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Supplemental Material

Risk-Based Chemical Ranking and Generating a Prioritized Human Exposome Database

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Additional File- Excel Document

Text S1. Graphical User Interface (GUI) installation

The GUI installer requires Java 8 (<https://www.oracle.com/java/technologies/javase/javase-jdk8-downloads.html>) under Windows or Mac OS operating system. Our first version of GUI package can be downloaded in the Supplementary Information named “HExpMetDB.rar”. The most updated GUI package is also available as an open access Java library at:

<https://github.com/FangLabNTU/HExpMetDB>

Step 1: Download package “HExpMetDB.zip for Win” or “HExpMetDB.zip for Mac” and unzip the file.

Step 2: For Windows system: Open the file → Double click the “run.bat” file, then the GUI will be automatically opened (maybe wait for a few seconds);

For **Mac OS** system: The snapshot of the file list can be found below. Open “Terminal.app” → Enter “cd+space+file path of “run.sh” in HExpMetDB package + carriage return” (e.g., cd+space+/Users/fan/Desktop/BIO/HExpMetDB_for_Mac+carriage return) → Enter “./run.sh”, then the GUI will be opened (shown as following figure).

copyright	2020/6/21 3:00
cyp450_AB	2020/11/23 15:50
ecbased_AB	2020/11/23 15:46
HExpMetDB.class	2020/11/25 15:44
HExpMetDB.java	2020/11/25 15:44
hgut_AB	2020/11/23 15:42
Index\$1.class	2020/11/25 15:44
Index\$2.class	2020/11/25 15:44
Index\$3.class	2020/11/25 15:44
Index.class	2020/11/25 15:44
phaseI_AB	2020/11/23 15:48
run	2020/11/25 15:46
run.sh	2020/11/25 15:50
total_matter	2020/11/25 11:00

HEExpMetDB_for_Mac — java — 80x24


```
Last login: Wed Nov 25 19:21:08 on console
fandeMacBook-Pro:~ fan$ cd /Users/fan/Desktop/BIO/HExpMetDB_for_Mac
fandeMacBook-Pro:HExpMetDB_for_Mac fan$ ./run.sh
```

HEExpMetDB

Search Database

Select a Search Type: Select a Input Type:

Tolerance Charge Adducts



HEExpMetDB
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Text S2. HExpMetDB Functionality

We have developed a Java GUI client program running on JVM 1.8 under Windows and Mac OS operating system. Upon startup, it preloads the detailed information of all substances into a table. Users can pose queries by specifying a few keywords and retrieve their desired information in milliseconds. The HExpMetDB GUI contains compound search tab and database tab: When users open the database tab, users can browse our database and choose the parameters they want to display on the interface (Figure S2). Under the search tab, users can search chemicals as demonstrated in Figure S3. Specifically, the GUI allows users to do the following functions: (1) a single chemical search using a Chemical Abstracts Service Registry Number (CASRN), molecular formula, mass-charge-ratio (m/z) or adduct (Figure S3A); (2) searching predicted metabolites of a single chemical using the metabolite search module (Figure S3B); (3) searching predicted metabolites using the m/z, adducts or molecular formula (Figure S3C). Information including human exposure, animal toxicity LD₅₀, ToxPi Score, their HQ (Hazard Quotient, LD₅₀ based) and Risk Index (ToxPi based) values as well as their ranking and confidence intervals were all given in “HExpMetDB” GUI. This platform would assist in a broad array of human exposure research and to facilitate chemical risk prioritization and metabolite identification.

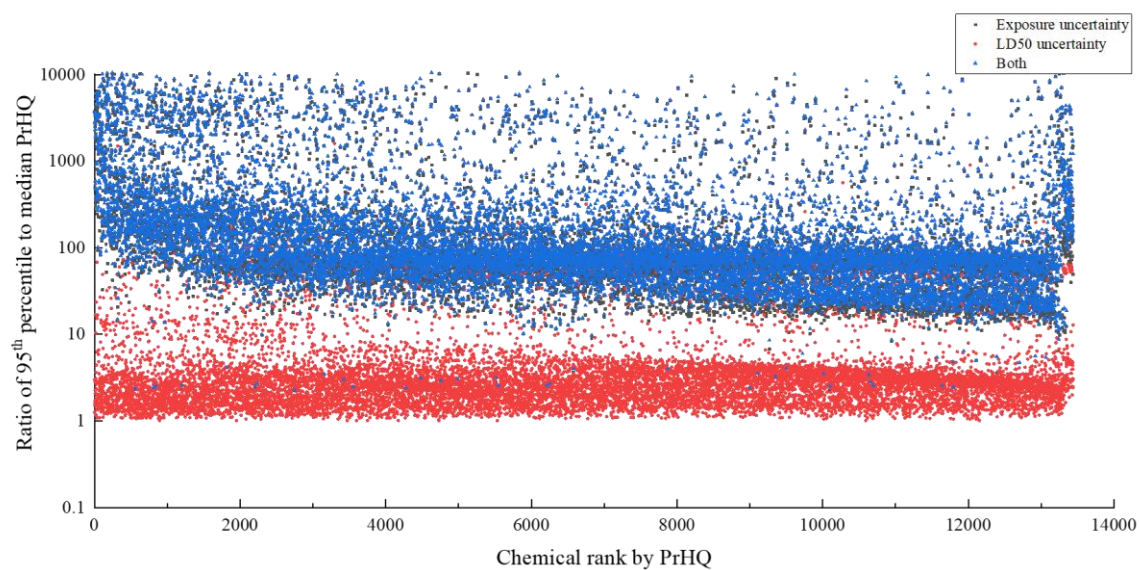


Figure S1. Relative contributions of exposure and LD₅₀ prediction uncertainty to differences between the 95th percentile and median PrHQ. Monte Carlo analysis of both exposure and LD₅₀ prediction uncertainty gives distributions that can be characterized by the ratio of the PrHQ for the 95th percentile to the median.

HEXpMetDB

Search Database

ID CASRN DTXSID Name IUPAC NAME Molecular formula Average mass Monoisotopic mass HLB (h) SEEM3 (mg/kg-BW/day) SEEM3 95%CI Oral rat LD50 mol/kg
 Oral rat LD50 95%CI ToxCast number of active assay/total Toxpi ToxPI 95% CI PrRID PrRID 95%CI PrHQ PrHQ 95%CI PrHQ Rank RI RI 95%CI RI Rank SMILES
 QSAR ready SMILES InChI String InChIKey logKow logKoa


ID	CASRN	DTXSID	Name	HLB (h)	SEEM3 (mg/kg--)	Toxpi	PrRID	PrHQ	PrHQ Rank	RI	RI Rank
10	60-33-3	DTXSID2025505	Linoleic acid	2.30	7.40E-06	0.24	4.79E-01	1.54E-05	7515	0.15	394
11	84-66-2	DTXSID7021780	Diethyl phthalate	1.92	2.27E-04	0.05	9.53E-02	2.39E-03	638	0.15	394
12	85-68-7	DTXSID3020205	Benzyl butyl phth...	2.23	1.62E-04	0.18	8.45E-01	1.91E-04	2	0.15	394
13	80-05-7	DTXSID7020182	Bisphenol A	7.11	5.50E-05	0.38	2.07E-01	2.65E-04	2	0.15	394
14	100-02-7	DTXSID0021834	4-Nitrophenol	0.90	1.12E-05	0.14	2.17E-02	5.19E-04	1616	0.09	1998
15	101-20-2	DTXSID4026214	Triclocarban	156.52	1.15E-07	0.34	4.28E-02	2.68E-06	11294	0.17	192
16	10265-92-6	DTXSID6024177	Methamidophos	4.84	2.48E-06	0.12	4.70E-04	5.28E-03	308	0.07	2637
17	106-48-9	DTXSID1021871	4-Chlorophenol	11.02	3.82E-06	0.07	2.96E-02	1.29E-04	3189	0.04	4060
18	107-66-4	DTXSID3040728	Phosphoric acid...	5.51	5.98E-05	0.10	6.53E-02	9.15E-04	1181	0.07	2892
19	108-95-2	DTXSID5021124	Phenol	3.30	3.17E-04	0.18	1.61E-02	1.97E-02	98	0.13	716
20	120-83-2	DTXSID1020439	2,4-Dichloroph...	1.42	1.66E-05	0.22	3.35E-02	4.95E-04	1664	0.14	563
21	131-57-7	DTXSID3022405	2-Hydroxy-4-met...	1.81	2.83E-04	0.18	2.30E-01	1.23E-03	964	0.13	805
22	134-62-3	DTXSID2021995	DEET	1.70	1.52E-06	0.02	8.40E-02	1.81E-05	7164	0.01	7011
23	135-19-3	DTXSID5027061	2-Naphthalenol	1.90	9.59E-06	0.25	5.91E-02	1.62E-04	2868	0.15	349
24	140-66-9	DTXSID9022360	4,4',1,1',3,3'-Tetra...	5.99	9.88E-07	0.33	9.48E-02	1.02E-05	8381	0.18	121
25	1563-38-8	DTXSID2027414	2,3-Dihydro-2,2...	2.14	4.41E-06	0.08	1.81E-02	2.43E-04	2361	0.05	3672
26	1912-24-9	DTXSID9020112	Atrazine	63.54	1.08E-06	0.29	5.45E-02	1.98E-05	6999	0.16	253

Select what you need in the interface

Select a Metabolic Transformation: CYP450

Molecular_fo...	Major_Isotop...	InChI	Synonyms	InChIKey	ALogP	Precursor_ID	Precursor_In...	Precursor_In...	Precursor_A...	Reaction	Reaction_ID	Metabolite_ID	Enzyme(s)	Biosystem
C15H16O3	244.109944...	InChI=1S/C1...		HHOUSCIE...	2.89189999...		InChI=1S/C1...	IISBACLAFK...		Hydroxylatio...	BTMR1061	BTM00001	CYP1A2CYP...	HUMAN
C15H16O3	244.109944...	InChI=1S/C1...		YGFAMQHM...	3.71520000...		InChI=1S/C1...	IISBACLAFK...		O-Hydroxylati...	BTMR1037	BTM00002	CYP1A2CYP...	HUMAN

Results: 2 records



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1 **Figure S2.** Database parameter selection display function.

HEXpMetDB

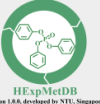
Search Database

Select a Search Type: Parent compound Select an Input Type: Mass 389.277

Tolerance 50 Charge Negative Adducts M-H

ID	CASRN	DTXSID	Name	IUPAC	Molecular f...	HLB (h)	SEEM3 (...)	Oral rat LD...	Toxpi	PrRID	PrHQ	PrHQ	RI	RI Ra...	In...	L...	
320	117-81-7	DTXSID0520607	D[2]-ethylhexyl phthalate	Bis(2-C24H38O4	...	4.50	2.72E-03	5.92E-02	0.21	1.36E+00	2.00E-03	700	0.16	236	
321	117-84-0	DTXSID1021956	Di-n-octyl phthalate	Dioc...	C24H38O4	...	1.92	3.94E-06	6.17E-02	0.18	1.21E+00	3.24E-06	10901	0.11	1321
1047	6422-86-2	DTXSID7027625	Bis(2-ethylhexyl) terephtha...	Bis(2-C24H38O4	...	4.50	1.12E-01	4.57E-02	0.17	9.00E-01	1.24E-01	18	0.15	389	
20456	131-15-7	DTXSID0051655	Bis(1-methylheptyl) phthal...	Dioc...	C24H38O4	...	4.35E-06	6.68E-02	-	1.32E+00	3.31E-06	10856	-	-	
20457	137-89-3	DTXSID7024619	Bis(2-ethylhexyl) isophthal...	Bis(2-C24H38O4	1.03E-05	5.70E-02	-	1.12E+00	9.20E-06	8602	-	-	
20458	25724-58-7	DTXSID70874013	Hexyl decyl phthalate	Decyl...	C24H38O4	6.34E-02	-	1.28E+00	-	-	-	-	
20459	81702-81-6	DTXSID2099492	Hexyl isodecyl phthalate	Hexyl...	C24H38O4	...	3.95E-06	6.38E-02	-	1.26E+00	3.14E-06	10984	-	-	
16546	54547-81-8	DTXSID08202959	1-(7-Hexyl-9,10-dihydro-2...	1-(7-C28H38O	...	37.10	2.89E-07	3.30E-05	-	6.50E-04	4.44E-04	1749	-	-	
16552	54454-95-4	DTXSID5099618	1-(7-Octyl-9,10-dihydroph...	C28H38O	...	37.10	-	-	-	-	-	-	-	-	

Select a Metabolic Transformation:



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B HExpMetDB

Search Database

Select a Search Type: Parent compound Select an Input Type: Mass 389.277 Search

Tolerance: 50 Charge: Negative Adducts: M-H

ID	CASRN	DTXSID	Name	IUPA	Molecular f	HLB (h)	SEEM3	Oral rat LD	Toxic	PRD	PHQ	PHQ	RI	RI Ra	In	L
20	117-81-7	DTXSID5020967	Dib(2-ethylhexyl) phthalate	Bis(2-C24H38O4	4.50	2.72E-03	6.92E-02	0.21	1.32E+00	2.00E-03	700	0.16	236			
121	117-81-7	DTXSID7021955	Dib(2-ethylhexyl) phthalate	Bis(2-C24H38O4	4.50	3.94E-06	6.17E-02	0.18	1.21E+00	3.22E-06	1050	0.11	1521			
1047	6422-86-2	DTXSID7027625	Bis(2-ethylhexyl) terephthalate	Bis(2-C24H38O4	4.50	1.12E-01	4.57E-02	0.17	9.00E-01	1.24E-01	18	0.15	389			
20456	131-15-7	DTXSID0051655	Bis(1-methylheptyl) phthalate	Diocd-C24H38O4	...	4.35E-06	6.68E-02	...	1.32E+00	3.31E-06	10856	-	-			
20457	137-89-3	DTXSID7024619	Bis(2-ethylhexyl) isophthalate	Bis(2-C24H38O4	...	1.03E-05	5.70E-02	...	1.12E+00	9.20E-06	8602	-	-			
20458	25724-58-7	DTXSID70874013	Hexyl decyl phthalate	Decyl-C24H38O4	6.34E-02	...	1.25E+00	-	-			
20459	81702-81-6	DTXSID2069492	Hexyl isodecyl phthalate	Hexyl-C24H38O4	...	3.95E-06	6.38E-02	...	1.25E+00	3.14E-06	10984	-	-			
16546	54547-81-8	DTXSID80202969	1-(7-Hexyl-9,10-dihydro-2	1-(7-C28H38O	37.10	2.89E-07	3.30E-05	...	6.50E-04	4.44E-04	1749	-	-			
16552	54454-95-4	DTXSID50969618	1-(7-Octyl-9,10-dihydroph	C28H38O	37.10	-	-			

Select a Metabolic Transformation: CYP450 Click

Molecular_fo	Major_Isotop	InChI	Synonyms	InChIKey	ALogP	Precursor_ID	Precursor_In	Precursor_In	Precursor_A	Reaction	Reaction_ID	Metabolite_ID	Enzyme(s)	Biosystem
C24H38O5	406.271924	InChI=1S/C2	FAPSLTONK	-0.51319999			InChI=1S/C2	BJOHLKABX		Hydroxylation	BTMR1045	BTM00001	CYP2C8CYP	HUMAN
C24H38O5	406.271924	InChI=1S/C2	VEVSWAOR	-0.51319999			InChI=1S/C2	BJOHLKABX		Hydroxylation	BTMR1047	BTM00002	CYP2C8CYP	HUMAN
C24H38O5	406.271924	InChI=1S/C2	VVVVPAJEU	-0.46849999			InChI=1S/C2	BJOHLKABX		Hydroxylation	BTMR1074	BTM00003	CYP2C8CYP	HUMAN
C24H38O5	406.271924	InChI=1S/C2	XEWFUJZKJ	-0.46849999			InChI=1S/C2	BJOHLKABX		Hydroxylation	BTMR1074	BTM00004	CYP2C8CYP	HUMAN
C24H38O5	406.271924	InChI=1S/C2	FNBFFOZGW	-0.74580000			InChI=1S/C2	BJOHLKABX		Hydroxylation	BTMR1061	BTM00005	CYP2C8CYP	HUMAN
C24H38O5	406.271924	InChI=1S/C2	VBHVVLXWI	-0.74580000			InChI=1S/C2	BJOHLKABX		Hydroxylation	BTMR1061	BTM00006	CYP2C8CYP	HUMAN
C24H36O4	388.261359	InChI=1S/C2	DTVJUBFLG	1.24200000			InChI=1S/C2	BJOHLKABX		Terminal de	BTMR1190	BTM00007	CYP2C8CYP	HUMAN
C24H36O4	388.261359	InChI=1S/C2	HGLVLYPXB	0.69840000			InChI=1S/C2	BJOHLKABX		Terminal de	BTMR1190	BTM00008	CYP2C8CYP	HUMAN
C24H38O5	406.271924	InChI=1S/C2	ALSKJINZS	-1.4933			InChI=1S/C2	BJOHLKABX		Epoxidation	BTMR1028	BTM00009	CYP2C8CYP	HUMAN
C24H38O5	406.271924	InChI=1S/C2	VDPSPBYB	-0.68489999			InChI=1S/C2	BJOHLKABX		Hydroxylation	BTMR0053	BTM00010	CYP2C8CYP	HUMAN

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C HExpMetDB

Search Database

Select a Search Type: metabolite Select an Input Type: Mass 406.2719 Search

Tolerance: 20 Charge: Neutral Adducts:

Molecular_fo	Major_Isotop	InChI	Synonyms	InChIKey	ALogP	Precursor_ID	Precursor_In	Precursor_In	Precursor_A	Reaction	Reaction_ID	Metabolite_ID	Enzyme(s)	Biosystem	Source
C24H38O5	406.271924	InChI=1S/C	VVVVPAJEU	-0.46849999			InChI=1S/C	BJOHLKAB		Hydroxylation	BTMR1074	BTM00003	CYP2C8CYP	HUMAN	CYP450: C
C24H38O5	406.271924	InChI=1S/C	OSULZORP	-2.24280000			InChI=1S/C	MOIUGAXC		Hydroxylation	BTMR1047	BTM00001	CYP3A4	HUMAN	CYP450: C
C24H38O5	406.271924	InChI=1S/C	BNTRAWD	-1.4933			InChI=1S/C	RWPCVVB		Epoxidation	BTMR1028	BTM00006	CYP2C8CYP	HUMAN	CYP450: C
C24H38O5	406.271924	InChI=1S/C	VDPSPBYB	-0.68489999			InChI=1S/C	BJOHLKAB		Hydroxylation	BTMR0053	BTM00010	CYP2C8CYP	HUMAN	CYP450: C
C24H38O5	406.271924	InChI=1S/C	VYVZCOUJ	-0.46849999			InChI=1S/C	RWPCVVB		Hydroxylation	BTMR1074	BTM00003	CYP2C8CYP	HUMAN	CYP450: C
C24H38O5	406.271924	InChI=1S/C	COQAJUDJ	-3.22290000			InChI=1S/C	MOIUGAXC		Epoxidation	BTMR1028	BTM00003	CYP3A4	HUMAN	CYP450: C
C24H38O5	406.271924	InChI=1S/C	ALSKJINZS	-1.4933			InChI=1S/C	BJOHLKAB		Epoxidation	BTMR1028	BTM00009	CYP2C8CYP	HUMAN	CYP450: C
C24H38O5	406.271924	InChI=1S/C	FAPSLTONK	-0.51319999			InChI=1S/C	BJOHLKAB		Hydroxylation	BTMR1045	BTM00001	CYP2C8CYP	HUMAN	CYP450: C
C24H38O5	406.271924	InChI=1S/C	PYEJENGZ	-0.74580000			InChI=1S/C	RWPCVVB		Hydroxylation	BTMR1061	BTM00005	CYP2C8CYP	HUMAN	CYP450: C
C24H38O5	406.271924	InChI=1S/C	QPAGZXGJ	-2.24280000			InChI=1S/C	MOIUGAXC		Hydroxylation	BTMR1045	BTM00004	CYP3A4	HUMAN	CYP450: C
C24H38O5	406.271924	InChI=1S/C	VEVSWAOR	-0.51319999			InChI=1S/C	BJOHLKAB		Hydroxylation	BTMR1047	BTM00002	CYP2C8CYP	HUMAN	CYP450: C
C24H38O5	406.271924	InChI=1S/C	VBHVVLXWI	-0.74580000			InChI=1S/C	BJOHLKAB		Hydroxylation	BTMR1061	BTM00006	CYP2C8CYP	HUMAN	CYP450: C
C24H38O5	406.271924	InChI=1S/C	ALOZYZYW	-0.46849999			InChI=1S/C	RWPCVVB		Hydroxylation	BTMR1074	BTM00002	CYP2C8CYP	HUMAN	CYP450: C
C24H38O5	406.271924	InChI=1S/C	WKAAYQY	-0.74580000			InChI=1S/C	RWPCVVB		Hydroxylation	BTMR1061	BTM00004	CYP2C8CYP	HUMAN	CYP450: C
C24H38O5	406.271924	InChI=1S/C	VCMNQOQB	-0.68489999			InChI=1S/C	RWPCVVB		Hydroxylation	BTMR0053	BTM00007	CYP2C8CYP	HUMAN	CYP450: C
C24H38O5	406.271924	InChI=1S/C	UYCZPSUV	-2.19909999			InChI=1S/C	MOIUGAXC		Hydroxylation	BTMR1074	BTM00005	CYP3A4	HUMAN	CYP450: C
C24H38O5	406.271924	InChI=1S/C	WLQJWJGX	-0.51319999			InChI=1S/C	RWPCVVB		Hydroxylation	BTMR1045	BTM00001	CYP2C8CYP	HUMAN	CYP450: C
C24H38O5	406.271924	InChI=1S/C	XEWFUJZKJ	-0.46849999			InChI=1S/C	BJOHLKAB		Hydroxylation	BTMR1074	BTM00004	CYP2C8CYP	HUMAN	CYP450: C
C24H38O5	406.271924	InChI=1S/C	FNBFFOZGW	-0.74580000			InChI=1S/C	BJOHLKAB		Hydroxylation	BTMR1061	BTM00005	CYP2C8CYP	HUMAN	CYP450: C
C24H38O5	406.271924	InChI=1S/C	ZWNMEQY	-2.47539999			InChI=1S/C	MOIUGAXC		Hydroxylation	BTMR1061	BTM00002	CYP3A4	HUMAN	CYP450: C

HExpMetDB
Version 1.0.0, developed by NTL, Singapore

Figure S3. Searching functions of HExpMetDB GUI. Using DHEP (117-81-7) as an example: (A) searching a chemical and its parameters by mass-charge-ratio (m/z); (B) searching predicted metabolites of a single chemical using the metabolite search module; and (C) searching predicted metabolites by the m/z.