

# Package ‘EpiTxDb’

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**Type** Package

**Title** Storing and accessing epitranscriptomic information using the AnnotationDbi interface

**Version** 1.3.0

**Description** EpiTxDb facilitates the storage of epitranscriptomic information. More specifically, it can keep track of modification identity, position, the enzyme for introducing it on the RNA, a specifier which determines the position on the RNA to be modified and the literature references each modification is associated with.

**License** Artistic-2.0

**Encoding** UTF-8

**LazyData** false

**biocViews** Software, Epitranscriptomics

**Depends** R (>= 4.0), AnnotationDbi, Modstrings

**Imports** methods, utils, httr, xml2, curl, GenomicFeatures, GenomicRanges, GenomeInfoDb, BiocGenerics, BiocFileCache, S4Vectors, IRanges, RSQLite, DBI, Biostrings, tRNAdbImport

**Suggests** BiocStyle, knitr, rmarkdown, testthat, httpptest, AnnotationHub, ensemblDb, ggplot2, EpiTxDb.Hs.hg38, BSgenome.Hsapiens.UCSC.hg38, BSgenome.Scerevisiae.UCSC.sacCer3, TxDb.Hsapiens.UCSC.hg38.knownGene

**Collate** 'AllGenerics.R' 'EpiTxDb-SELECT-helpers.R' 'EpiTxDb-schema.R' 'EpiTxDb.R' 'EpiTxDb-class.R' 'makeEpiTxDb.R' 'makeEpiTxDbFromGRanges.R' 'shiftGenomicToTranscript.R' 'makeEpiTxDbFromRMBase.R' 'makeEpiTxDbFromtRNAdb.R' 'modifications.R' 'modificationsBy.R' 'ranges-helpers.R' 'select-methods.R'

**RoxygenNote** 7.1.0

**BugReports** <https://github.com/FelixErnst/EpiTxDb/issues>

**URL** <https://github.com/FelixErnst/EpiTxDb>

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EpiTxDb-package	<i>EpiTxDb - Storing and accessing epitranscriptomic information using the AnnotationDbi interface</i>
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## Description

title

## Author(s)

Felix G M Ernst [aut]

## References

Jia-Jia Xuan, Wen-Ju Sun, Ke-Ren Zhou, Shun Liu, Peng-Hui Lin, Ling-Ling Zheng, Liang-Hu Qu, Jian-Hua Yang (2017): "RMBase v2.0: Deciphering the Map of RNA Modifications from Epitranscriptome Sequencing Data." *Nucleic Acids Research*, Volume 46, Issue D1, 4 January 2018, Pages D327–D334. doi: 10.1093/nar/gkx934

Jühling, Frank; Mörl, Mario; Hartmann, Roland K.; Sprinzl, Mathias; Stadler, Peter F.; Pütz, Joern (2009): "TRNAdb 2009: Compilation of tRNA Sequences and tRNA Genes." *Nucleic Acids Research* 37 (suppl\_1): D159–D162. doi: 10.1093/nar/gkn772

Sprinzl, Mathias; Vassilenko, Konstantin S. (2005): "Compilation of tRNA Sequences and Sequences of tRNA Genes." *Nucleic Acids Research* 33 (suppl\_1): D139–D140. doi: 10.1093/nar/gki012

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EpiTxDb-class

*EpiTxDb objects*


---

### Description

The EpiTxDb class is a [AnnotationDb](#) type container for storing Epitranscriptomic information.

The information are typically stored on a per transcript and not as genomic coordinates, but the EpiTxDb class is agnostic to this. In case of genomic coordinates `transcriptsBy` will return modifications per chromosome.

### Usage

```
## S4 method for signature 'EpiTxDb'
organism(object)
```

```
## S4 method for signature 'EpiTxDb'
seqinfo(x)
```

```
## S4 method for signature 'EpiTxDb'
seqlevels(x)
```

```
## S4 method for signature 'EpiTxDb'
as.list(x)
```

### Arguments

`x, object`      a EpiTxDb object

### Value

For

- `organism()` and `seqlevels()` a character vector
- `seqinfo()` a [Seqinfo](#) object
- `as.list()` a list

### See Also

- [makeEpiTxDbFromGRanges](#) for creating a EpiTxDb object from a [GRanges](#) object and it's metadata columns
- [makeEpiTxDbFromRMBase](#) for creating a EpiTxDb object from RMBase online resources
- [makeEpiTxDbFromtRNadb](#) for creating a EpiTxDb object from tRNadb online resources
- [makeEpiTxDb](#) for creating a EpiTxDb object from `data.frames`
- [modifications](#), [modificationsBy](#) for getting epitranscriptomic modification locations
- [select](#) for using the default interface of [AnnotationDb](#) objects.
- [shiftGenomicToTranscript](#) and [shiftTranscriptToGenomic](#) for transferring genomic to transcript coordinates and back again.

**Examples**

```

etdb_file <- system.file("extdata", "EpiTxDb.Hs.hg38.snoRNadb.sqlite",
                        package="EpiTxDb")
etdb <- loadDb(etdb_file)
etdb

# general methods
seqinfo(etdb) #
seqlevels(etdb) # easy access to all transcript names

```

---

EpiTxDb-data	<i>EpiTxDb internal data</i>
--------------	------------------------------

---

**Description**

EpiTxDb internal data

**Usage**

```
data(rmbase_data)
```

**Format**

data.frame

---

makeEpiTxDb	<i>Creating a EpiTxDb from user supplied annotations as data.frames</i>
-------------	---

---

**Description**

makeEpiTxDb is a low-level constructor for creating a [EpiTxDb](#) object from user supplied annotations.

This functions typically will not be used by regular users.

**Usage**

```

makeEpiTxDb(
  modifications,
  reactions = NULL,
  specifiers = NULL,
  references = NULL,
  metadata = NULL,
  reassign.ids = FALSE
)

```

**Arguments**

- modifications** A data.frame containing the following columns:
- **mod\_id**: a unique integer value per modification.
  - **mod\_type**: the modification type as a character or factor value. Must be a value from `shortName(ModRNAString())`.
  - **mod\_name**: a character or factor name for the specific modification
  - **mod\_start**: the start position for the modification as integer value. Usually `mod_start = mod_end`
  - **mod\_end**: the end position for the modification as integer value. Usually `mod_start = mod_end`
  - **mod\_strand**: the strand information for the modification as a character or factor.
  - **sn\_id**: a integer value per unique sequence
  - **sn\_name**: a character or factor as sequence name, e.g a chromosome or a transcript identifier like `chr1`.
- The first six are mandatory, whereas one of the last two has to be set. `sn_id` will be generated from `sn_name`, if `sn_id` is not set.
- reactions** An optional data.frame containing the following columns:
- **mod\_id**: a integer value per modification and the link to the modification data.frame.
  - **rx\_genename**: a character or factor referencing a genename for the enzyme incorporating the modification.
  - **rx\_rank**: a integer for sorting enzyme reactions, if multiple enzymes are involved in the modification's incorporation/maintenance.
  - **rx\_ensembl**: a character or factor with an ensembl identifier for the genename of the enzyme.
  - **rx\_ensembltrans**: a character or factor with an ensembl identifier for the transcript being translated into the enzyme.
  - **rx\_entrezid**: a character or factor with an entrezid for the genename of the enzyme.
- (default: `reactions = NULL`)
- specifiers** An optional data.frame containing the following columns:
- **mod\_id**: a integer value per modification and the link to the modification data.frame.
  - **spec\_type**: a character or factor referencing a type of specifier, e.g. snoRNA. Not checked for validity.
  - **spec\_genename**: a character or factor referencing a genename for the specifier directing an enzyme to the specific location for the modification to be incorporated.
  - **spec\_ensembl**: a character or factor with an ensembl identifier for the genename of the specifier.
  - **spec\_ensembltrans**: a character or factor with an ensembl identifier for the transcript being translated into the specifier.
  - **spec\_entrezid**: a character or factor with an entrezid for the genename of the specifier.
- (default: `specifiers = NULL`)
- references** An optional data.frame containing the following columns:

	<ul style="list-style-type: none"> <li>• <code>mod_id</code>: a integer value per modification and the link to the modification data.frame.</li> <li>• <code>ref_type</code>: a character or factor with a reference type, e.g. PMID. Is not checked for validity.</li> <li>• <code>ref</code>: a character or factor with a reference value, e.g. a specific pubmed id or an journal article. Is not checked for validity.</li> </ul>
	(default: <code>references = NULL</code> )
<code>metadata</code>	<p>An optional data.frame containing the following columns:</p> <ul style="list-style-type: none"> <li>• <code>name</code>: a character value used as name</li> <li>• <code>value</code>: a character value</li> </ul> <p>This dataframe will be returned by <code>metadata()</code> (default: <code>metadata = NULL</code>)</p>
<code>reassign.ids</code>	TRUE or FALSE Controls how internal <code>mod_ids</code> should be assigned. If <code>reassign.ids</code> is FALSE (the default) and if the ids are supplied, then they are used as the internal ids, otherwise the internal ids are assigned in a way that is compatible with the order defined by ordering the modifications first by chromosome, then by strand, then by start, and finally by end.

### Value

a EpiTxDb object.

### See Also

- [makeEpiTxDbFromGRanges](#) for creating a EpiTxDb object from a [GRanges](#) object and it's metadata columns
- [makeEpiTxDbFromRMBase](#) for creating a EpiTxDb object from RMBase online resources
- [makeEpiTxDbFromtRNadb](#) for creating a EpiTxDb object from tRNadb online resources
- [shortName](#) and [ModRNAString](#) for information on ModRNAString objects.

### Examples

```

mod <- data.frame("mod_id" = 1L,
                 "mod_type" = "m1A",
                 "mod_name" = "m1A_1",
                 "mod_start" = 1L,
                 "mod_end" = 1L,
                 "mod_strand" = "+",
                 "sn_id" = 1L,
                 "sn_name" = "test")
rx <- data.frame(mod_id = 1L,
                 rx_genename = "test",
                 rx_rank = 1L,
                 rx_ensembl = "test",
                 rx_ensembltrans = "test",
                 rx_entrezid = "test")
spec <- data.frame(mod_id = 1L,
                  spec_type = "test",
                  spec_genename = "test",
                  spec_ensembl = "test",
                  spec_ensembltrans = "test",
                  spec_entrezid = "test")
ref <- data.frame(mod_id = 1L,

```

```
      ref_type = "test",
      ref = "test")
etdb <- makeEpiTxDb(mod,rx,spec,ref)
```

---

makeEpiTxDbFromGRanges

*Create a EpiTxDb object from a GRanges object*

---

## Description

makeEpiTxDbFromGRanges extracts informations from a [GRanges](#) object. The following metadata columns can be used:

- mod\_id, mod\_type, mod\_name and tx\_ensembl. The first three are mandatory, whereas tx\_ensembl is optional.
- rx\_genename, rx\_rank, rx\_ensembl, rx\_ensembltrans and rx\_entrezid
- spec\_type, spec\_genename, spec\_ensembl, spec\_ensembltrans and spec\_entrezid
- ref\_type and ref

... and passed on the [makeEpiTxDb](#).

## Usage

```
makeEpiTxDbFromGRanges(gr, metadata = NULL, reassign.ids = FALSE)
```

## Arguments

gr	A <a href="#">GRanges</a> object, which contains at least the mandatory columns.
metadata	A 2-column data.frame containing meta information to be included in the EpiTxDb object. This data.frame is just passed to <a href="#">makeEpiTxDb</a> . See <a href="#">makeEpiTxDb</a> for more information about the format of metadata. (default: metadata = NULL)
reassign.ids	= FALSE

## Value

a EpiTxDb object.

## Examples

```
library(GenomicRanges)
gr <- GRanges(seqnames = "test",
              ranges = IRanges::IRanges(1,1),
              strand = "+",
              DataFrame(mod_id = 1L,
                       mod_type = "Am",
                       mod_name = "Am_1"))
etdb <- makeEpiTxDbFromGRanges(gr)
```

---

makeEpiTxDbFromRMBase *Create a EpiTxDb object from RMBase v2.0 online resources*

---

## Description

makeEpiTxDbFromRMBase will make use of the RMBase v2.0 online resources.

## Usage

```
EPITXDB_RMBASE_URL
```

```
downloadRMBaseFiles(organism, genome, modtype)
```

```
makeEpiTxDbFromRMBase(  
  organism,  
  genome,  
  modtype,  
  tx = NULL,  
  sequences = NULL,  
  metadata = NULL,  
  reassign.ids = FALSE  
)
```

```
getRMBaseDataAsGRanges(files)
```

```
makeEpiTxDbFromRMBaseFiles(  
  files,  
  tx = NULL,  
  sequences = NULL,  
  metadata = NULL,  
  reassign.ids = FALSE  
)
```

```
listAvailableOrganismsFromRMBase()
```

```
listAvailableGenomesFromRMBase(organism)
```

```
listAvailableModFromRMBase(organism, genome)
```

## Arguments

organism	A character value, which must match an organism descriptor on the RMBase download website.
genome	A character value, which must match a genome descriptor on the RMBase download website.
modtype	A character value, which must match one or more modification descriptors on the RMBase download website.
tx	A <a href="#">GRangesList</a> object which will be used to shift the genomic coordinates to transcript coordinates. This is optional, but highly recommended. (default: tx = NULL).



sequences	A named DNASTringSet or RNASTringSet, which will be used to check whether the defined modifications are compatible with the original base. This uses <a href="#">removeIncompatibleModi</a> function from the Modstrings package.
metadata, reassign.ids	See <a href="#">makeEpiTxDb</a>
files	From organism, genome and modtype the available files will be downloaded using the <a href="#">BiocFileCache</a> interface and passed on to makeEpiTxDbFromRMBaseFiles. However, individual files can be provided as well.

### Format

An object of class character of length 1.

### Value

a EpiTxDb object.

---

makeEpiTxDbFromtRNAdb *Create a EpiTxDb object from tRNAdb resources*

---

### Description

makeEpiTxDbFromtRNAdb will make use of the tRNAdb online resources and extract the modification information from the RNA database.

If a named [DNASTringSet](#) is provided as sequences, the result from the tRNAdb will be matched against the sequences. Valid matches will be used as transcript identifiers and returned after a check of modification compatibility with the provided sequence. By this process multiple copies of transcripts can be associated with a single modification.

makeEpiTxDbFromtRNAdb uses the functions provided by the [tRNAdbImport](#) package. [import.tRNAdb](#) will be used with database = "RNA" and the three different values for origin.

### Usage

```
gettRNAdbDataAsGRanges(
  organism,
  sequences = NULL,
  dbURL = tRNAdbImport::TRNA_DB_URL
)

makeEpiTxDbFromtRNAdb(
  organism,
  sequences = NULL,
  metadata = NULL,
  dbURL = tRNAdbImport::TRNA_DB_URL
)

listAvailableOrganismsFromtRNAdb()
```

**Arguments**

organism	A character value for an organism available on the tRNAdb website.
sequences	A named DNASTringSet or RNASTringSet, which will be used to associate a tRNAdb result with a specific transcript.
dbURL	The URL to the tRNA db website.
metadata	See <a href="#">makeEpiTxDb</a>

**Value**

a EpiTxDb object.

**References**

Juehling F, Moerl M, Hartmann RK, Sprinzl M, Stadler PF, Puetz J. 2009. "tRNAdb 2009: compilation of tRNA sequences and tRNA genes." *Nucleic Acids Research*, Volume 37 (suppl\_1): D159–162. doi:10.1093/nar/gkn772.

**Examples**

```
# getting just the annotation data
etdb <- makeEpiTxDbFromtRNAdb("Saccharomyces cerevisiae")

# For associating the result with transcripts, provide and additional
# named DNASTringSet object. Matching will be done against each sequence
# allowing 5 mismatches and indels. The final result will be checked for
# validity regarding the identity of the modifications
## Not run:
etdb <- makeEpiTxDbFromtRNAdb("Saccharomyces cerevisiae",
                             some_transcript_sequences)

## End(Not run)
```

---

modifications

*Getting modification data from a EpiTxDb-object*

---

**Description**

modifications and modificationsBy are functions to extract modification annotation from a [EpiTxDb](#) object.

modifiedSeqsByTranscript returns a [ModRNASTringSet](#) from a EpiTxDb object and compatible RNASTringSet object. This used the [combineIntoModstrings\(\)](#) function from the Modstrings package.

**Usage**

```
modifications(
  x,
  columns = c("mod_id", "mod_type", "mod_name"),
  filter = NULL,
  use.names = FALSE,
  ...
```

```

)

modificationsBy(
  x,
  by = c("seqnames", "mod_type", "reaction", "specifier", "specifier_type"),
  ...
)

modifiedSeqsByTranscript(x, sequences, ...)

## S4 method for signature 'EpiTxDb'
modifications(
  x,
  columns = c("mod_id", "mod_type", "mod_name"),
  filter = NULL,
  use.names = FALSE
)

## S4 method for signature 'EpiTxDb'
modificationsBy(
  x,
  by = c("seqnames", "modtype", "reaction", "specifier", "specifiertype")
)

## S4 method for signature 'EpiTxDb,DNAStringSet'
modifiedSeqsByTranscript(x, sequences)

```

## Arguments

x	a <a href="#">EpiTxDb</a>
columns	Columns to include in the result. If the vector is named, those names are used for the corresponding column in the element metadata of the returned object. (default: <code>columns = c("mod_id", "mod_type", "mod_name")</code> )
filter	Either NULL or a named list of vectors to be used to restrict the output. Valid names for this list are: "mod_id", "mod_type", "mod_name", "sn_id", "sn_name", "rx_genename", "rx_ensembl", "rx_ensembltrans", "rx_entrezid", "spec_genename", "spec_type", "spec_ensembl", "spec_ensembltrans", "spec_entrezid", "ref_type" and "ref". (default: <code>filter = NULL</code> )
use.names	TRUE or FALSE. If TRUE, the modification names are set as the names of the returned object. (default: <code>use.names = FALSE</code> )
...	Not used.
by	By which information type should the result be split into? A character value from one of the following values: <ul style="list-style-type: none"> <li>• seqnames</li> <li>• mod_type</li> <li>• reaction</li> <li>• specifier</li> <li>• specifier_type</li> </ul>
sequences	A <a href="#">RNAStringSet</a> , which can be used as input for <a href="#">combineIntoModstrings()</a> . See <a href="#">?combineIntoModstrings</a> for additional details.

**Value**

a [GRanges](#) object for modifications and a [GRangesList](#) for modificationsBy.

**Examples**

```
etdb_file <- system.file("extdata", "EpiTxDb.Hs.hg38.snoRNADB.sqlite",
                        package="EpiTxDb")
etdb <- loadDb(etdb_file)
etdb
```

---

positionSequence	<i>Generate integer sequences from position information of Ranges</i>
------------------	---

---

**Description**

positionSequence generates sequences of integer values along the range information of x. This can be used for navigating specific positions on a range information.

**Usage**

```
positionSequence(x, order = FALSE, decreasing = FALSE)

## S4 method for signature 'Ranges'
positionSequence(x, order = FALSE, decreasing = FALSE)

## S4 method for signature 'RangesList'
positionSequence(x, order = FALSE, decreasing = FALSE)

## S4 method for signature 'Ranges'
as.integer(x)
```

**Arguments**

x	a Ranges object, like a <a href="#">GRanges</a> or <a href="#">IRanges</a> , or a RangesList object, like a <a href="#">GRangesList</a> or <a href="#">IRangesList</a>
order	TRUE or FALSE: Should the position be ordered? (default: order = FALSE)
decreasing	TRUE or FALSE: If order = TRUE Should the position be ordered in a decreasing order? (default: order = FALSE)

**Value**

a integer vector if x is a [GRanges](#) object and a IntegerList if x is a [GRangesList](#)

**Examples**

```
library(GenomicRanges)
# Returns an integer vector
gr <- GRanges("chr1:1-5:+")
positionSequence(gr)
gr2 <- GRanges("chr1:1-5:-")
positionSequence(gr)
# returns an IntegerList
```

```
gr1 <- GRangesList("1" = gr,"2" = gr,"3" = gr2) # must be named
positionSequence(gr1)
```

---

rescale

*Rescaling Ranges object*

---

### Description

rescale() rescales IRanges, GRanges, IRangesList and GRangesList by using minima and maxima derived from to and from.

### Usage

```
rescale(x, to = 1L, from = 1L)

## S4 method for signature 'IRanges'
rescale(x, to = 1L, from = 1L)

## S4 method for signature 'IRangesList'
rescale(x, to = 1L, from = 1L)

## S4 method for signature 'GRanges'
rescale(x, to = 1L, from = 1L)

## S4 method for signature 'GRangesList'
rescale(x, to = 1L, from = 1L)
```

### Arguments

x	a IRanges, GRanges, IRangesList and GRangesList object
to, from	an IRanges object, a character vector coercible to IRanges or a integer vector parallel to x or with length = 1L.

### Value

an object of the same type and dimensions as x

### Author(s)

H. Pagès, F. Ernst

### See Also

[IRanges](#) for details on character vectors coercible to IRanges.

### Examples

```
x <- IRanges("5-10")
# widen the ranges
rescale(x, 100, 10)
# widen and shift
rescale(x, "31-60", "5-14")
```

---

select *Using the "select" interface on EpiTxDb objects*

---

### Description

As expected for a `AnnotationDb` object, the general accessors `select`, `keys`, `columns` and `keytypes` can be used to get information from a `EpiTxDb` object.

### Usage

```
## S4 method for signature 'EpiTxDb'
select(x, keys, columns, keytype, ...)

## S4 method for signature 'EpiTxDb'
columns(x)

## S4 method for signature 'EpiTxDb'
keys(x, keytype, ...)

## S4 method for signature 'EpiTxDb'
keytypes(x)
```

### Arguments

`x` a `EpiTxDb` object  
`keys`, `columns`, `keytype`, ...  
 See `AnnotationDb` for more comprehensive description of the methods `select`, `keys`, `columns` and `keytypes` and their arguments.

### Value

a `data.frame` object for `select()` and a character vector for `keytypes()`, `keys()` and `columns()`.

### Examples

```
etdb_file <- system.file("extdata", "EpiTxDb.Hs.hg38.snoRNadb.sqlite",
                        package="EpiTxDb")
etdb <- loadDb(etdb_file)
etdb
```

---

shiftTranscriptToGenomic  
*Shift GRanges coordinates based on another GRanges object*

---

### Description

`shiftGenomicToTranscript` shifts positions of a `GRanges` object based on coordinates of another `GRanges` object. The most common application is to shift genomic coordinates to transcript coordinates, which is reflected in the name. `shiftTranscriptToGenomic` implements the reverse operation.

Matches are determined by `findOverlaps` for `shiftGenomicToTranscript` and by `findMatches` for `shiftTranscriptToGenomic` using the `seqnames` of the subject and the names of `tx`.

**Usage**

```

shiftTranscriptToGenomic(subject, tx)

shiftGenomicToTranscript(subject, tx)

## S4 method for signature 'GRanges,GRangesList'
shiftTranscriptToGenomic(subject, tx)

## S4 method for signature 'GRangesList,GRangesList'
shiftTranscriptToGenomic(subject, tx)

## S4 method for signature 'GRanges,GRangesList'
shiftGenomicToTranscript(subject, tx)

## S4 method for signature 'GRangesList,GRangesList'
shiftGenomicToTranscript(subject, tx)

```

**Arguments**

```

subject      a GRanges or GRangesList object
tx           a named GRangesList object.

```

**Value**

a [GRanges](#) or [GRangesList](#) object depending on the type of subject

**Examples**

```

library(GenomicRanges)
# Construct some example data
subject1 <- GRanges("chr1", IRanges(3, 6),
  strand = "+")
subject2 <- GRanges("chr1", IRanges(c(17,23), width=3),
  strand = c("+","-"))
subject3 <- GRanges("chr2", IRanges(c(51, 54), c(53, 59)),
  strand = "-")
subject <- GRangesList(a=subject1, b=subject2, c=subject3)
tx1 <- GRanges("chr1", IRanges(1, 40),
  strand="+")
tx2 <- GRanges("chr1", IRanges(10, 30),
  strand="+")
tx3 <- GRanges("chr2", IRanges(50, 60),
  strand="-")
tx <- GRangesList(a=tx1, b=tx2, c=tx3)

# shift to transcript coordinates. Since the third subject does not have
# a match in tx it is dropped with a warning
shifted_gr1 <- shiftGenomicToTranscript(subject,tx)

# ... and back
shifted_gr12 <- shiftTranscriptToGenomic(shifted_gr1,tx)

# comparison of ranges work. However the seqlevels differ
ranges(shifted_gr12) == ranges(subject[[list(1,c(1,1),c(1,2))]])

```

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