## MiMeDB: The Human Microbial Metabolome Database

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**Abstract:** The Human Microbial Metabolome DataBase or MiMeDB (https://mimedb.org) is a comprehensive, multi-omic, microbiome resource that connects: 1) microbes to microbial genomes; 2) microbial genomes to microbial metabolites; 3) microbial metabolites to the human exposome; and 4) all of these "omes" to human health. MiMeDB was established to consolidate the growing body of data connecting the human microbiome and the chemicals it produces to both health and disease. MiMeDB contains detailed taxonomic, microbiological and body-site location data on most known human microbes (bacteria and fungi). This microbial data is linked to extensive genomic and proteomic sequence data that is closely coupled to colourful interactive chromosomal maps. The database also houses detailed information about all the known metabolites generated by these microbes, their structural, chemical and spectral properties, the reactions and enzymes responsible for these metabolites and the primary exposome sources (food, drug, cosmetic, pollutant, etc.) that ultimately lead to the observed microbial metabolites in humans. Additional, extensively referenced data about the known or presumptive health effects, measured biosample concentrations and human protein targets for these compounds is provided. All of this information is housed in richly annotated, highly interactive, visually pleasing database that has been designed to be easy to search, easy to browse and easy to navigate. Currently MiMeDB contains data on 626 health effects or bioactivities, 1,904 microbes, 3,112 references, 22,054 reactions, 24,254 metabolites or exposure chemicals, 648,861 MS and NMR spectra, 6.4 million genes and 7.6 billion DNA bases. We believe that MiMeDB represents the kind of integrated, multi-omic or systems biology database that is needed to enable comprehensive multi-omic integration.

#### Why This Database?

Over the past decade, many significant associations have been found between human gut microflora and gastrointestinal disorders, obesity, mood and immunity. While most human microbiome studies continue to focus on connecting health outcomes to measures of microbial taxonomy (such as microbe types or measures of microbial diversity), there is increasing awareness that it's not the microbes themselves that lead to specific health effects, it's the chemicals they produce. It was because of this fact that we decided to create MiMeDB – the Human Microbial Metabolome DataBase.

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M'M - D				MiMeDB	Browse <del>-</del>	Searc
MiMeD	Browse - Search - Downloads About - Contact Us	Metabolites Y Search	Search	Detected in Host		
Showing meta	abocard for Indoxyl sulfate (MMDBc0000661)				Host and Biospecimen	5
Record Informatio	n		^		Human urine	1
/ersion	1.0				Human urine	(
reated at	2021-07-26 19:24:25 UTC					
Updated at	2021-07-26 19:24:25 UTC				Human blood	1
Mime	MMDBc0000661					
Metabolite Identification			~		Human urine	
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# Medbe and adult Method adult <th colspan="2"<

MiMeDB is designed to be a fully integrated multi-omic database that links the human microbial (meta)genome, proteome and metabolome to the human exposome – and human health. Our goal in creating MiMeDB was to create a resource that researchers with genomic, proteomic, metabolomic or exposomic data could use to query and interactively explore, visualize and interpret their data with other known multi-omic data on the human microbiome. In developing MiMeDB, we attempted to bring many of the best features of other databases such as VMH, HMDB, KEGG, GenBank, UniProt, BacMap, FooDB and HMDB, together into a single resource. These data have then been reformatted and integrated into a web-friendly database that allows users to perform sophisticated queries and interactive visualizations.

#### The Microbiome, Diet & The Metabolome Are Closely Linked



Description Indoxyl sulfate, also known as 3-indoxyl sulfate, is a member of the class of organic compounds known as arylsulfates. These are organic compo containing a sulfate group that carries an aryl group through an ether group. Indoxyl sulfate is a metabolite of the common amino acid tryptophan and is derived through the consumption, digestion and microbial processing of protein-rich foods. Indoxyl sulfate is technically a bacterial co-metabolite, meaning that it is derived from both bacterial and host metabolism. Specifically, it is generated from dietary L-tryptophan which is converted to indole in the large testine via tryptophanase-expressing gastrointestinal bacteria (PMID: 27102537). The resulting indole is converted to indoxyl in the liver via enzyme by the CYP450 enzyme CYP2E1 (PMID 11808865). Subsequently, indoxyl is converted into indoxyl sulfate by the SULT1A1 whe in the liver (PMID: 12064372). Indoxyl sulfate has been identified as a uremic toxin according to the European Uremic Toxi and is classified as a protein-bound uremic solute. Indoxyl sulfate is known to bind to serum albumin (PMID: 226268 insported by the OAT1 transporter (PMID: 34678967 🕥 and to be an adoptist for the anylhydrocarbon recentor (AbR) (PMIC centrations of indoxyl sulfate in whole blood or blood plasma are known to be associated with the development and progression of ase (CKD) as well as the development of cardiovascular disease (CVD) in humans and other mammals (PMID: 28754616 🖤). As a 38205 🕼). Indoxyl sulfate upregulates signal transducers and activators of transcription 3 phosphorylation leading to nonocyte chemotactic protein-1 and alpha-smooth muscle actin production, all of which participate in interstitial inflammation, renal prosis and, consequently, CKD progression (PMID: 33138205 🕜). Indoxyl sulfate is also a known cardiotoxin (PMID: 30200452 🕜). In plasma, indoxyl MiMeDB – Reactions MIMEDB Browse - Search - Downloads About - Contact Us Metabolites 🖌 Search Showing metabocard for Indoxyl sulfate (MMDBc0000661 tabolite Identificat etabolic Reaction ase-II biotransformatio Exposure Source Reference otein fiber ra high CVD risk

MiMeDB – Pathways

		creatinine					
Human blood	Detected and Quantified	14 +/- 4.2 micromolar	adult	Male	healthy	HMDB	<ul> <li>● details</li> </ul>
Human blood	Detected and Quantified	2.49 +/- 1.36 micromolar	1-13yo	Both	healthy	HMDB	<ul> <li>details</li> </ul>
Human urine	Detected and Quantified	129 (45-191) micromol/mmol creatinine	adult	Both	healthy	HMDB	© details
Human urine	Detected and Quantified	19.74 +/- 5.26 micromol/mmol creatinine	adult	Male	healthy	HMDB	© details
Human urine	Detected and Quantified	17.76 +/- 6.58 micromol/mmol creatinine	adult	Female	healthy	HMDB	

#### **MiMeDB – Health Effects**

MeDB	Browse - Sea	rch <del>-</del> Downloads	About+ Con	tact Us	Metabolites	✓ Search	Search
nd Bioactivity							^
	Health outcome	Metabolite Response	Related Health Condition	Evidence Type	Measured in Matrix	Reference	
	Mild cognitive impairment	Increased	CKD	Association	Human serum	PMID:26797588	details
	Bioactivity	Metabolite effect	Related Health Condition	Evidence Type	Measured in Matrix	Reference	
	Nuclear factor-kb	agonist	Neuroinflammation CKD	Cell culture	astrocyte cells	PMID:28659803	♥ details
	Aryl hydrocarbon receptor	agonist		Cell culture	Mouse CaCo-2 intestinal cells	PMID:34137156	details
	Aryl hydrocarbon receptor	agonist	Neuroinflammation	Cell culture	astrocyte cells	PMID:30336612	details
	Neurotoxin		Neuroinflammation CKD	Animal_model	Mouse brain tissue	PMID:28659803	letails
	Pro-inflammatory		CKD	Cell culture	renal tubular cells	PMID: 22610984	<ul> <li>♥ details</li> </ul>
	Pro-inflammatory		Neuroinflammation	Cell culture	astrocyte cells	PMID:30336612	<ul> <li>✓ details</li> </ul>
	Pro-inflammatory		Neuroinflammation CKD	Animal_model	Mouse brain tissue	PMID:28659803	👁 details
	ROS production	induces	Neuroinflammation CKD	Cell culture	astrocyte cells	PMID:28659803	
	ROS production	induces	CKD	Cell culture	renal tubular cells	PMID: 29474405	• details





### **MiMeDB – Food Sources**

MiMeDI	Browse - Sea	arch <del>-</del> Downloads	About <del>-</del> Cor	ntact Us	Metabolites	✓ Search	Searc
alth and Bioacti	vity						^
	Health Type	Evidence Type	Related Health Condition	Metabolite Response	Measured in Matrix	Reference	
	Health outcome	Association	Alzheimer disease	decreased	Human plasma	PMID:33269100	
posure Sources							~
	Exposure Type	Exposure Source	Source Sub-type	Species	Taxonomy	Reference	
	Ingestion	Animal	Fish	Salmon	NCBI:504568	FooDB	details
	Ingestion	Animal	Fish	Smelt	NCBI:8012	FooDB	• details
	Ingestion	Animal	Crustaceans	Snow crab	NCBI:41210	FooDB	• details
	Ingestion	Animal		Cow	NCBI:9913	FooDB	• details
	Ingestion	Food	Coffee	Coffea arabica	NCBI:13443	FooDB	( details
	Ingestion	Food	Tofu	Soy	NCBI:3847	FooDB	👁 details
	Ingestion	Plant		Cashew nuts	NCBI:171929	FooDB	
	Indection	Diant	Reas	0	NOD-2014	FeeDR	-



#### Conclusion

MiMeDB represents one of the most comprehensive, interconnected, multi-omic databases ever constructed. Currently MiMeDB contains data on 626 health effects or bioactivities, 1,904 microbes, 3,112 references, 22,054 reactions, 24,254 metabolites or exposure chemicals, 648,861 MS and NMR spectra, 6.4 million genes and 7.6 billion DNA bases Overall, we believe MiMeDB represents an important first step in the path to providing the integrated, multi-omic resources needed to advance their understanding of the human microbiome, the human microbial metabolome, the human exposome and their combined impacts on human health and disease.



#### **MiMeDB – Home Page**

