

# Package ‘immunotation’

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**Type** Package

**Title** Tools for working with diverse immune genes

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## Description

MHC (major histocompatibility complex) molecules are cell surface complexes that present antigens to T cells. The repertoire of antigens presented in a given genetic background largely depends on the sequence of the encoded MHC molecules, and thus, in humans, on the highly variable HLA (human leukocyte antigen) genes of the hyperpolymorphic HLA locus. More than 28,000 different HLA alleles have been reported, with significant differences in allele frequencies between human populations worldwide. Reproducible and consistent annotation of HLA alleles in large-scale bioinformatics workflows remains challenging, because the available reference databases and software tools often use different HLA naming schemes. The package immunotation provides tools for consistent annotation of HLA genes in typical immunoinformatics workflows such as for example the prediction of MHC-presented peptides in different human donors. Converter functions that provide mappings between different HLA naming schemes are based on the MHC restriction ontology (MRO). The package also provides automated access to HLA alleles frequencies in worldwide human reference populations stored in the Allele Frequency Net Database.

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'MRO\_interface\_helper.R' 'MRO\_interface.R' 'MACUI\_interface.R'  
'nomenclature\_queries.R' 'AFND\_queries.R' 'visualization.R'

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---

|                                 |  |
|---------------------------------|--|
| assemble_protein_complex        |  |
| <i>Assemble protein complex</i> |  |

---

### Description

Assemble a table or MHC protein complexes for a given organism.

### Usage

```
assemble_protein_complex(organism)
```

### Arguments

|          |                                                                                                                                                                          |
|----------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| organism | Organism for which the lookup should be built (e.g. "human", "mouse", ...). The list of valid organisms can be found using the function <code>get_valid_organisms</code> |
|----------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

### Value

a data frame with the MHC complexes annotated in MRO (only completely annotated complexes are returned)

### Examples

```
assemble_protein_complex(organism = "mouse")
```

---

|                    |                                            |
|--------------------|--------------------------------------------|
| build_allele_group | <i>Building a list of alleles to cover</i> |
|--------------------|--------------------------------------------|

---

**Description**

build\_allele\_group e.g. A\*01:01 -> A\*01:01:01, A\*01:01:02, A\*01:01:03

**Usage**

```
build_allele_group(allele_selection)
```

**Arguments**

|                  |                                                        |
|------------------|--------------------------------------------------------|
| allele_selection | HLA allele for which the allele group should be built. |
|------------------|--------------------------------------------------------|

**Value**

list of alleles

**Examples**

```
build_allele_group("A*01:01")
```

---

|                   |                                                       |
|-------------------|-------------------------------------------------------|
| check_geographics | <i>check_geographics, stops if input not adequate</i> |
|-------------------|-------------------------------------------------------|

---

**Description**

check\_geographics, stops if input not adequate

**Usage**

```
check_geographics(country, region, ethnic)
```

**Arguments**

|         |                                                         |
|---------|---------------------------------------------------------|
| country | country used for allele frequency selection             |
| region  | geographical region used for allele frequency selection |
| ethnic  | ethnic origin used for allele frequency selection       |

**Value**

TRUE

---

|                 |                                                     |
|-----------------|-----------------------------------------------------|
| check_hla_locus | <i>check_hla_locus, stops if input not adequate</i> |
|-----------------|-----------------------------------------------------|

---

**Description**

check\_hla\_locus, stops if input not adequate

**Usage**

check\_hla\_locus(hla\_locus)

**Arguments**

hla\_locus        locus of hla frequencies to query

**Value**

TRUE

---

|                     |                                                         |
|---------------------|---------------------------------------------------------|
| check_hla_selection | <i>check_hla_selection, stops if input not adequate</i> |
|---------------------|---------------------------------------------------------|

---

**Description**

check\_hla\_selection, stops if input not adequate

**Usage**

check\_hla\_selection(hla\_selection, query\_type)

**Arguments**

hla\_selection    HLA alleles used for selection  
query\_type       ["allele"|"haplotype"] type of AFND query

**Value**

TRUE

---

|                  |                                                      |
|------------------|------------------------------------------------------|
| check_population | <i>check_population, stops if input not adequate</i> |
|------------------|------------------------------------------------------|

---

**Description**

check\_population, stops if input not adequate

**Usage**

check\_population(hla\_population)

**Arguments**

hla\_population    population id

**Value**

TRUE

---

|                   |                                                       |
|-------------------|-------------------------------------------------------|
| check_sample_size | <i>check_sample_size, stops if input not adequate</i> |
|-------------------|-------------------------------------------------------|

---

**Description**

check\_sample\_size, stops if input not adequate

**Usage**

check\_sample\_size(hla\_sample\_size\_pattern, hla\_sample\_size)

**Arguments**

hla\_sample\_size\_pattern  
                          one of "bigger\_than", "equal", "less\_than", "less\_equal\_than", "bigger\_equal\_than", "different"  
hla\_sample\_size  
                          integer number used for population size

**Value**

TRUE

---

|                |                                                    |
|----------------|----------------------------------------------------|
| check_standard | <i>check_standard, stops if input not adequate</i> |
|----------------|----------------------------------------------------|

---

**Description**

check\_standard, stops if input not adequate

**Usage**

check\_standard(standard)

**Arguments**

standard          one of "a" - all, "s" - silver, "g" - gold

**Value**

TRUE

---

|                      |                             |
|----------------------|-----------------------------|
| create_encode_handle | <i>create_encode_handle</i> |
|----------------------|-----------------------------|

---

**Description**

create\_encode\_handle

**Usage**

create\_encode\_handle(allele\_names)

**Arguments**

allele\_names      list of HLA alleles

**Value**

curl handle

---

`decode_MAC`*Decode MAC*

---

**Description**

Decode a multiple allele code (MAC) into a list of HLA alleles. #' The National Marrow Donor Program (NMDP) uses [MAC](<https://bioinformatics.bethematchclinical.org/hla-resources/allele-codes/allele-code-lists/>) to facilitate the reporting and comparison of HLA alleles. MAC represent groups of HLA alleles and are useful when the HLA typing is ambiguous and does not allow to narrow down one single allele from a list of alleles.

**Usage**

```
decode_MAC(MAC)
```

**Arguments**

MAC                      multiple allele code (e.g. "A\*01:ATJNV")

**Value**

list of HLA alleles

**Examples**

```
MAC <- "A*01:ATJNV"
decode_MAC(MAC)
```

---

`encode_MAC`*Encode MAC*

---

**Description**

Encode a list of HLA alleles into multiple allele code (MAC). The National Marrow Donor Program (NMDP) uses [MAC](<https://bioinformatics.bethematchclinical.org/hla-resources/allele-codes/allele-code-lists/>) to facilitate the reporting and comparison of HLA alleles. MAC represent groups of HLA alleles and are useful when the HLA typing is ambiguous and does not allow to narrow down one single allele from a list of alleles.

**Usage**

```
encode_MAC(allele_list)
```

**Arguments**

allele\_list            list of HLA alleles (e.g. c("A\*01:01:01", "A\*02:01:01", "A\*03:01"))

**Value**

encoded MAC

**Examples**

```
allele_list <- c("A*01:01:01", "A*02:01:01", "A*03:01")
encode_MAC(allele_list)
```

---

`extract_population_id` *extract\_population\_id*

---

**Description**

extract the population ids from the html result

**Usage**

```
extract_population_id(data)
```

**Arguments**

data                      html from AFND website

**Value**

population ids

---

`extract_population_info`  
*extract\_population\_info*

---

**Description**

`extract_population_info`

**Usage**

```
extract_population_info(data)
```

**Arguments**

data                      html input page

**Value**

population information

---

|                                |
|--------------------------------|
| extract_population_name        |
| <i>extract_population_name</i> |

---

**Description**

extract\_population\_name

**Usage**

extract\_population\_name(data)

**Arguments**

|      |                 |
|------|-----------------|
| data | html input page |
|------|-----------------|

**Value**

population name

---

|                     |                            |
|---------------------|----------------------------|
| extract_sample_info | <i>extract_sample_info</i> |
|---------------------|----------------------------|

---

**Description**

extract\_sample\_info

**Usage**

extract\_sample\_info(data)

**Arguments**

|      |                 |
|------|-----------------|
| data | html input page |
|------|-----------------|

**Value**

sample information

---

|                   |                          |
|-------------------|--------------------------|
| fetch_encoded_MAC | <i>fetch_encoded_MAC</i> |
|-------------------|--------------------------|

---

**Description**

fetch\_encoded\_MAC

**Usage**

fetch\_encoded\_MAC(handle)

**Arguments**

|        |             |
|--------|-------------|
| handle | curl handle |
|--------|-------------|

**Value**

curl handle fetch

---

|        |               |
|--------|---------------|
| getURL | <i>getURL</i> |
|--------|---------------|

---

**Description**

getURL

**Usage**

```
getURL(  
  URL,  
  N.TRIES = 2L,  
  read_method = c("delim", "lines", "html"),  
  skip = 0,  
  delim = "\\t",  
  col_names = TRUE  
)
```

**Arguments**

|             |                                                                                                                                      |
|-------------|--------------------------------------------------------------------------------------------------------------------------------------|
| URL         | Indicated the url that will be read                                                                                                  |
| N.TRIES     | Integer, how often should the function try to read the URL?                                                                          |
| read_method | Method to be used for reading of URL content ("delim" -> readr::read_delim, "lines" -> readr::read_lines, "html" -> xml2::read_html) |
| skip        | integer indicating how many lines to skip when reading URL                                                                           |
| delim       | pattern used for delim (passed to delim of read functions)                                                                           |
| col_names   | list of colnames to use                                                                                                              |

**Value**

returns a the content of the URL. The format of the return object depends on the read\_method that was used.

---

|                   |                          |
|-------------------|--------------------------|
| get_external_file | <i>get_external_file</i> |
|-------------------|--------------------------|

---

**Description**

get\_external\_file

**Usage**

```
get_external_file(file, skip = 0, delim = "\t", col_names = TRUE)
```

**Arguments**

|           |                                                            |
|-----------|------------------------------------------------------------|
| file      | Indicated the file that will be read                       |
| skip      | integer indicating how many lines to skip when reading URL |
| delim     | pattern used for delim (passed to delim of read functions) |
| col_names | list of colnames to use                                    |

**Value**

returns a the content of the file. The format of the return object depends on the read\_method that was used.

---

|             |                 |
|-------------|-----------------|
| get_G_group | <i>G groups</i> |
|-------------|-----------------|

---

**Description**

Get the G groups for a list of HLA alleles. [G groups]([http://hla.alleles.org/alleles/g\\_groups.html](http://hla.alleles.org/alleles/g_groups.html)) are groups of HLA alleles that have identical nucleotide sequences across the exons encoding the peptide binding domains.

**Usage**

```
get_G_group(allele_list)
```

**Arguments**

|             |                  |
|-------------|------------------|
| allele_list | List of alleles. |
|-------------|------------------|

**Value**

Named list of G-groups the input alleles belong to.

**Examples**

```
allele_list <- c("DQB1*02:02:01", "DQB1*06:09:01")
get_G_group(allele_list)
```

---

|                  |                                       |
|------------------|---------------------------------------|
| get_mhcpan_input | <i>Get format for NetMHCpan tools</i> |
|------------------|---------------------------------------|

---

**Description**

NetMHCpan tools for MHC-peptide binding prediction require HLA complex names in a specific format. `get_mhcpan_input` formats a list of HLA alleles into a list of NetMHC-formated complexes.

**Usage**

```
get_mhcpan_input(allele_list, mhc_class)
```

**Arguments**

|             |                                                                         |
|-------------|-------------------------------------------------------------------------|
| allele_list | list of HLA alleles (e.g. <code>c("A*01:01:01", "B*27:01")</code> )     |
| mhc_class   | <code>["MHC-I" "MHC-II"]</code> indicated which NetMHC you want to use. |

**Value**

protein chain list as formatted for MHCpan input

**Examples**

```
allele_list <- c("A*01:01:01", "B*27:01")
get_mhcpan_input(allele_list, mhc_class = "MHC-I")
```

---

|              |                     |
|--------------|---------------------|
| get_nb_pages | <i>get_nb_pages</i> |
|--------------|---------------------|

---

**Description**

get\_nb\_pages

**Usage**

```
get_nb_pages(page_tbl)
```

**Arguments**

page\_tbl          html input page

**Value**

integer number of pages in the html input

---

|             |                 |
|-------------|-----------------|
| get_P_group | <i>P groups</i> |
|-------------|-----------------|

---

**Description**

Get the P groups for a list of HLA alleles. [P groups]([http://hla.alleles.org/alleles/p\\_groups.html](http://hla.alleles.org/alleles/p_groups.html)) are groups of HLA alleles that have identical protein sequences in the peptide binding domains.

**Usage**

```
get_P_group(allele_list)
```

**Arguments**

allele\_list      list of HLA alleles

**Value**

Named list of P-groups the input alleles belong to.

**Examples**

```
allele_list <- c("DQB1*02:02:01", "DQB1*06:09:01")
get_P_group(allele_list)
```

---

|               |                  |
|---------------|------------------|
| get_serotypes | <i>Serotypes</i> |
|---------------|------------------|

---

**Description**

Get the serotypes of the MHC complexes encoded by a list of MHC alleles.

**Usage**

```
get_serotypes(allele_list, organism = "human", mhc_type)
```

**Arguments**

|             |                                                                                                                  |
|-------------|------------------------------------------------------------------------------------------------------------------|
| allele_list | List of allele                                                                                                   |
| organism    | Organism to be used for MRO lookup. If the organism does not match the given allele, a empty object is returned. |
| mhc_type    | ["MHC-I" or "MHC-II"] MHC class to use for MRO lookup.                                                           |

**Value**

Named list of serotypes, which only contains complexes contained in the MRO. If no serotype is annotated for a given complex, the list element is NA.

**Examples**

```
allele_list <- c("A*01:01:01", "B*27:01")
get_serotypes(allele_list, mhc_type = "MHC-I")
```

---

|                       |                              |
|-----------------------|------------------------------|
| get_valid_geographics | <i>get_valid_geographics</i> |
|-----------------------|------------------------------|

---

**Description**

get a list of valid countries, regions and ethnic origins

**Usage**

```
get_valid_geographics()
```

**Value**

list of valid countries, regions and ethnic origin

---

|                     |                            |
|---------------------|----------------------------|
| get_valid_organisms | <i>get_valid_organisms</i> |
|---------------------|----------------------------|

---

**Description**

get the list of organisms that are part of the MRO annotation

**Usage**

get\_valid\_organisms()

**Value**

list of organisms

**Examples**

get\_valid\_organisms()

---

|                                    |
|------------------------------------|
| human_protein_complex_table        |
| <i>human_protein_complex_table</i> |

---

**Description**

human\_protein\_complex\_table

**Usage**

human\_protein\_complex\_table

**Format**

An object of class data.frame with 12385 rows and 8 columns.

**Details**

human\_protein\_complex\_table: human\_protein\_complex\_table.

**Examples**

```
# The human protein complex table is available in the following
# exported variable
human_protein_complex_table
```

---

|          |                 |
|----------|-----------------|
| load_mro | <i>load_mro</i> |
|----------|-----------------|

---

**Description**

load\_mro

**Usage**

load\_mro()

**Value**

MRO in ontology\_index format

---

|         |            |
|---------|------------|
| mro.obo | <i>MRO</i> |
|---------|------------|

---

**Description**

mro.obo: MHC Restriction Ontology obo file.

**Usage**

mro.obo

**Format**

An object of class ontology\_index of length 18.

---

|                        |                               |
|------------------------|-------------------------------|
| parse_allele_freq_html | <i>parse_allele_freq_html</i> |
|------------------------|-------------------------------|

---

**Description**

format the allele frequency table and select columns of interest

**Usage**

parse\_allele\_freq\_html(allele\_freq\_table)

**Arguments**

allele\_freq\_table  
allele frequency table parsed from AFND website

**Value**

allele\_freq\_table reformatted

---

parse\_haplotype\_freq\_html  
*parse\_haplotype\_freq\_html*

---

**Description**

format the haplotype frequency table and select columns of interest

**Usage**

parse\_haplotype\_freq\_html(haplotype\_freq\_table)

**Arguments**

haplotype\_freq\_table  
haplotype frequency table parsed from AFND website

**Value**

haplotype\_freq\_table reformatted

---

plot\_allele\_frequency *Plotting allele frequencies*

---

**Description**

plot\_allele\_frequency Generate a World map displaying the frequency of a given table of HLA alleles. Use the function [query\\_allele\\_frequencies](#) to generate a table with allele frequencies.

**Usage**

plot\_allele\_frequency(allele\_frequency)

**Arguments**

allele\_frequency  
returned by [query\\_allele\\_frequencies](#)

**Value**

ggplot2 object displaying the allele frequencies on a world map.

**Examples**

```
# select frequency of given allele
sel_allele_freq <- query_allele_frequencies(hla_selection = "A*02:01",
hla_sample_size_pattern = "bigger_than",
hla_sample_size = 10000, standard="g")

plot_allele_frequency(sel_allele_freq)
```

---

query\_allele\_frequencies

*Query allele frequencies*


---

**Description**

Query allele frequencies

**Usage**

```
query_allele_frequencies(
  hla_locus = NA,
  hla_selection = NA,
  hla_population = NA,
  hla_country = NA,
  hla_region = NA,
  hla_ethnic = NA,
  hla_sample_size_pattern = NA,
  hla_sample_size = NA,
  standard = "a"
)
```

**Arguments**

|                |                                                                                                                                        |
|----------------|----------------------------------------------------------------------------------------------------------------------------------------|
| hla_locus      | HLA locus that will be used for filtering data. A, B, C, DPA1, DPB1, DQA1, DQB1, DRB1                                                  |
| hla_selection  | Allele that will be used for filtering data. e.g. A*01:01                                                                              |
| hla_population | Numeric identifier of the population that will be used for filtering. This identifier is defined by the Allele Frequency Net Database. |
| hla_country    | Country of interest (e.g. Germany, France, ...).                                                                                       |
| hla_region     | Geographic region of interest (e.g. Europe, North Africa, ...)                                                                         |
| hla_ethnic     | Ethnic origin of interest (e.g. Caucasoid, Siberian, ...)                                                                              |

|                         |                                                                                                                                                       |
|-------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------|
| hla_sample_size_pattern | Keyword used to define the filtering for a specific population size. e.g. "bigger_than", "equal", "less_than", "less_equal_than", "bigger_equal_than" |
| hla_sample_size         | Integer number used to define the filtering for a specific population size, together with the hla_sample_size_pattern argument.                       |
| standard                | Population standards, as defined in the package vignette. "g" - gold, "s" - silver, "a" - all                                                         |

**Value**

data.frame object containing the result of the allele frequency query

**Examples**

```
# select frequencies of the A*02:01 allele,
# for gold standard population with more than 10,000 individuals
sel <- query_allele_frequencies(hla_selection = "A*02:01",
hla_sample_size_pattern = "bigger_than", hla_sample_size = 10000,
standard="g")
```

---

query\_haplotype\_frequencies

*Query haplotype frequencies*

---

**Description**

Query haplotype frequencies

**Usage**

```
query_haplotype_frequencies(
  hla_selection = NA,
  hla_population = NA,
  hla_country = NA,
  hla_region = NA,
  hla_ethnic = NA,
  hla_sample_size_pattern = NA,
  hla_sample_size = NA
)
```

**Arguments**

**hla\_selection** Alleles that will be used to build the haplotype query. One entry per locus. If no entry for a given locus, the function will search for haplotypes that do not include specifications for this locus. If any allele for a given locus should be considered, the list entry should be "A\*" or other locus in same format.

|                         |                                                                                                                                                       |
|-------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------|
| hla_population          | Numeric identifier of the population that will be used for filtering. This identifier is defined by the Allele Frequency Net Database.                |
| hla_country             | Country of interest (e.g. Germany, France, ...).                                                                                                      |
| hla_region              | Geographic region of interest (e.g. Europe, North Africa, ...)                                                                                        |
| hla_ethnic              | Ethnic origin of interest (e.g. Caucasoid, Siberian, ...)                                                                                             |
| hla_sample_size_pattern | Keyword used to define the filtering for a specific population size. e.g. "bigger_than", "equal", "less_than", "less_equal_than", "bigger_equal_than" |
| hla_sample_size         | Integer number used to define the filtering for a specific population size, together with the hla_sample_size_pattern argument.                       |

**Value**

data.frame object containing the result of the allele frequency query

**Examples**

```
# works only for one haplotype at a time
query_haplotype_frequencies(hla_selection = c("A*02:01", "B*", "C*"),
hla_region = "Europe")
```

---

query\_population\_detail

*Query population metainformation*

---

**Description**

Query population metainformation

**Usage**

```
query_population_detail(population_ids)
```

**Arguments**

population\_ids List of numeric identifiers of the population that will be used for filtering. The identifier is defined by the Allele Frequency Net Database.

**Value**

data.frame object containing the result of the population detail query

**Examples**

```
population_detail <- query_population_detail(0001986)
```

---

|                                 |
|---------------------------------|
| read_complete_freq_table        |
| <i>read_complete_freq_table</i> |

---

**Description**

read\_complete\_freq\_table

**Usage**

read\_complete\_freq\_table(url, type)

**Arguments**

|      |                                               |
|------|-----------------------------------------------|
| url  | URL of the website containing frequency table |
| type | ["allele" "haplotype"]                        |

**Value**

frequency table

---

|                               |
|-------------------------------|
| read_population_detail        |
| <i>read_population_detail</i> |

---

**Description**

read\_population\_detail

**Usage**

read\_population\_detail(url, population\_id)

**Arguments**

|               |                                                   |
|---------------|---------------------------------------------------|
| url           | url of the page containing population information |
| population_id | numeric population identifier                     |

**Value**

population information

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|                             |                                        |
|-----------------------------|----------------------------------------|
| retrieve_chain_lookup_table | <i>Retrieve MHC chain lookup table</i> |
|-----------------------------|----------------------------------------|

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**Description**

Retrieve MHC chain lookup table

**Usage**

```
retrieve_chain_lookup_table(organism)
```

**Arguments**

|          |                                 |
|----------|---------------------------------|
| organism | name of organism (e.g. "human") |
|----------|---------------------------------|

**Value**

Table containing MHC chain information for the organism. It contains chain names, MHC restriction and protein sequence.

**Examples**

```
retrieve_chain_lookup_table("mouse")
```

---

|                   |                          |
|-------------------|--------------------------|
| verify_parameters | <i>verify_parameters</i> |
|-------------------|--------------------------|

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**Description**

verify\_parameters

**Usage**

```
verify_parameters(  
  hla_locus,  
  hla_selection,  
  hla_population,  
  hla_country,  
  hla_region,  
  hla_ethnic,  
  hla_sample_size_pattern,  
  hla_sample_size,  
  standard = "a",  
  query_type  
)
```

**Arguments**

|                         |                                                                                                 |
|-------------------------|-------------------------------------------------------------------------------------------------|
| hla_locus               | locus of hla frequencies to query                                                               |
| hla_selection           | HLA alleles used for selection                                                                  |
| hla_population          | population id                                                                                   |
| hla_country             | country used for allele frequency selection                                                     |
| hla_region              | geographical region used for allele frequency selection                                         |
| hla_ethnic              | ethical origin used for allele frequency selection                                              |
| hla_sample_size_pattern | one of "bigger_than", "equal", "less_than", "less_equal_than", "bigger_equal_than", "different" |
| hla_sample_size         | integer number used for population size                                                         |
| standard                | one of "a" - all, "s" - silver, "g" - gold                                                      |
| query_type              | "allele" or "haplotype"                                                                         |

**Value**

boolean to indicate, whether tests were passed

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