci, 11	GL2Tab.Sub, 31
cci.pval, 12	GL2Tab.wrapper, 31
cci.pval.list, 13	GLSconvert, 32
Check.Cores, 13	
Check.Data, 14	H.MC, 32
Check. Params, 14	H.MC.wrapper, 33
Check.Params.GLS, 15	HLA_data, 34
CheckAlleles, 16	HWE, 34
CheckHLA, 17	HWE.ChiSq, 35
CheckLoci, 17	HWE.wrapper, 35
CheckRelease, 18	
CheckString.Allele, 18	L, 36
CheckString.Locus, 19	L.wrapper, 36
Condense . EPL, 19	
Create.Null.Table, 20	make2x2, 37
or cate.mail.rable, 20	makeComb, 37
DRB345.Check.Wrapper, 20	MergeData_Output, 38
DRB345.Check.Zygosity, 21	
DRB345.Exp, 21	PgrpExtract, 38
DRB345.parser, 22	PgrpFormat, 39
	PreCheck, 39
Err.Log, 22	prepData, $40$

INDEX 47

```
rmABstrings, 40
RunChiSq, 41
RunChiSq_c, 41
Stripper, 42
summaryGeno.2, 42
Tab2GL.Loci, 43
Tab2GL.Sub, 43
Tab2GL.wrapper, 44
TableMaker, 44
UpdateRelease, 45
```