SUPPLEMENTARY TABLES AND FIGURES

Tool	Reference Database	Multi-omic pathway analysis with mixed ID input	Multi-omic pathway analysis using multiple knowledge sources	Inclusion of extensive chemical/lipid annotations
RaMP	HMDB, Reactome, Wikipathways	Yes	Yes	Yes
MetaboAnalyst	KEGG, Pathbank	No	Yes	No
3Omics	KEGG, HumanCyc	No	Yes	No
IMPaLA	11 total including KEGG, Reactome, BioCyc, Wiki-Pathways, SMPDB	No	Yes	No
ConsensusPathDB	30 different sources including Reactome, KEGG, WikiPathways and HumanCyc	No	Yes	No
MetaBox	KEGG	No	No	Yes
PathNet	KEGG	No	No	No
GO-Elite	GO, WikiPathways, PathwayCommons, KEGG	Yes	Yes	No

Supplementary Table 1: Publicly available tools for functional enrichment analysis of metabolomic and transcriptomic data

RaMP package function	Query result	Page of GUI used	Tables used	API link
getAnalyteFromPathway()	A dataframe of analytes associated with input pathway(s)	https://ramp-alpha.ncats.io/analytes-from-pathways	source, analytehaspathway, pathway	https://rampdb.nih.gov/api/analytes-from-pathways
getPathwayFromAnalyte()	A dataframe of pathways associated with the input analyte(s)	https://ramp-alpha.ncats.io/pathways-from-analytes	source, analytehaspathway, pathway	https://rampdb.nih.gov/api/pathways-from-analytes
getMetaFromOnto()	A dataframe of metabolites associated with the input ontology/ies	https://ramp-alpha.ncats.io/metabolites-from-ontologies	source, analytehasontology, ontology	https://rampdb.nih.gov/api/metabolites-from-ontologies
getOntoFromMeta()	A dataframe of ontologies associated with the the input metabolite(s)	https://ramp-alpha.ncats.io/ontologies-from-metabolites	source, analytehasontology, ontology	https://rampdb.nih.gov/api/ontologies-from-metabolites
rampFastCata()	A dataframe of reaction partners associated with the input analyte(s)	https://ramp-alpha.ncats.io/common-reaction-analytes	source, catalyzed, analytesynonym	https://rampdb.nih.gov/api/common-reaction-analytes
getChemicalProperties()	A dataframe of chemical properties associated with the input metabolite. Includes InCHI, InCHIKey, formula, mass, and SMILES	https://ramp-alpha.ncats.io/properties-from-metabolites	chem_props	https://rampdb.nih.gov/api/chemical-properties
chemicalClassSurvey()	A dataframe of ClassyFire chemical classes (up to level 4) associated with the input metabolite(s) of interest	https://ramp-alpha.ncats.io/classes-from-metabolites	source, metabolite_class	https://rampdb.nih.gov/api/chemical-classes

Supplementary Table 2: Queries supported by RaMP 2.0, including MySQL queries, corresponding R package functions, and API links

HMDBOntologyType (Parent Term)	Number of Distinct Descendant Ontology Terms	Notes on captured descendant term	Example terms
Source	10	Specific endpoint terms reported: Endogenous, Food, Plant, Animal, Microbe, Synthetic, Environmental, Saccharomyces cerevisiae, Fungi, Exogenous	Endogenous, Food, Plant, Animal
Biofluid and excreta	14	Capturing all descendent terms	Saliva, Feces, Urine, Blood
Organ and components	34	Capturing all descendent terms	Prostate, Brain, Liver, Intestines
Tissue and substructures	16	Capturing all descendent terms	Muscle, Placenta, Hepatic tissue, Epidermis
Subcellular	16	Capturing all descendent terms	Cytoplasm, Membrane, Mitochondria, Nucleus
Health condition	465	Capturing all descendent terms	Kidney disease, Obesity, Cancer, Schizophrenia
Industrial application	144	Capturing all descendent terms	Pharmaceutical, Surfactant, Emulsifier, Anticonvulsant

Supplementary Table 3: Portions of the HMDB Chemical Functional Ontology incorporated into RaMP
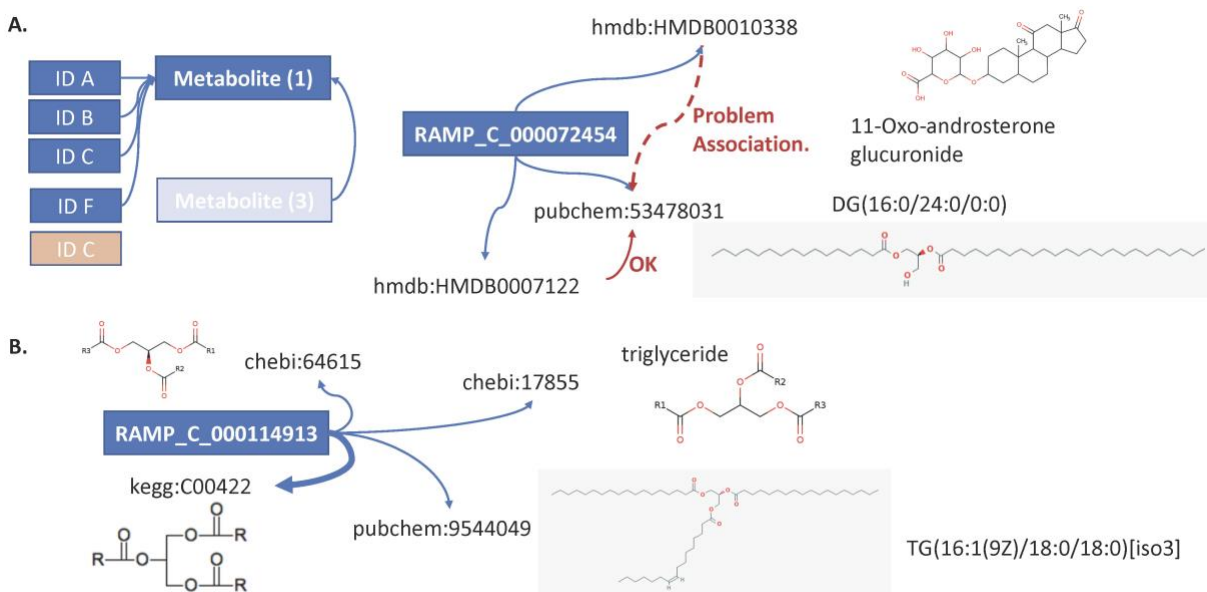
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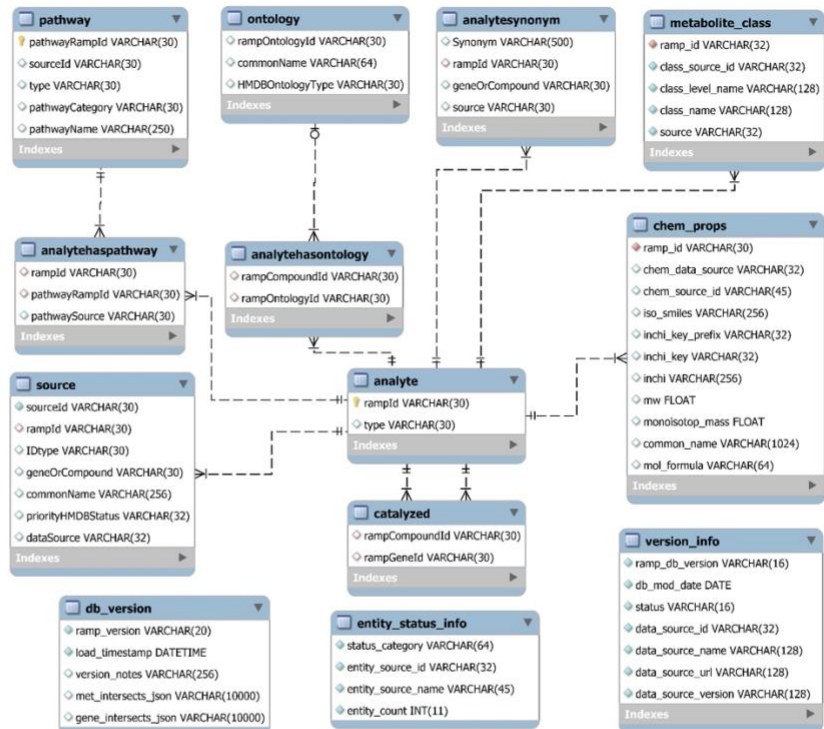
B.
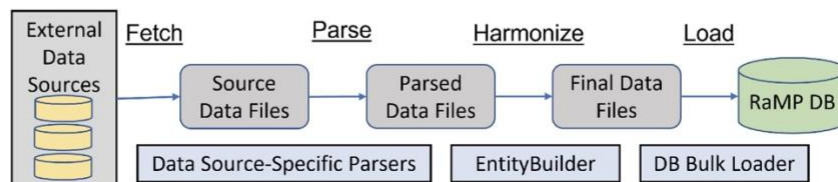
Supplementary Figure 1: **A)** RaMP-DB 2.0 Schema (and data models). **B)** Overview of the process underlying the backend code used to create RaMP .

Supplementary Figure 2: Example errors in mappings. A) Two completely different structures are mapping to the same PubChem ID. B) Specific structures are mapping to generic structures (triglycerides with R groups rather than specific chains). 118 of 125 HMDB triglycerides map to the generic KEGG triglyceride ID (C00422).