

**Step 1: ORA database generation  
and  
Step 2: Gene-Protein-Reaction (GPR) rules**

**Reaction / pathway identifiers [txt]:**

- EC
- KO (KEGG orthology ID)
- RID (KEGG reaction ID)
- KEGG pathway map

**Manual editing**  
of sequences,  
reactions and GPRs

**User-defined ORAdb**

**Step 3: Ortholog clustering**

- Protein sequence data [FASTA]
- Species id

Orthofinder

Cluster of orthologs

**Step 4: Functional annotation**

Relaxed search

DIAMOND BLAST

Reduced cluster  
of orthologs

Restrictive search

DIAMOND BLAST

Annotated sequences

**Step 5: Putative interactions  
and exploration**

**Interactive  
network  
visualization**

**Functional  
potential [CSV]**

**Putative species  
interactions [CSV]**

**Task 1**

**Task 2**

**Task 3**

Optional step  
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Input [format]

Key tools

Output [format]