

# Package ‘genotypeeval’

April 23, 2016

**Title** QA/QC of a gVCF or VCF file

**Version** 1.0.0

**Description** Takes in a gVCF or VCF and reports metrics to assess quality of calls.

**Depends** R (>= 3.2.0), VariantAnnotation

**Imports** ggplot2, rtracklayer, BiocGenerics, GenomicRanges, GenomeInfoDb, IRanges, methods, BiocParallel

**Collate** GoldDataParam.R GoldData.R VCFData.R VCFQAParam.R VCFQAReport.R PopulationSummary.R

**License** file LICENSE

**LazyData** true

**Suggests** knitr, testthat, SNPlocs.Hsapiens.dbSNP141.GRCh38, TxDb.Hsapiens.UCSC.hg38.knownGene

**VignetteBuilder** knitr

**Author** Jennifer Tom [aut, cre]

**Maintainer** Jennifer Tom <tom.jennifer@gene.com>

**biocViews** Genetics, BatchEffect, Sequencing, SNP, VariantAnnotation, DataImport

**NeedsCompilation** no

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didSamplePass	<i>Getter for VCFEvaluate class to check if Sample Passed. Using thresholds from VCFQAParam object return a list. First return whether each test was passed (TRUE) or failed (FALSE). Then return an overall pass (TRUE) or fail (FALSE).</i>
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## Description

Getter for VCFEvaluate class to check if Sample Passed. Using thresholds from VCFQAParam object return a list. First return whether each test was passed (TRUE) or failed (FALSE). Then return an overall pass (TRUE) or fail (FALSE).

## Usage

```
didSamplePass(Object)
```

## Arguments

Object            an object of type VCFQAReport

## Value

Vector of True and False

## Examples

```
vcffn <- system.file("ext-data", "chr22.GRCh38.vcf.gz", package="genotypeeval")
mydir <- paste(dirname(vcffn), "/", sep="")
myfile <- basename(vcffn)
svp <- ScanVcfParam(which=GRanges("22", IRanges(0,200e5)), geno="GT")
vcfparams <- VCFQAParam(count.limits=c(301458000, Inf), readdepth.target = 30)
vcf <- ReadVCFData(mydir, myfile, "GRCh38")
ev <- VCFEvaluate(vcf, vcfparams)
didSamplePass(ev)
```

---

`didSamplePassOverall` *Getter for VCFEvaluate class to check if Sample Passed. Using thresholds from VCFQAParam object return a list. First return whether each test was passed (TRUE) or failed (FALSE). Then return an overall pass (TRUE) or fail (FALSE).*

---

### Description

Getter for VCFEvaluate class to check if Sample Passed. Using thresholds from VCFQAParam object return a list. First return whether each test was passed (TRUE) or failed (FALSE). Then return an overall pass (TRUE) or fail (FALSE).

### Usage

```
didSamplePassOverall(Object)
```

### Arguments

`Object` an object of type VCFQARepor

### Value

True or False if sample passed all thresholds

### Examples

```
vcffn <- system.file("ext-data", "chr22.GRCh38.vcf.gz", package="genotypeeval")
mydir <- paste(dirname(vcffn), "/", sep="")
myfile <- basename(vcffn)
svp <- ScanVcfParam(which=GRanges("22", IRanges(0,200e5)), geno="GT")
vcfparams <- VCFQAParam(count.limits=c(301458000, Inf), readdepth.target = 30)
vcf <- ReadVCFData(mydir, myfile, "GRCh38")
ev <- VCFEvaluate(vcf, vcfparams)
didSamplePassOverall(ev)
```

---

`getName` *Getter for VCFQARepor class to return filename slot*

---

### Description

Getter for VCFQARepor class to return filename slot

### Usage

```
getName(Object)
```

**Arguments**

Object                    Object of class VCFQARepor

**Value**

Name of file

**Examples**

```
vcffn <- system.file("ext-data", "chr22.GRCh38.vcf.gz", package="genotypeeval")
mydir <- paste(dirname(vcffn), "/", sep="")
myfile <- basename(vcffn)
svp <- ScanVcfParam(which=GRanges("22", IRanges(0,200e5)), geno="GT")
vcfparams <- VCFQAParam(count.limits=c(301458000, Inf), readdepth.target = 30)
vcf <- ReadVCFData(mydir, myfile, "GRCh38")
ev <- VCFEvaluate(vcf, vcfparams)
getName(ev)
```

---

getPlots

*Getter for VCFQARepor class to return plots slot.*

---

**Description**

Getter for VCFQARepor class to return plots slot.

**Usage**

```
getPlots(Object)
```

**Arguments**

Object                    Object of Class VCFQARepor

**Value**

List of named ggplots

**Examples**

```
vcffn <- system.file("ext-data", "chr22.GRCh38.vcf.gz", package="genotypeeval")
mydir <- paste(dirname(vcffn), "/", sep="")
myfile <- basename(vcffn)
svp <- ScanVcfParam(which=GRanges("22", IRanges(0,200e5)), geno="GT")
vcfparams <- VCFQAParam(count.limits=c(301458000, Inf), readdepth.target = 30)
vcf <- ReadVCFData(mydir, myfile, "GRCh38")
ev <- VCFEvaluate(vcf, vcfparams)
getPlots(ev)
```

---

getResults	<i>Getter for VCFQAReport class to return results. Return a list showing values that the sample was evaluated on.</i>
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---

**Description**

Getter for VCFQAReport class to return results. Return a list showing values that the sample was evaluated on.

**Usage**

```
getResults(Object)
```

**Arguments**

Object            an object of type VCFQAReport

**Value**

numeric vector of results

**Examples**

```
vcffn <- system.file("ext-data", "chr22.GRCh38.vcf.gz", package="genotypeeval")
mydir <- paste(dirname(vcffn), "/", sep="")
myfile <- basename(vcffn)
svp <- ScanVcfParam(which=GRanges("22", IRanges(0,200e5)), geno="GT")
vcfparams <- VCFQAParam(count.limits=c(301458000, Inf), readdepth.target = 30)
vcf <- ReadVCFData(mydir, myfile, "GRCh38")
ev <- VCFEvaluate(vcf, vcfparams)
getResults(ev)
```

---

getVR	<i>getVr is a Getter. Returns vr slot.</i>
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**Description**

getVr is a Getter. Returns vr slot.

**Usage**

```
getVR(x)
```

**Arguments**

x                    VCFData object

**Value**

VRanges

**Examples**

```
vcffn <- system.file("ext-data", "chr22.GRCh38.vcf.gz", package="genotypeeval")
mydir <- paste(dirname(vcffn), "/", sep="")
myfile <- basename(vcffn)
svp <- ScanVcfParam(which=GRanges("22", IRanges(0,1e5)), geno="GT")
vcf <- ReadVCFData(mydir, myfile, "GRCh38")
getVR(vcf)
```

---

GoldData-class	<i>Declare class Gold to store information from Gold" (1000 Genomes for example) along with the GoldDataParam</i>
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---

**Description**

Declare class Gold to store information from Gold" (1000 Genomes for example) along with the GoldDataParam

**Arguments**

genome	Genome build, GRCh37 or GRCh38
track	Where the gold data is stored
goldparams	The Param file with the limits to be applied
track.rare	Stores the Gold data with MAF < 0.01 if MAF exists

**Value**

Object of class GoldData

---

GoldDataFromGRanges	<i>User Constructor for class. Used to associate the gold params object with the gold granges and to check if MAF is present.</i>
---------------------	---

---

**Description**

User Constructor for class. Used to associate the gold params object with the gold granges and to check if MAF is present.

**Usage**

```
GoldDataFromGRanges(genome, gold.granges, goldparams)
```

**Arguments**

genome            Genome build, GRCh37 or GRCh38  
gold.granges      Gold file as GRanges  
goldparams        GoldDataParam object setting thresholds for evaluation

**Value**

Object of class GoldData

**Examples**

```
gparam <- GoldDataParam(percent.confirmed=0.792, percent.het.rare = 0.93)
gr <- GRanges(seqnames="22", IRanges(1e7,5e7))
gold <- GoldDataFromGRanges("GRCh38", gr, gparam)
```

---

GoldDataParam            *User Constructor for class*

---

**Description**

User Constructor for class

**Usage**

```
GoldDataParam(titv.coding.confirmed.l = 0, titv.coding.confirmed.u = 5,
  titv.noncoding.confirmed.l = 0, titv.noncoding.confirmed.u = 5,
  titv.coding.unconfirmed.l = 0, titv.coding.unconfirmed.u = 5,
  titv.noncoding.unconfirmed.l = 0, titv.noncoding.unconfirmed.u = 5,
  percent.confirmed.limits = 0, percent.het.rare.limits = 0)
```

**Arguments**

titv.coding.confirmed.l  
                         Lower limit of transition transversion ratio in coding confirmed  
titv.coding.confirmed.u  
                         upper limit of transition transverion ratio coding confirmed  
titv.noncoding.confirmed.l  
                         Lower limit of transition transversion ratio in noncoding confirmed  
titv.noncoding.confirmed.u  
                         upper limit of transition transverion ratio noncoding confirmed  
titv.coding.unconfirmed.l  
                         Lower limit of transition transversion ratio in coding unconfirmed  
titv.coding.unconfirmed.u  
                         upper limit of transition transverion ratio coding unconfirmed  
titv.noncoding.unconfirmed.l  
                         Lower limit of transition transversion ratio in noncoding unconfirmed

`titv.noncoding.unconfirmed.u`  
     upper limit of transition transversion ratio noncoding unconfirmed  
`percent.confirmed.limits`  
     lower limit, upper limit, percent confirmed in Gold comparator  
`percent.het.rare.limits`  
     lower limit, upper limit, (Percent Het in Rare, MAF < 0.01 in Gold) / Total  
     number of Heterozygotes

**Value**

Object of type GoldDataParam

**Examples**

```
gparam <- GoldDataParam(percent.confirmed=0.792, percent.het.rare = 0.93)
```

---

**GoldDataParam-class**    *Declare class GoldDataParam which will store thresholds to apply to VCFEvaluate object. This is intended for use in batch mode when a large number of vcf files needs to be screened and individual vcf files that fail flagged. All limits follow the format lower limit than upper limit*

---

**Description**

Declare class GoldDataParam which will store thresholds to apply to VCFEvaluate object. This is intended for use in batch mode when a large number of vcf files needs to be screened and individual vcf files that fail flagged. All limits follow the format lower limit than upper limit

**Arguments**

`titv.confirmed.limits`  
     lower limit coding, upper limit coding, lower limit noncoding, upper limit non-coding, Transition transversion ratios for confirmed snps  
`titv.unconfirmed.limits`  
     lower limit coding, upper limit coding, lower limit noncoding, upper limit non-coding, Transition transversion ratios for unconfirmed snps  
`percent.confirmed.limits`  
     lower limit, upper limit, percent confirmed in Gold comparator  
`percent.het.rare.limits`  
     lower limit, upper limit, (Percent Het in Rare, MAF < 0.01 in Gold) / Total  
     number of Heterozygotes

**Value**

Object of type GoldDataParam



---

ReadGoldData	<i>User Constructor for class</i>
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---

**Description**

User Constructor for class

**Usage**

```
ReadGoldData(genome, vcffilename, goldparams)
```

**Arguments**

genome	Genome build, GRCh37 or GRCh38
vcffilename	path and filename of vcf file
goldparams	GoldDataParam object setting thresholds for evaluation

**Value**

Object of class GoldData

**Examples**

```
gparam <- GoldDataParam(percent.confirmed=0.792, percent.het.rare = 0.93)
g1000fn <- system.file("ext-data", "example_gold_file.vcf", package="genotypeeval")
g1000 <- ReadGoldData("GRCh38", g1000fn, gparam)
```

---

ReadVCFData	<i>User Constructor for class. Calls VCFData constructor: ReadVCFData is a wrapper for readVcfAsVRanges. It removes indels, GL chromosomes, and MULTI calls. It scans the header of the vcf file and adds in the following fields for analysis if present: AD, GT, DP, GQ. Looks for the "END" tag in the header and reads in file as gVCF if necessary.</i>
-------------	--

---

**Description**

User Constructor for class. Calls VCFData constructor: ReadVCFData is a wrapper for readVcfAsVRanges. It removes indels, GL chromosomes, and MULTI calls. It scans the header of the vcf file and adds in the following fields for analysis if present: AD, GT, DP, GQ. Looks for the "END" tag in the header and reads in file as gVCF if necessary.

**Usage**

```
ReadVCFData(mydir, myfile, genome)
```

**Arguments**

mydir	Directory of vcf file
myfile	Filename of vcf file
genome	GRCh37 or GRCh38

**Value**

Object of class VCFData

**Examples**

```
vcffn <- system.file("ext-data", "chr22.GRCh38.vcf.gz", package="genotypeeval")
mydir <- paste(dirname(vcffn), "/", sep="")
myfile <- basename(vcffn)
vcf <- ReadVCFData(mydir, myfile, "GRCh38")
```

**ReadVCFDataChunk**


---

*User Constructor for class. Calls VCFData constructor: ReadVCFDataChunk is a wrapper for readVcfAsVRanges. It removes indels, GL chromosomes, and MULTI calls. It scans the header of the vcf file and adds in the following fields for analysis if present: AD, GT, DP, GQ. Looks for the "END" tag in the header and reads in file as gVCF if necessary. This is a multi core version of readVCFData. Note, input file must have been zipped and have a corresponding tabix file. It will drop all hom ref sites not in the admixture file but retain the counts of homref and multi in the VCF file. This means that a few of the metrics and the hom ref plot can no longer be calculated in VCFQARreport. If the metrics can no longer be calculated, it will not be output. Please note that if using a filter on the data (eg gq.filter) this will not be applied to the hom ref and total number of calls. The filter is applied in the VCFQARreport step and the metrics number of hom ref and total number of calls is calculated while reading in the file. When calling this function keep in mind the memory requirements. For example, if numcores=6, then when submitting the job you may request 12 Gb each core (72 Gb total). However the VCF in memory will need to fit back onto a single core or else R will not be able to allocate the memory. The given example here does not make sense to run as it includes only chromosome 22.*

---

**Description**

User Constructor for class. Calls VCFData constructor: ReadVCFDataChunk is a wrapper for readVcfAsVRanges. It removes indels, GL chromosomes, and MULTI calls. It scans the header of the vcf file and adds in the following fields for analysis if present: AD, GT, DP, GQ. Looks for the "END" tag in the header and reads in file as gVCF if necessary. This is a multi core version of readVCFData. Note, input file must have been zipped and have a corresponding tabix file. It

will drop all hom ref sites not in the admixture file but retain the counts of homref and multi in the VCF file. This means that a few of the metrics and the hom ref plot can no longer be calculated in VCFQAReport. If the metrics can no longer be calculated, it will not be output. Please note that if using a filter on the data (eg `gq.filter`) this will not be applied to the hom ref and total number of calls. The filter is applied in the VCFQAReport step and the metrics number of hom ref and total number of calls is calculated while reading in the file. When calling this function keep in mind the memory requirements. For example, if `numcores=6`, then when submitting the job you may request 12 Gb each core (72 Gb total). However the VCF in memory will need to fit back onto a single core or else R will not be able to allocate the memory. The given example here does not make sense to run as it includes only chromosome 22.

## Usage

```
ReadVCFDataChunk(mydir, myfile, genome, admixture.ref, numcores)
```

## Arguments

<code>mydir</code>	Directory of vcf file
<code>myfile</code>	Filename of vcf file (zipped)
<code>genome</code>	GRCh37 or GRCh38
<code>admixture.ref</code>	VRanges with MAF for superpopulations (EAS, AFR, EUR)
<code>numcores</code>	Number of cores to read in VCF (passed to <code>bplapply</code> )

## Value

Object of type `VCFData`

## Examples

```
vcffn <- system.file("ext-data", "chr22.GRCh38.vcf.gz", package="genotypeeval")
mydir <- paste(dirname(vcffn), "/", sep="")
myfile <- basename(vcffn)
svp <- ScanVcfParam(which=GRanges("22", IRanges(0,1e5)), geno="GT")
vcf <- ReadVCFData(mydir, myfile, "GRCh38")
admix.var <- getVR(vcf)[getVR(vcf)$GT %in% c("0|1", "1|0", "1|1"),][,1:2]
admix.var$EAS_AF <- ifelse(admix.var$GT %in% c("1|1"), 1, .5)
admix.var$AFR_AF <- 0
admix.var$EUR_AF <- 0
admix.hom <- getVR(vcf)[getVR(vcf)$GT %in% c("0|0"),][,1:2]
admix.hom$EAS_AF <- 0
admix.hom$AFR_AF <- 1
admix.hom$EUR_AF <- 1
admix.ref <- c(admix.var, admix.hom)
ReadVCFDataChunk(mydir, myfile, "GRCh38", admix.ref, numcores=2)
```

---

reformatData	<i>Take in the results from the population data and re-format it</i>
--------------	--

---

**Description**

Take in the results from the population data and re-format it

**Usage**

```
reformatData(results)
```

**Arguments**

results	The list of results from running the package using BatchJobs
---------	--

**Value**

list, data frame of logical (passed or not), data frame of numeric (all results)

---

VCFData-class	<i>Declare class Reads in VCF using readVCFAsVRanges</i>
---------------	--

---

**Description**

Declare class Reads in VCF using readVCFAsVRanges

**Arguments**

mydir	Directory of vcf file
myfile	Filename of vcf file
vr.homref	All SNPs from VCF with INDELS, MULTIs (seperately removed for variant and non variant), weird chromosomes removed
genoString	A character vector of all genotype fields present (looks for AD, GQ, GT, DP)
infoString	A character vector looking for "END" tag indicating file is a gVCF
genome	Declare if the genome is GRCh37 or GRCh38
n.dup	Counts the number of MULTIs removed
chunked	Whether data was read in using ReadVCFDataChunk which means hom refs not in the admixture file were dropped

**Value**

Object of class VCFData

---

VCFEvaluate	<i>Constructor for class. Calls constructor for class. Using the GENO fields present in the vcf header will evaluate the vcf file using metrics and generate plots. Each metric will be tested against the params specified in the params class. For example, if Read Depth is in the GENO header will calculate median read depth, percent in target (50 percent to 200 percent of the target specified in the params file) and generate a histogram of Read Depth.</i>
-------------	--

---

### Description

Constructor for class. Calls constructor for class. Using the GENO fields present in the vcf header will evaluate the vcf file using metrics and generate plots. Each metric will be tested against the params specified in the params class. For example, if Read Depth is in the GENO header will calculate median read depth, percent in target (50 percent to 200 percent of the target specified in the params file) and generate a histogram of Read Depth.

### Usage

```
VCFEvaluate(myvcf, vcfparams, gold.ref = NA, cds.ref = NA,
  masked.ref = NA, admixture.ref = NA)
```

### Arguments

myvcf	Vcf file to evaluate
vcfparams	object of VCFQAParam class. Sets thresholds to evaluate the VCF File against.
gold.ref	Object of class Gold that contains the 1000 Genomes reference
cds.ref	Coding Region as GRanges
masked.ref	optional regions as GRanges to mask eg repeats, self chain, paralogs, etc.
admixture.ref	VRanges with MAF for superpopulations (EAS, AFR, EUR)

### Value

Object of VCFQAReport.

### Examples

```
vcffn <- system.file("ext-data", "chr22.GRCh38.vcf.gz", package="genotypeeval")
mydir <- paste(dirname(vcffn), "/", sep="")
myfile <- basename(vcffn)
svp <- ScanVcfParam(which=GRanges("22", IRanges(0,200e5)), geno="GT")
vcfparams <- VCFQAParam(count.limits=c(301458000, Inf), readdepth.target = 30)
vcf <- ReadVCFData(mydir, myfile, "GRCh38")
ev <- VCFEvaluate(vcf, vcfparams)
```

---

VCFQAParam

*User Constructor for class. Call limits are set as default to pass.*


---

## Description

User Constructor for class. Call limits are set as default to pass.

## Usage

```
VCFQAParam(homref.limits = c(-Inf, Inf), het.limits = c(-Inf, Inf),
  homvar.limits = c(-Inf, Inf), percenthets.limits = c(-Inf, Inf),
  titv.noncoding.limits = c(-Inf, Inf), titv.coding.limits = c(-Inf, Inf),
  readdepth.target = -1, readdepth.limits = c(-Inf, Inf),
  readdepth.percent.limits = 0, gq.limit = 0, masked.limits = c(-Inf,
  Inf), non.masked.limits = c(-Inf, Inf), het.gap.limits = rep(Inf, 24),
  count.limits = c(-Inf, Inf), gq.filter = 0, dp.filter = -1)
```

## Arguments

homref.limits	lower limit, upper limit, number of homozygous reference
het.limits	lower limit, upper limit, number of heterozygous calls
homvar.limits	lower limit, upper limit, number of homozygous alternative
percenthets.limits	lower limit, upper limit, Number of Heterozygous / (Total Number of Counts) or percent het
titv.noncoding.limits	lower limit, upper limit, Transition transversion ratio in noncoding regions
titv.coding.limits	lower limit, upper limit, Transition transversion ratio in coding regions
readdepth.target	The sequencing depth target (eg 30x)
readdepth.limits	lower limit, upper limit, Mean read depth
readdepth.percent.limits	lower limit, upper limit, Percent read depth in target (50 percent to 200 percent of target read depth)
gq.limit	lower limit, Mean genotype quality (does not make sense to have an upper limit)
masked.limits	lower limit, upper limit, (Number of heterozygous in self chained regions)/(Total number of heterozygotes)
non.masked.limits	lower limit, upper limit, (Number of heterozygous in non-self chained regions)/(Total number of heterozygotes)
het.gap.limits	lower limit, upper limit, Largest gap within chromosome between two heterozygous calls

count.limits lower limit, upper limit, total number of counts  
 gq.filter filter for the VCF file on genotype quality (eg only GQ > 90)  
 dp.filter filter for the VCF file on read depth (eg only DP > 0)

**Value**

Object of class VCFQAParam

**Examples**

```
vcfparams <- VCFQAParam(count.limits=c(301458000, Inf), readdepth.target = 30)
```

---

VCFQAParam-class	<i>Declare class VCFQAParam which will store thresholds to apply to VCFEvaluate object. This is intended for use in batch mode when a large number of vcf files needs to be screened and individual vcf files that fail flagged. All limits follow the format lower limit than upper limit</i>
------------------	--

---

**Description**

Declare class VCFQAParam which will store thresholds to apply to VCFEvaluate object. This is intended for use in batch mode when a large number of vcf files needs to be screened and individual vcf files that fail flagged. All limits follow the format lower limit than upper limit

**Arguments**

homref.limits lower limit, upper limit, number of homozygous reference  
 het.limits lower limit, upper limit, number of heterozygous calls  
 homvar.limits lower limit, upper limit, number of homozygous alternative  
 count.limits lower limit, upper limit, total number of counts  
 percenthets.limits  
 lower limit, upper limit, Number of Heterozygous / (Total Number of Counts)  
 or percent het  
 titv.noncoding.limits  
 lower limit, upper limit, Transition transversion ratio in noncoding regions  
 titv.coding.limits  
 lower limit, upper limit, Transition transversion ratio in coding regions  
 readdepth.target  
 The sequencing depth target (eg 30x)  
 readdepth.limits  
 lower limit, upper limit, Mean read depth  
 readdepth.percent.limits  
 lower limit, upper limit, Percent read depth in target (50 percent to 200 percent  
 of target read depth)

gq.limit	lower limit, Mean genotype quality (does not make sense to have an upper limit)
masked.limits	lower limit, upper limit, (Number of heterozygous in masked regions)/(Total number of heterozygotes)
non.masked.limits	lower limit, upper limit, (Number of heterozygous in non-self chained regions)/(Total number of heterozygotes)
het.gap.limits	lower limit, upper limit, Largest gap within chromosome between two heterozygous calls
gq.filter	filter for the VCF file on genotype quality (eg only GQ > 90)
dp.filter	filter for the VCF file on read depth (eg only DP > 0)

**Value**

VCFQAParam object

---

VCFQAReport-class      *Declare class VCFQAReport which will evaluate a VCF stored as a ReadData object.*

---

**Description**

Declare class VCFQAReport which will evaluate a VCF stored as a ReadData object.

**Arguments**

printnames	List of tests applied to VCF
results	Numeric vector of metrics calculated from VCF file
plots	List of plots created from VCF File
tests	TRUE (passed) or FALSE (failed) logical vector of whether VCF passed metrics using thresholds from VCFQAParam
fn	Filename of VCF evaluated (for plot titles)



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