

# Package ‘mLLMCelltype’

May 11, 2026

**Type** Package

**Title** Cell Type Annotation Using Large Language Models

**Version** 2.0.5

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**Description** Automated cell type annotation for single-cell RNA sequencing data using consensus predictions from multiple large language models. Integrates with Seurat objects and provides uncertainty quantification for annotations. Supports various LLM providers including OpenAI, Anthropic, and Google. For details see Yang et al. (2025) <[doi:10.1101/2025.04.10.647852](https://doi.org/10.1101/2025.04.10.647852)>.

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**BugReports** <https://github.com/cafferychen777/mLLMCelltype/issues>

**URL** <https://cafferyyang.com/mLLMCelltype/>

**Encoding** UTF-8

**Imports** dplyr, httr (>= 1.4.0), jsonlite (>= 1.7.0), R6 (>= 2.5.0), digest (>= 0.6.25), magrittr, stats, tools, utils

**Suggests** knitr, rmarkdown, Seurat, testthat

**RoxygenNote** 7.3.3

**Config/build/clean-inst-doc** TRUE

**VignetteBuilder** knitr

**NeedsCompilation** no

**Repository** CRAN

**Date/Publication** 2026-05-11 07:30:07 UTC

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annotate\_cell\_types     *Cell Type Annotation with Multi-LLM Framework*

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## Description

A comprehensive function for automated cell type annotation using multiple Large Language Models (LLMs). This function supports both Seurat's differential gene expression results and custom gene lists as input. It implements a sophisticated annotation pipeline that leverages state-of-the-art LLMs to identify cell types based on marker gene expression patterns.

- A data frame from Seurat's FindAllMarkers() function containing differential gene expression results (must have columns: 'cluster', 'gene', and 'avg\_log2FC'). The function will select the top genes based on avg\_log2FC for each cluster.
- A list where each element has a 'genes' field containing marker genes for a cluster. This can be in one of these formats:
  - Named with cluster IDs: list("0" = list(genes = c(...)), "1" = list(genes = c(...)))
  - Named with cell type names: list(t\_cells = list(genes = c(...)), b\_cells = list(genes = c(...)))
  - Unnamed list: list(list(genes = c(...)), list(genes = c(...)))

- Cluster IDs are preserved as-is. The function does not modify or re-index cluster IDs. ('mouse brain'). This helps provide context for more accurate annotations.
- OpenAI: 'gpt-5.5', 'gpt-5.4', 'gpt-5.4-mini'
- Anthropic: 'claude-opus-4-7', 'claude-opus-4-6', 'claude-sonnet-4-6', 'claude-haiku-4-5-20251001'
- DeepSeek: 'deepseek-v4-flash', 'deepseek-v4-pro'
- Google: 'gemini-3.1-pro-preview', 'gemini-3-flash-preview', 'gemini-3.1-flash-lite'
- Alibaba: 'qwen3.6-max-preview', 'qwen3.6-plus', 'qwen3.6-flash'
- Stepfun: 'step-3.5-flash', 'step-3.5-flash-2603', 'step-3'
- Zhipu/Z.AI: 'glm-5.1', 'glm-5-turbo', 'glm-5'
- MiniMax: 'MiniMax-M2.7', 'MiniMax-M2.7-highspeed', 'MiniMax-M2.5'
- X.AI: 'grok-4.3', 'grok-4.3-latest', 'grok-latest'
- OpenRouter: Provides access to models from multiple providers through a single API. Format: 'provider/model-name'
  - OpenAI models: 'openai/gpt-5.5', 'openai/gpt-5.4-mini'
  - Anthropic models: 'anthropic/claude-opus-4.7', 'anthropic/claude-sonnet-4.6'
  - Google models: 'google/gemini-3.1-pro-preview', 'google/gemini-3-flash-preview'
  - X.AI models: 'x-ai/grok-4.3'
  - Stepfun models: 'stepfun/step-3.5-flash' Each provider requires a specific API key format and authentication method:
- OpenAI: "sk-..." (obtain from OpenAI platform)
- Anthropic: "sk-ant-..." (obtain from Anthropic console)
- Google: A Google API key for Gemini models (obtain from Google AI)
- DeepSeek: API key from DeepSeek platform
- Qwen: API key from Alibaba Cloud
- Stepfun: API key from Stepfun AI
- Zhipu: API key from Zhipu AI
- MiniMax: API key from MiniMax
- X.AI: API key for Grok models
- OpenRouter: "sk-or-..." (obtain from OpenRouter) OpenRouter provides access to multiple models through a single API key

The API key can be provided directly or stored in environment variables:

```
# Direct API key
result <- annotate_cell_types(input, tissue_name, model="gpt-5.5",
                             api_key="sk-...")

# Using environment variables
Sys.setenv(OPENAI_API_KEY="sk-...")
Sys.setenv(ANTHROPIC_API_KEY="sk-ant-...")
Sys.setenv(OPENROUTER_API_KEY="sk-or-...")
```

```
# Then use with environment variables
result <- annotate_cell_types(input, tissue_name, model="claude-sonnet-4-6",
                             api_key=Sys.getenv("ANTHROPIC_API_KEY"))
```

If NA, returns the generated prompt without making an API call, which is useful for reviewing the prompt before sending it to the API. when input is from Seurat's FindAllMarkers(). Default: 10

- A single character string: Applied to all providers (e.g., "https://api.proxy.com/v1")
- A named list: Provider-specific URLs (e.g., list(openai = "https://openai-proxy.com/v1", anthropic = "https://anthropic-proxy.com/v1")). This is useful for:
  - Users accessing international APIs through proxies
  - Enterprise users with internal API gateways
  - Development/testing with local or alternative endpoints If NULL (default), uses official API endpoints for each provider.

### Usage

```
annotate_cell_types(
  input,
  tissue_name,
  model = "gpt-5.5",
  api_key = NA,
  top_gene_count = 10,
  debug = FALSE,
  base_urls = NULL
)
```

### Arguments

input	Either a data frame from Seurat's FindAllMarkers() containing columns 'cluster', 'gene', and 'avg_log2FC', or a list with 'genes' field for each cluster
tissue_name	Required tissue context (e.g., 'human PBMC', 'mouse brain') for more accurate annotations
model	Model name to use. Default: 'gpt-5.5'. See details for supported models
api_key	API key for the selected model provider as a non-empty character scalar. If NA, returns prompt only.
top_gene_count	Number of top genes to use per cluster when input is from Seurat. Default: 10
debug	Logical indicating whether to enable debug output. Default: FALSE
base_urls	Optional base URLs for API endpoints. Can be a string or named list for custom endpoints

### Value

When api\_key is provided, the provider response split by newline as a character vector. When api\_key is NA, the generated prompt string.

**See Also**

- [Seurat::FindAllMarkers\(\)](#)
- [get\\_provider\(\)](#)
- [process\\_openai\(\)](#)

**Examples**

```
# Example 1: Using custom gene lists, returning prompt only (no API call)
annotate_cell_types(
  input = list(
    t_cells = list(genes = c('CD3D', 'CD3E', 'CD3G', 'CD28')),
    b_cells = list(genes = c('CD19', 'CD79A', 'CD79B', 'MS4A1')),
    monocytes = list(genes = c('CD14', 'CD68', 'CSF1R', 'FCGR3A'))
  ),
  tissue_name = 'human PBMC',
  model = 'gpt-5.5',
  api_key = NA # Returns prompt only without making API call
)

# Example 2: Using with Seurat pipeline and OpenAI model
## Not run:
library(Seurat)

# Load example data
data("pbmc_small")

# Find marker genes
all.markers <- FindAllMarkers(
  object = pbmc_small,
  only.pos = TRUE,
  min.pct = 0.25,
  logfc.threshold = 0.25
)

# Set API key in environment variable (recommended approach)
Sys.setenv(OPENAI_API_KEY = "your-openai-api-key")

# Get cell type annotations using OpenAI model
openai_annotations <- annotate_cell_types(
  input = all.markers,
  tissue_name = 'human PBMC',
  model = 'gpt-5.5',
  api_key = Sys.getenv("OPENAI_API_KEY"),
  top_gene_count = 15
)

# Example 3: Using Anthropic Claude model
Sys.setenv(ANTHROPIC_API_KEY = "your-anthropic-api-key")

claude_annotations <- annotate_cell_types(
  input = all.markers,
```

```

tissue_name = 'human PBMC',
model = 'claude-opus-4-7',
api_key = Sys.getenv("ANTHROPIC_API_KEY"),
top_gene_count = 15
)

# Example 4: Using OpenRouter to access multiple models
Sys.setenv(OPENROUTER_API_KEY = "your-openrouter-api-key")

# Access OpenAI models through OpenRouter
openrouter_gpt4_annotations <- annotate_cell_types(
  input = all.markers,
  tissue_name = 'human PBMC',
  model = 'openai/gpt-5.5', # Note the provider/model format
  api_key = Sys.getenv("OPENROUTER_API_KEY"),
  top_gene_count = 15
)

# Access Anthropic models through OpenRouter
openrouter_claude_annotations <- annotate_cell_types(
  input = all.markers,
  tissue_name = 'human PBMC',
  model = 'anthropic/claude-opus-4.6', # Note the provider/model format
  api_key = Sys.getenv("OPENROUTER_API_KEY"),
  top_gene_count = 15
)

# Example 5: Using with mouse brain data
mouse_annotations <- annotate_cell_types(
  input = mouse_markers, # Your mouse marker genes
  tissue_name = 'mouse brain', # Specify correct tissue for context
  model = 'gpt-5.5',
  api_key = Sys.getenv("OPENAI_API_KEY"),
  top_gene_count = 20, # Use more genes for complex tissues
  debug = TRUE # Enable debug output
)

## End(Not run)

```

---

AnthropicProcessor      *Anthropic API Processor*

---

## Description

Anthropic API Processor

Anthropic API Processor

## Details

Concrete implementation of BaseAPIProcessor for Anthropic models. Handles Anthropic-specific API calls, authentication, and response parsing.

## Super class

mLLMCelltype: [BaseAPIProcessor](#) -> AnthropicProcessor

## Methods

### Public methods:

- [AnthropicProcessor\\$new\(\)](#)
- [AnthropicProcessor\\$get\\_default\\_api\\_url\(\)](#)
- [AnthropicProcessor\\$make\\_api\\_call\(\)](#)
- [AnthropicProcessor\\$extract\\_response\\_content\(\)](#)
- [AnthropicProcessor\\$clone\(\)](#)

**Method** `new()`: Initialize Anthropic processor

*Usage:*

```
AnthropicProcessor$new(base_url = NULL)
```

**Method** `get_default_api_url()`: Get default Anthropic API URL

*Usage:*

```
AnthropicProcessor$get_default_api_url()
```

**Method** `make_api_call()`: Make API call to Anthropic

*Usage:*

```
AnthropicProcessor$make_api_call(chunk_content, model, api_key)
```

**Method** `extract_response_content()`: Extract response content from Anthropic API response

*Usage:*

```
AnthropicProcessor$extract_response_content(response, model)
```

**Method** `clone()`: The objects of this class are cloneable with this method.

*Usage:*

```
AnthropicProcessor$clone(deep = FALSE)
```

*Arguments:*

`deep` Whether to make a deep clone.

---

BaseAPIProcessor	<i>Base API Processor Class</i>
------------------	---------------------------------

---

## Description

Base API Processor Class

Base API Processor Class

## Details

Abstract base class for API processors that provides common functionality including unified logging, error handling, input processing, and response validation. This eliminates code duplication across all provider-specific processors.

## Public fields

provider\_name Name of the API provider

logger Unified logger instance

base\_url Custom base URL for API endpoints

## Methods

### Public methods:

- [BaseAPIProcessor\\$new\(\)](#)
- [BaseAPIProcessor\\$process\\_request\(\)](#)
- [BaseAPIProcessor\\$get\\_api\\_url\(\)](#)
- [BaseAPIProcessor\\$get\\_default\\_api\\_url\(\)](#)
- [BaseAPIProcessor\\$make\\_api\\_call\(\)](#)
- [BaseAPIProcessor\\$extract\\_response\\_content\(\)](#)
- [BaseAPIProcessor\\$clone\(\)](#)

**Method** new(): Initialize the base API processor

*Usage:*

BaseAPIProcessor\$new(provider\_name, base\_url = NULL)

**Method** process\_request(): Main entry point for processing API requests

*Usage:*

BaseAPIProcessor\$process\_request(prompt, model, api\_key)

**Method** get\_api\_url(): Get the API URL to use for requests

*Usage:*

BaseAPIProcessor\$get\_api\_url()

**Method** get\_default\_api\_url(): Abstract method to be implemented by subclasses for getting default API URL

*Usage:*

BaseAPIProcessor\$get\_default\_api\_url()

**Method** `make_api_call()`: Abstract method to be implemented by subclasses for making the actual API call

*Usage:*

BaseAPIProcessor\$make\_api\_call(chunk\_content, model, api\_key)

**Method** `extract_response_content()`: Abstract method to be implemented by subclasses for extracting content from response Make API call and extract response content

*Usage:*

BaseAPIProcessor\$extract\_response\_content(response, model)

**Method** `clone()`: The objects of this class are cloneable with this method.

*Usage:*

BaseAPIProcessor\$clone(deep = FALSE)

*Arguments:*

deep Whether to make a deep clone.

---

CacheManager

*Cache Manager Class*

---

## Description

Manages caching of consensus analysis results

## Public fields

`cache_dir` Directory to store cache files. Options:

- NULL (default): Uses system cache directory
- "local": Uses `.mlmcelltype_cache` in current directory
- "temp": Uses temporary directory
- Custom path: Any other string is used as directory path

`cache_version` Current cache version

## Methods

### Public methods:

- [CacheManager\\$new\(\)](#)
- [CacheManager\\$get\\_cache\\_dir\(\)](#)
- [CacheManager\\$generate\\_key\(\)](#)
- [CacheManager\\$save\\_to\\_cache\(\)](#)
- [CacheManager\\$load\\_from\\_cache\(\)](#)

- `CacheManager$has_cache()`
- `CacheManager$get_cache_stats()`
- `CacheManager$clear_cache()`
- `CacheManager$validate_cache()`
- `CacheManager$clone()`

**Method** `new()`: Initialize cache manager

- `NULL` (default): Uses system cache directory via `tools::R_user_dir()`
- `"local"`: Uses `.mlmcelltype_cache` in current directory
- `"temp"`: Uses temporary directory (cleared on R restart)
- Custom path: Any other string is used as directory path

*Usage:*

```
CacheManager$new(cache_dir = NULL)
```

**Method** `get_cache_dir()`: Get actual cache directory path

*Usage:*

```
CacheManager$get_cache_dir()
```

**Method** `generate_key()`: Generate cache key from input parameters (improved version)

*Usage:*

```
CacheManager$generate_key(  
  input,  
  models,  
  cluster_id,  
  tissue_name = "",  
  top_gene_count = 10  
)
```

**Method** `save_to_cache()`: Save results to cache

*Usage:*

```
CacheManager$save_to_cache(key, data)
```

**Method** `load_from_cache()`: Load results from cache

*Usage:*

```
CacheManager$load_from_cache(key)
```

**Method** `has_cache()`: Check if results exist in cache

*Usage:*

```
CacheManager$has_cache(key)
```

**Method** `get_cache_stats()`: Get cache statistics

*Usage:*

```
CacheManager$get_cache_stats()
```

**Method** `clear_cache()`: Clear all cache

*Usage:*

```
CacheManager$clear_cache(confirm = FALSE)
```

**Method** `validate_cache()`: Validate cache content Extract genes from input in a standardized way Create stable hash from genes list Create stable hash from models list Create stable hash from tissue\_name and top\_gene\_count Create stable hash from cluster ID

*Usage:*

```
CacheManager$validate_cache(key)
```

**Method** `clone()`: The objects of this class are cloneable with this method.

*Usage:*

```
CacheManager$clone(deep = FALSE)
```

*Arguments:*

`deep` Whether to make a deep clone.

compare\_model\_predictions

*Compare predictions from different models*

**Description**

This function runs the same input through multiple models and compares their predictions. It provides both individual predictions and a consensus analysis.

**Usage**

```
compare_model_predictions(
  input,
  tissue_name,
  models = c("claude-opus-4-7", "gpt-5.5", "gemini-3.1-pro-preview", "deepseek-v4-flash",
    "qwen3.6-plus", "grok-4.3"),
  api_keys,
  top_gene_count = 10,
  consensus_threshold = 0.5,
  base_urls = NULL
)
```

**Arguments**

<code>input</code>	Either a data frame from Seurat's <code>FindAllMarkers()</code> containing columns 'cluster', 'gene', and 'avg_log2FC', or a list with 'genes' field for each cluster
<code>tissue_name</code>	Tissue context (e.g., 'human PBMC', 'mouse brain') for more accurate annotations
<code>models</code>	Vector of model names to use for comparison. Default includes top models from each provider

api_keys	Named list of API keys for the models, with provider or model names as keys. Every model in models must resolve to a non-NULL API key.
top_gene_count	Number of top genes to use per cluster when input is from Seurat. Default: 10
consensus_threshold	Minimum agreement threshold for consensus (0-1). Default: 0.5. Consensus is only evaluated when at least two non-missing model predictions are available for a cluster.
base_urls	Optional base URLs for API endpoints. Can be a string or named list for provider-specific custom endpoints.

**Value**

List containing individual model predictions and consensus analysis. If a cluster has fewer than two valid predictions after alignment/padding, its consensus-related outputs are NA.

**Note**

This function uses create\_standardization\_prompt from prompt\_templates.R. Supported models:

- OpenAI: 'gpt-5.5', 'gpt-5.4', 'gpt-5.4-mini'
  - Anthropic: 'claude-opus-4-7', 'claude-opus-4-6', 'claude-sonnet-4-6', 'claude-haiku-4-5-20251001'
  - DeepSeek: 'deepseek-v4-flash', 'deepseek-v4-pro'
  - Google: 'gemini-3.1-pro-preview', 'gemini-3-flash-preview', 'gemini-3.1-flash-lite'
  - Alibaba: 'qwen3.6-max-preview', 'qwen3.6-plus', 'qwen3.6-flash'
  - Stepfun: 'step-3.5-flash', 'step-3.5-flash-2603', 'step-3'
  - Zhipu/Z.AI: 'glm-5.1', 'glm-5-turbo', 'glm-5'
  - MiniMax: 'MiniMax-M2.7', 'MiniMax-M2.7-highspeed', 'MiniMax-M2.5'
  - X.AI: 'grok-4.3', 'grok-4.3-latest', 'grok-latest'
  - OpenRouter: Provides access to models from multiple providers through a single API. Format: 'provider/model-name'
    - OpenAI models: 'openai/gpt-5.5', 'openai/gpt-5.4-mini'
    - Anthropic models: 'anthropic/claude-opus-4.7', 'anthropic/claude-sonnet-4.6'
    - Google models: 'google/gemini-3.1-pro-preview', 'google/gemini-3-flash-preview'
    - X.AI models: 'x-ai/grok-4.3'
    - Stepfun models: 'stepfun/step-3.5-flash'
1. With provider names as keys: list("openai" = "sk-...", "anthropic" = "sk-ant-...", "openrouter" = "sk-or-...")
  2. With model names as keys: list("gpt-5.5" = "sk-...", "claude-sonnet-4-6" = "sk-ant-...")

The system first tries to find the API key using the provider name. If not found, it then tries using the model name. Example:

```
api_keys <- list(
  "openai" = Sys.getenv("OPENAI_API_KEY"),
  "anthropic" = Sys.getenv("ANTHROPIC_API_KEY"),
  "openrouter" = Sys.getenv("OPENROUTER_API_KEY"),
  "claude-opus-4-7" = "your-claude-opus-key"
)
```

### Examples

```
## Not run:
# Compare predictions using different models
api_keys <- list(
  "claude-sonnet-4-6" = "your-anthropic-key",
  "deepseek-v4-pro" = "your-deepseek-key",
  "gemini-3.1-pro-preview" = "your-gemini-key",
  "qwen3.6-plus" = "your-qwen-key"
)

results <- compare_model_predictions(
  input = list(gs1=c('CD4','CD3D'), gs2='CD14'),
  tissue_name = 'PBMC',
  api_keys = api_keys
)

## End(Not run)
```

---

configure_logger	<i>Set global logger configuration</i>
------------------	----------------------------------------

---

### Description

Set global logger configuration

### Usage

```
configure_logger(level = "INFO", console_output = FALSE, json_format = TRUE)
```

### Arguments

level	Logging level: "DEBUG", "INFO", "WARN", or "ERROR". Default: "INFO"
console_output	Whether to enable console output. Default: FALSE
json_format	Whether to use JSON format for log messages. Default: TRUE

### Value

Invisible logger object

---

```
create_annotation_prompt
```

*Create prompt for cell type annotation*

---

### Description

Create prompt for cell type annotation

### Usage

```
create_annotation_prompt(input, tissue_name, top_gene_count = 10)
```

### Arguments

input	Either a data frame from Seurat's FindAllMarkers() or a list for each cluster where each element is either a character vector of genes or a list containing a genes field Cluster IDs in named inputs are preserved as-is; unnamed list input receives sequential IDs starting at "0".
tissue_name	Tissue context for the annotation (e.g., 'human PBMC', 'mouse brain')
top_gene_count	Number of top genes to use per cluster when input is from Seurat. Default: 10

### Value

A list with prompt (formatted prompt text), expected\_count (number of clusters), and gene\_lists (cluster ID to marker genes mapping).

---

DeepSeekProcessor      *DeepSeek API Processor*

---

### Description

DeepSeek API Processor

DeepSeek API Processor

### Details

Concrete implementation of BaseAPIProcessor for DeepSeek models. Handles DeepSeek-specific API calls, authentication, and response parsing.

### Super class

[mLLMCelltype::BaseAPIProcessor](#) -> DeepSeekProcessor

**Methods****Public methods:**

- [DeepSeekProcessor\\$new\(\)](#)
- [DeepSeekProcessor\\$get\\_default\\_api\\_url\(\)](#)
- [DeepSeekProcessor\\$make\\_api\\_call\(\)](#)
- [DeepSeekProcessor\\$extract\\_response\\_content\(\)](#)
- [DeepSeekProcessor\\$clone\(\)](#)

**Method** `new()`: Initialize DeepSeek processor

*Usage:*

`DeepSeekProcessor$new(base_url = NULL)`

**Method** `get_default_api_url()`: Get default DeepSeek API URL

*Usage:*

`DeepSeekProcessor$get_default_api_url()`

**Method** `make_api_call()`: Make API call to DeepSeek

*Usage:*

`DeepSeekProcessor$make_api_call(chunk_content, model, api_key)`

**Method** `extract_response_content()`: Extract response content from DeepSeek API response

*Usage:*

`DeepSeekProcessor$extract_response_content(response, model)`

**Method** `clone()`: The objects of this class are cloneable with this method.

*Usage:*

`DeepSeekProcessor$clone(deep = FALSE)`

*Arguments:*

`deep` Whether to make a deep clone.

---

GeminiProcessor

*Gemini API Processor*

---

**Description**

Gemini API Processor

Gemini API Processor

**Details**

Concrete implementation of BaseAPIProcessor for Gemini models. Handles Gemini-specific API calls, authentication, and response parsing.

**Super class**

mLLMCelltype::BaseAPIProcessor -> GeminiProcessor

**Methods****Public methods:**

- GeminiProcessor\$new()
- GeminiProcessor\$get\_default\_api\_url()
- GeminiProcessor\$get\_api\_url\_for\_model()
- GeminiProcessor\$make\_api\_call()
- GeminiProcessor\$extract\_response\_content()
- GeminiProcessor\$clone()

**Method** new(): Initialize Gemini processor

*Usage:*

GeminiProcessor\$new(base\_url = NULL)

**Method** get\_default\_api\_url(): Get default Gemini API URL template

*Usage:*

GeminiProcessor\$get\_default\_api\_url()

**Method** get\_api\_url\_for\_model(): Get API URL for specific model

*Usage:*

GeminiProcessor\$get\_api\_url\_for\_model(model)

**Method** make\_api\_call(): Make API call to Gemini

*Usage:*

GeminiProcessor\$make\_api\_call(chunk\_content, model, api\_key)

**Method** extract\_response\_content(): Extract response content from Gemini API response

*Usage:*

GeminiProcessor\$extract\_response\_content(response, model)

**Method** clone(): The objects of this class are cloneable with this method.

*Usage:*

GeminiProcessor\$clone(deep = FALSE)

*Arguments:*

deep Whether to make a deep clone.

---

`get_api_key`*Utility functions for API key management*

---

**Description**

This file contains utility functions for managing API keys and related operations. Get API key for a specific model

**Usage**

```
get_api_key(model, api_keys)
```

**Arguments**

<code>model</code>	Model name to get API key for
<code>api_keys</code>	Named list of API keys with provider or model names as keys

**Details**

This function retrieves the appropriate API key for a given model by first checking the provider name and then the model name in the provided API keys list.

**Value**

API key string for the specified model

---

`get_logger`*Get the global logger instance*

---

**Description**

Get the global logger instance

**Usage**

```
get_logger()
```

---

get_provider	Determine provider from model name
--------------	------------------------------------

---

## Description

This function determines the appropriate provider (e.g., OpenAI, Anthropic, Google, OpenRouter) based on the model name. Uses prefix-based matching for efficient and maintainable provider detection. New models following existing naming conventions are automatically supported.

## Usage

```
get_provider(model)
```

## Arguments

model            Character string specifying the model name (e.g., "gpt-5.5", "claude-opus-4-7").

## Details

Supported providers and model prefixes:

- OpenAI: gpt-, o1, o3\*, o4\*, chatgpt-, *codex*- (e.g., 'gpt-5.5', 'gpt-5.4-mini')
- Anthropic: claude-\* (e.g., 'claude-opus-4-7', 'claude-sonnet-4-6')
- DeepSeek: deepseek-\* (e.g., 'deepseek-v4-flash', 'deepseek-v4-pro')
- Google: gemini-\* (e.g., 'gemini-3.1-pro-preview', 'gemini-3-flash-preview')
- Qwen: qwen\*, qwq-\* (e.g., 'qwen3.6-plus', 'qwen3.6-flash')
- Stepfun: step-\* (e.g., 'step-3.5-flash', 'step-3')
- Zhipu: glm-, *chatglm* (e.g., 'glm-5.1', 'glm-5-turbo')
- MiniMax: minimax-\* (e.g., 'MiniMax-M2.7', 'MiniMax-M2.5')
- Grok: grok-\* (e.g., 'grok-4.3', 'grok-4.3-latest')
- OpenRouter: Any model with '/' in the name (e.g., 'openai/gpt-5.5', 'anthropic/claude-opus-4.7')

## Value

Character string of the provider name (e.g., "openai", "anthropic").

---

GrokProcessor

*Grok API Processor*

---

## Description

Grok API Processor

Grok API Processor

## Details

Concrete implementation of BaseAPIProcessor for Grok models. Handles Grok-specific API calls, authentication, and response parsing.

## Super class

`mLLMCelltype::BaseAPIProcessor` -> GrokProcessor

## Methods

### Public methods:

- `GrokProcessor$new()`
- `GrokProcessor$get_default_api_url()`
- `GrokProcessor$make_api_call()`
- `GrokProcessor$extract_response_content()`
- `GrokProcessor$clone()`

**Method** `new()`: Initialize Grok processor

*Usage:*

`GrokProcessor$new(base_url = NULL)`

**Method** `get_default_api_url()`: Get default Grok API URL

*Usage:*

`GrokProcessor$get_default_api_url()`

**Method** `make_api_call()`: Make API call to Grok

*Usage:*

`GrokProcessor$make_api_call(chunk_content, model, api_key)`

**Method** `extract_response_content()`: Extract response content from Grok API response

*Usage:*

`GrokProcessor$extract_response_content(response, model)`

**Method** `clone()`: The objects of this class are cloneable with this method.

*Usage:*

`GrokProcessor$clone(deep = FALSE)`

*Arguments:*

`deep` Whether to make a deep clone.

---

`interactive_consensus_annotation`*Interactive consensus building for cell type annotation*

---

## Description

This function implements an interactive voting and discussion mechanism where multiple LLMs collaborate to reach a consensus on cell type annotations, particularly focusing on clusters with low agreement. The process includes:

1. Initial voting by all LLMs
2. Identification of controversial clusters
3. Detailed discussion for controversial clusters
4. Final summary by a designated LLM (default: Claude)

## Usage

```
interactive_consensus_annotation(  
  input,  
  tissue_name,  
  models = c("claude-opus-4-7", "gpt-5.5", "gemini-3.1-pro-preview", "deepseek-v4-flash",  
            "grok-4.3"),  
  api_keys,  
  top_gene_count = 10,  
  controversy_threshold = 0.7,  
  entropy_threshold = 1,  
  max_discussion_rounds = 3,  
  consensus_check_model = NULL,  
  log_dir = "logs",  
  cache_dir = NULL,  
  use_cache = TRUE,  
  base_urls = NULL,  
  clusters_to_analyze = NULL,  
  force_rerun = FALSE  
)
```

## Arguments

<code>input</code>	Either a data frame from Seurat's <code>FindAllMarkers()</code> function containing differential gene expression results (must have columns: <code>'cluster'</code> , <code>'gene'</code> , and <code>'avg_log2FC'</code> ), or a list where each element is either a character vector of genes or a list containing a genes field.
<code>tissue_name</code>	Character string specifying the tissue type for context-aware cell type annotation (e.g., <code>'human PBMC'</code> , <code>'mouse brain'</code> ). Required.

models	Character vector of model names to use for consensus annotation. Minimum 2 models required. Supports models from OpenAI, Anthropic, DeepSeek, Google, Alibaba, Stepfun, Zhipu, MiniMax, X.AI, and OpenRouter.
api_keys	Named, non-empty list of API keys. Can use provider names as keys (e.g., "openai", "anthropic") or model names as keys (e.g., "gpt-5").
top_gene_count	Integer specifying the number of top marker genes to use for annotation per cluster (default: 10).
controversy_threshold	Numeric value between 0 and 1 for consensus proportion threshold. Clusters below this threshold are considered controversial (default: 0.7).
entropy_threshold	Numeric value for entropy threshold. Higher entropy indicates more disagreement among models (default: 1.0).
max_discussion_rounds	Integer specifying maximum number of discussion rounds for controversial clusters (default: 3).
consensus_check_model	Character string specifying which model to use for consensus checking. If NULL, uses the first model that succeeds during initial annotation.
log_dir	Character scalar specifying directory for log files (default: "logs"). This function reinitializes the session logger with this directory at the start of each call.
cache_dir	Character string or NULL. Cache directory for storing results. NULL uses system cache, "local" uses current directory, "temp" uses temporary directory, or specify custom path.
use_cache	Logical indicating whether to use caching (default: TRUE).
base_urls	Named list or character string specifying custom API base URLs. Useful for proxies or alternative endpoints. If NULL, uses official endpoints.
clusters_to_analyze	Character or numeric vector specifying which clusters to analyze. If NULL (default), all clusters are analyzed.
force_rerun	Logical indicating whether to force rerun of all specified clusters, ignoring cache. Only affects controversial cluster discussions (default: FALSE).

## Value

A list containing:

- `initial_results`: Initial voting results, consensus checks, and controversial cluster IDs
- `final_annotations`: Final annotations keyed by cluster ID
- `controversial_clusters`: Clusters identified as controversial
- `discussion_logs`: Detailed discussion logs for controversial clusters
- `session_id`: Logger session identifier
- `voting_results`: Backward-compatible alias of `initial_results`
- `discussion_results`: Backward-compatible alias of `discussion_logs`
- `final_consensus`: Backward-compatible alias of `final_annotations`

---

`list_custom_models`      *Get list of registered custom models*

---

**Description**

Get list of registered custom models

**Usage**

```
list_custom_models()
```

---

`list_custom_providers`      *Get list of registered custom providers*

---

**Description**

Get list of registered custom providers

**Usage**

```
list_custom_providers()
```

---

`logging_functions`      *Convenience functions for logging*

---

**Description**

Convenience functions for logging

**Usage**

```
log_debug(message, context = NULL)
```

```
log_info(message, context = NULL)
```

```
log_warn(message, context = NULL)
```

```
log_error(message, context = NULL)
```

**Arguments**

<code>message</code>	Log message string
<code>context</code>	Optional context information (list or character)

**Value**

Invisible NULL

---

MinimaxProcessor	<i>Minimax API Processor</i>
------------------	------------------------------

---

## Description

Minimax API Processor

Minimax API Processor

## Details

Concrete implementation of BaseAPIProcessor for Minimax models. Handles Minimax-specific API calls, authentication, and response parsing.

## Super class

`mLLMCelltype::BaseAPIProcessor` -> MinimaxProcessor

## Methods

### Public methods:

- `MinimaxProcessor$new()`
- `MinimaxProcessor$get_default_api_url()`
- `MinimaxProcessor$make_api_call()`
- `MinimaxProcessor$extract_response_content()`
- `MinimaxProcessor$clone()`

**Method** `new()`: Initialize Minimax processor

*Usage:*

`MinimaxProcessor$new(base_url = NULL)`

**Method** `get_default_api_url()`: Get default Minimax API URL

*Usage:*

`MinimaxProcessor$get_default_api_url()`

**Method** `make_api_call()`: Make API call to Minimax

*Usage:*

`MinimaxProcessor$make_api_call(chunk_content, model, api_key)`

**Method** `extract_response_content()`: Extract response content from Minimax API response

*Usage:*

`MinimaxProcessor$extract_response_content(response, model)`

**Method** `clone()`: The objects of this class are cloneable with this method.

*Usage:*

`MinimaxProcessor$clone(deep = FALSE)`

*Arguments:*

`deep` Whether to make a deep clone.

---

`mllmcelltype_cache_dir`*Get mLLMCelltype cache location*

---

**Description**

Display the cache directory location

**Usage**

```
mllmcelltype_cache_dir(cache_dir = NULL)
```

**Arguments**

`cache_dir` Cache directory specification. NULL uses system default, "local" uses current dir, "temp" uses temp dir, or custom path

**Value**

Invisible cache directory path

**Examples**

```
## Not run:  
mllmcelltype_cache_dir()  
mllmcelltype_cache_dir("local")  
  
## End(Not run)
```

---

`mllmcelltype_clear_cache`*Clear mLLMCelltype cache*

---

**Description**

Clear the mLLMCelltype cache

**Usage**

```
mllmcelltype_clear_cache(cache_dir = NULL)
```

**Arguments**

`cache_dir` Cache directory specification. NULL uses system default, "local" uses current dir, "temp" uses temp dir, or custom path

**Value**

Invisible NULL

**Examples**

```
## Not run:
mllmcelltype_clear_cache()
mllmcelltype_clear_cache("local")

## End(Not run)
```

---

OpenAIProcessor	<i>OpenAI API Processor</i>
-----------------	-----------------------------

---

**Description**

OpenAI API Processor

OpenAI API Processor

**Details**

Concrete implementation of BaseAPIProcessor for OpenAI models. Handles OpenAI-specific API calls, authentication, and response parsing.

**Super class**

[mLLMCelltype::BaseAPIProcessor](#) -> OpenAIProcessor

**Methods****Public methods:**

- [OpenAIProcessor\\$new\(\)](#)
- [OpenAIProcessor\\$get\\_default\\_api\\_url\(\)](#)
- [OpenAIProcessor\\$make\\_api\\_call\(\)](#)
- [OpenAIProcessor\\$extract\\_response\\_content\(\)](#)
- [OpenAIProcessor\\$clone\(\)](#)

**Method** `new()`: Initialize OpenAI processor

*Usage:*

```
OpenAIProcessor$new(base_url = NULL)
```

**Method** `get_default_api_url()`: Get default OpenAI API URL

*Usage:*

```
OpenAIProcessor$get_default_api_url()
```

**Method** `make_api_call()`: Make API call to OpenAI

*Usage:*

OpenAIProcessor\$make\_api\_call(chunk\_content, model, api\_key)

**Method** extract\_response\_content(): Extract response content from OpenAI API response

*Usage:*

OpenAIProcessor\$extract\_response\_content(response, model)

**Method** clone(): The objects of this class are cloneable with this method.

*Usage:*

OpenAIProcessor\$clone(deep = FALSE)

*Arguments:*

deep Whether to make a deep clone.

---

OpenRouterProcessor    *OpenRouter API Processor*

---

## Description

OpenRouter API Processor

OpenRouter API Processor

## Details

Concrete implementation of BaseAPIProcessor for OpenRouter models. Handles OpenRouter-specific API calls, authentication, and response parsing.

## Super class

`mLLMCelltype::BaseAPIProcessor` -> OpenRouterProcessor

## Methods

### Public methods:

- `OpenRouterProcessor$new()`
- `OpenRouterProcessor$get_default_api_url()`
- `OpenRouterProcessor$make_api_call()`
- `OpenRouterProcessor$extract_response_content()`
- `OpenRouterProcessor$clone()`

**Method** new(): Initialize OpenRouter processor

*Usage:*

OpenRouterProcessor\$new(base\_url = NULL)

**Method** get\_default\_api\_url(): Get default OpenRouter API URL

*Usage:*

```
OpenRouterProcessor$get_default_api_url()
```

**Method** `make_api_call()`: Make API call to OpenRouter

*Usage:*

```
OpenRouterProcessor$make_api_call(chunk_content, model, api_key)
```

**Method** `extract_response_content()`: Extract response content from OpenRouter API response

*Usage:*

```
OpenRouterProcessor$extract_response_content(response, model)
```

**Method** `clone()`: The objects of this class are cloneable with this method.

*Usage:*

```
OpenRouterProcessor$clone(deep = FALSE)
```

*Arguments:*

`deep` Whether to make a deep clone.

---

QwenProcessor

*Qwen API Processor*

---

## Description

Qwen API Processor

Qwen API Processor

## Details

Concrete implementation of BaseAPIProcessor for Qwen models. Handles Qwen-specific API calls, authentication, and response parsing.

Qwen has two API endpoints:

- International: <https://dashscope-intl.aliyuncs.com/api/v1/services/aigc/text-generation/generation> (preferred)
- Domestic (China): <https://dashscope.aliyuncs.com/api/v1/services/aigc/text-generation/generation> (fallback) The processor automatically tries international first, then falls back to domestic if needed.

## Super class

`mLLMCelltype::BaseAPIProcessor` -> QwenProcessor

## Methods

### Public methods:

- [QwenProcessor\\$new\(\)](#)
- [QwenProcessor\\$get\\_default\\_api\\_url\(\)](#)
- [QwenProcessor\\$get\\_working\\_api\\_url\(\)](#)
- [QwenProcessor\\$make\\_api\\_call\(\)](#)
- [QwenProcessor\\$extract\\_response\\_content\(\)](#)
- [QwenProcessor\\$clone\(\)](#)

**Method** `new()`: Test if an endpoint is accessible  
Initialize Qwen processor

*Usage:*

```
QwenProcessor$new(base_url = NULL)
```

**Method** `get_default_api_url()`: Get default Qwen API URL with intelligent endpoint selection

*Usage:*

```
QwenProcessor$get_default_api_url()
```

**Method** `get_working_api_url()`: Get working Qwen API URL with automatic endpoint detection

*Usage:*

```
QwenProcessor$get_working_api_url(api_key)
```

**Method** `make_api_call()`: Make API call to Qwen

*Usage:*

```
QwenProcessor$make_api_call(chunk_content, model, api_key)
```

**Method** `extract_response_content()`: Extract response content from Qwen API response

*Usage:*

```
QwenProcessor$extract_response_content(response, model)
```

**Method** `clone()`: The objects of this class are cloneable with this method.

*Usage:*

```
QwenProcessor$clone(deep = FALSE)
```

*Arguments:*

`deep` Whether to make a deep clone.

---

register\_custom\_model *Register a custom model for a provider*

---

**Description**

Register a custom model for a provider

**Usage**

```
register_custom_model(model_name, provider_name, model_config = list())
```

**Arguments**

model_name	Unique name for the custom model
provider_name	Name of the provider this model belongs to
model_config	List of configuration parameters for the model (e.g., temperature, max_tokens)

**Value**

Invisible TRUE on success

**Examples**

```
## Not run:
register_custom_model(
  model_name = "my_model",
  provider_name = "my_provider",
  model_config = list(
    temperature = 0.7,
    max_tokens = 2000
  )
)

## End(Not run)
```

---

register\_custom\_provider  
*Register a custom LLM provider*

---

**Description**

Register a custom LLM provider

**Usage**

```
register_custom_provider(provider_name, process_fn, description = NULL)
```

**Arguments**

provider_name	Unique name for the custom provider
process_fn	Function that processes LLM requests. Must accept parameters: prompt, model, api_key; may optionally accept model_config
description	Optional description of the provider

**Value**

Invisible NULL

**Examples**

```
## Not run:
register_custom_provider(
  provider_name = "my_provider",
  process_fn = function(prompt, model, api_key) {
    # Custom implementation
    response <- httr::POST(
      url = "your_api_endpoint",
      body = list(prompt = prompt),
      encode = "json"
    )
    return(httr::content(response)$choices[[1]]$text)
  }
)

## End(Not run)
```

---

StepFunProcessor

*StepFun API Processor*

---

**Description**

StepFun API Processor

StepFun API Processor

**Details**

Concrete implementation of BaseAPIProcessor for StepFun models. Handles StepFun-specific API calls, authentication, and response parsing.

**Super class**

[mLLMCelltype::BaseAPIProcessor](#) -> StepFunProcessor

## Methods

### Public methods:

- `StepFunProcessor$new()`
- `StepFunProcessor$get_default_api_url()`
- `StepFunProcessor$make_api_call()`
- `StepFunProcessor$extract_response_content()`
- `StepFunProcessor$clone()`

**Method** `new()`: Initialize StepFun processor

*Usage:*

```
StepFunProcessor$new(base_url = NULL)
```

**Method** `get_default_api_url()`: Get default StepFun API URL

*Usage:*

```
StepFunProcessor$get_default_api_url()
```

**Method** `make_api_call()`: Make API call to StepFun

*Usage:*

```
StepFunProcessor$make_api_call(chunk_content, model, api_key)
```

**Method** `extract_response_content()`: Extract response content from StepFun API response

*Usage:*

```
StepFunProcessor$extract_response_content(response, model)
```

**Method** `clone()`: The objects of this class are cloneable with this method.

*Usage:*

```
StepFunProcessor$clone(deep = FALSE)
```

*Arguments:*

`deep` Whether to make a deep clone.

---

UnifiedLogger

*Unified Logger for mLLMCelltype Package*

---

## Description

Unified Logger for mLLMCelltype Package

Unified Logger for mLLMCelltype Package

## Details

This logger provides centralized, multi-level logging with structured output, log rotation, and performance monitoring capabilities.

**Public fields**

log\_dir Directory for storing log files  
log\_level Current logging level  
session\_id Unique identifier for the current session  
max\_log\_size Maximum log file size in MB (default: 10MB)  
max\_log\_files Maximum number of log files to keep (default: 5)  
enable\_console Whether to output to console (default: FALSE)  
enable\_json Whether to use JSON format (default: TRUE)  
performance\_stats Performance monitoring statistics

**Methods****Public methods:**

- [UnifiedLogger\\$new\(\)](#)
- [UnifiedLogger\\$debug\(\)](#)
- [UnifiedLogger\\$info\(\)](#)
- [UnifiedLogger\\$warn\(\)](#)
- [UnifiedLogger\\$error\(\)](#)
- [UnifiedLogger\\$log\\_api\\_call\(\)](#)
- [UnifiedLogger\\$log\\_api\\_request\\_response\(\)](#)
- [UnifiedLogger\\$log\\_cache\\_operation\(\)](#)
- [UnifiedLogger\\$log\\_cluster\\_progress\(\)](#)
- [UnifiedLogger\\$log\\_discussion\(\)](#)
- [UnifiedLogger\\$log\\_model\\_response\(\)](#)
- [UnifiedLogger\\$get\\_performance\\_summary\(\)](#)
- [UnifiedLogger\\$cleanup\\_logs\(\)](#)
- [UnifiedLogger\\$set\\_level\(\)](#)
- [UnifiedLogger\\$clone\(\)](#)

**Method** new(): Initialize the unified logger

*Usage:*

```
UnifiedLogger$new(  
  base_dir = "logs",  
  level = "INFO",  
  max_size = 10,  
  max_files = 5,  
  console_output = FALSE,  
  json_format = TRUE  
)
```

**Method** debug(): Log a debug message

*Usage:*

```
UnifiedLogger$debug(message, context = NULL)
```

**Method** info(): Log an info message

*Usage:*

```
UnifiedLogger$info(message, context = NULL)
```

**Method** warn(): Log a warning message

*Usage:*

```
UnifiedLogger$warn(message, context = NULL)
```

**Method** error(): Log an error message

*Usage:*

```
UnifiedLogger$error(message, context = NULL)
```

**Method** log\_api\_call(): Log API call performance

*Usage:*

```
UnifiedLogger$log_api_call(  
  provider,  
  model,  
  duration,  
  success = TRUE,  
  tokens = NULL  
)
```

**Method** log\_api\_request\_response(): Log complete API request and response for debugging and audit

*Usage:*

```
UnifiedLogger$log_api_request_response(  
  provider,  
  model,  
  prompt_content,  
  response_content,  
  request_metadata = NULL,  
  response_metadata = NULL  
)
```

**Method** log\_cache\_operation(): Log cache operations

*Usage:*

```
UnifiedLogger$log_cache_operation(operation, key, size = NULL)
```

**Method** log\_cluster\_progress(): Log cluster annotation progress

*Usage:*

```
UnifiedLogger$log_cluster_progress(cluster_id, stage, progress = NULL)
```

**Method** log\_discussion(): Log detailed cluster discussion with complete model conversations

*Usage:*

```
UnifiedLogger$log_discussion(cluster_id, event_type, data = NULL)
```

**Method** `log_model_response()`: Log model response with concise summary in main log and full text in file

*Usage:*

```
UnifiedLogger$log_model_response(
  provider,
  model,
  response,
  stage = "annotation",
  cluster_id = NULL
)
```

**Method** `get_performance_summary()`: Get performance summary

*Usage:*

```
UnifiedLogger$get_performance_summary()
```

**Method** `cleanup_logs()`: Clean up old log files

*Usage:*

```
UnifiedLogger$cleanup_logs(force = FALSE)
```

**Method** `set_level()`: Set logging level

*Usage:*

```
UnifiedLogger$set_level(level)
```

**Method** `clone()`: The objects of this class are cloneable with this method.

*Usage:*

```
UnifiedLogger$clone(deep = FALSE)
```

*Arguments:*

`deep` Whether to make a deep clone.

---

ZhipuProcessor

*Zhipu API Processor*

---

## Description

Zhipu API Processor

Zhipu API Processor

## Details

Concrete implementation of BaseAPIProcessor for Zhipu models. Handles Zhipu-specific API calls, authentication, and response parsing.

## Super class

[mLLMCelltype::BaseAPIProcessor](#) -> ZhipuProcessor

**Methods****Public methods:**

- [ZhipuProcessor\\$new\(\)](#)
- [ZhipuProcessor\\$get\\_default\\_api\\_url\(\)](#)
- [ZhipuProcessor\\$make\\_api\\_call\(\)](#)
- [ZhipuProcessor\\$extract\\_response\\_content\(\)](#)
- [ZhipuProcessor\\$clone\(\)](#)

**Method** `new()`: Initialize Zhipu processor

*Usage:*

```
ZhipuProcessor$new(base_url = NULL)
```

**Method** `get_default_api_url()`: Get default Zhipu API URL

*Usage:*

```
ZhipuProcessor$get_default_api_url()
```

**Method** `make_api_call()`: Make API call to Zhipu

*Usage:*

```
ZhipuProcessor$make_api_call(chunk_content, model, api_key)
```

**Method** `extract_response_content()`: Extract response content from Zhipu API response

*Usage:*

```
ZhipuProcessor$extract_response_content(response, model)
```

**Method** `clone()`: The objects of this class are cloneable with this method.

*Usage:*

```
ZhipuProcessor$clone(deep = FALSE)
```

*Arguments:*

`deep` Whether to make a deep clone.

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