



The FoodBAll online resources to support discovery of novel dietary biomarkers with metabolomics



FOODBALL PROJECT - THE FOOD BIOMARKER ALLIANCE



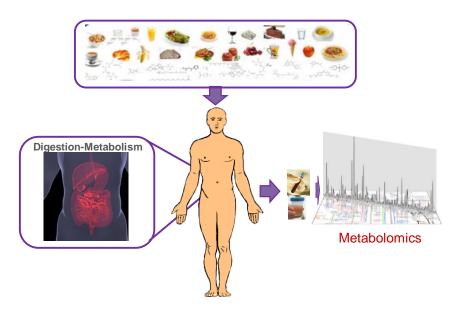
■ Janv 2015-Dec 2017. 4,38M€

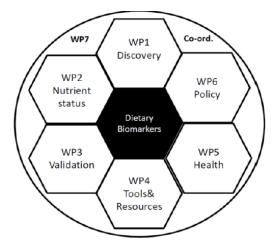


22 partners, PI: E. Feskens, Wageningen, NL

Aim: Identification and validation of

dietary biomarkers using metabolomics





- Intervention studies in 7 centers to identify new biomarkers of food intake
- Inventory of known dietary biomarkers and new validation scoring system
- New tools and resources for research on the food metabolome and biomarker discovery (WP4)



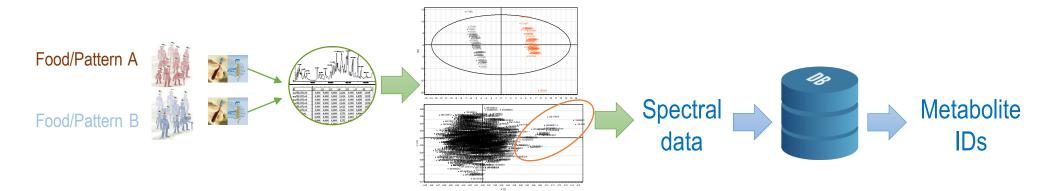
NEW TOOLS: PRIORITY NEEDS IDENTIFIED

- 1. A compound database with extensive coverage of the food metabolome
- 2. A food intake biomarkers database
- 3. A resource to facilitate sharing of standards
- A resource to facilitate knowledge and data sharing within the FoodBAll community and beyond



1- DATABASE WITH EXTENSIVE COVERAGE OF THE FOOD METABOLOME

 Compound databases are essential to obtain hypotheses of identification for discriminant ions associated with the intake of a given food or dietary pattern



Must be as <u>comprehensive</u> as possible, and contain <u>chemical</u>, <u>analytical</u>, <u>and biological data</u> that help to rapidly select the best hypotheses of identification to be further validated

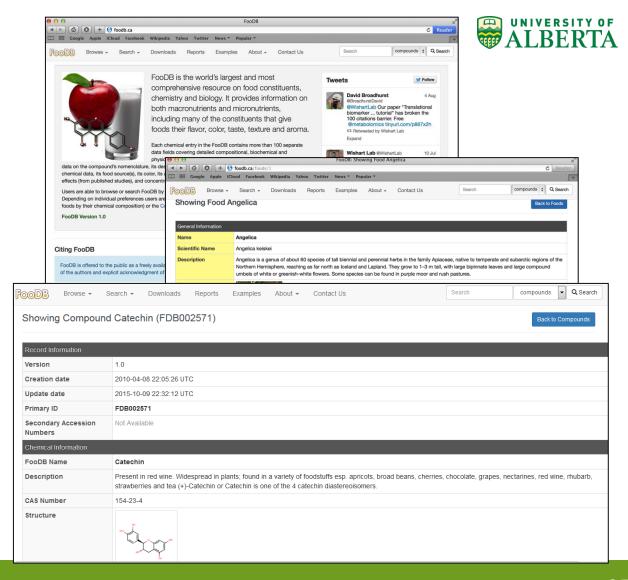








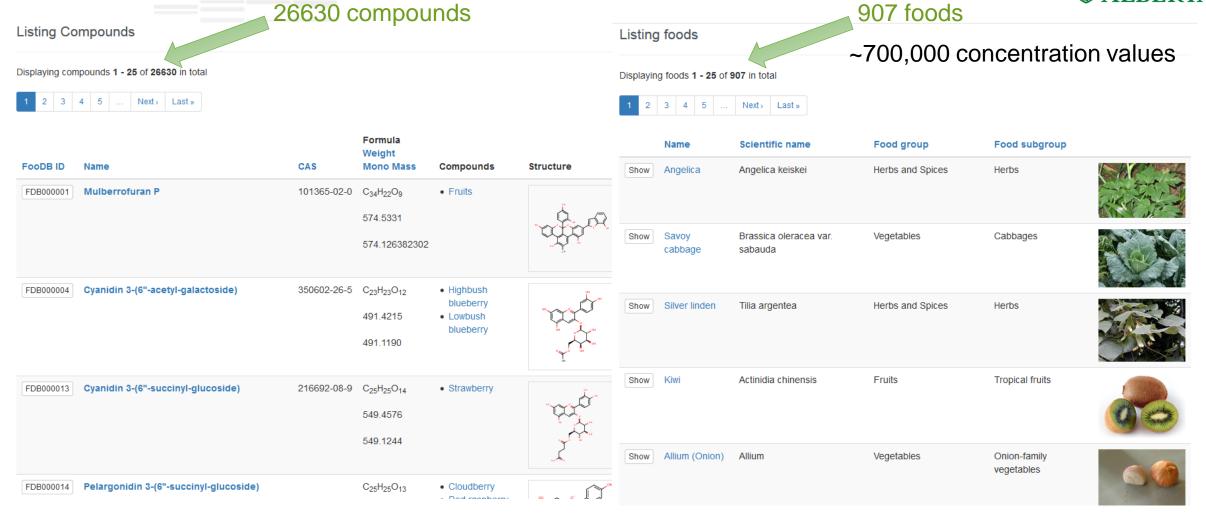
- ☐ Open access: www.foodb.ca/
- ☐ Developed by Univ of Alberta
- ☐ The most comprehensive database on food constituents
- ☐ Covers all types of food constituents

















☐ Every metabocards contains > 110 data fields

Showing Compound (±)-Catechin (FDB004453)



Record Information		
Version	1.0	
Creation date	2010-04-08 22:06:15 UTC	
Update date	2015-07-20 22:00:29 UTC	Chemical data
Primary ID	FDB004453	oriorinoar data
Secondary Accession Numbers	Not Available	
Chemical Information		
FooDB Name	(±)-Catechin	
Description	Isol. from various plants, e.g. Artocarpus integra, as artifact of epimerisation [CCD]	
CAS Number	7295-85-4	
Structure		Biological data

Chemical Names and synonyms
Chemical structures
Chemical taxonomies
Physical properties
NMR and MS spectra
Compound description
Associated foods
Biological effects (Duke's DB)
Flavor
Links





☐ Experimental spectra (Quercetin)

pectra			
Spectra	Spectrum Ty	peDescription	Splash Key
	GC-MS	GC-MS Spectrum - GC-MS (5 TMS)	splash10-0bt9-2611390000-f8e98c928a7ed82acda4 View in MoNA []
	LC-MS/MS	LC-MS/MS Spectrum - Quattro_QQQ 10V, Positive (Annotated)	splash10-0udi-0009000000-d4689b76f41c73487399 View in MoNA []
	LC-MS/MS	LC-MS/MS Spectrum - Quattro_QQQ 25V, Positive (Annotated)	splash10-0udi-0967000000-613e61ec0c69ed0ee630 View in MoNA []
	LC-MS/MS	LC-MS/MS Spectrum - Quattro_QQQ 40V, Positive (Annotated)	splash10-0uy0-5910000000-ee816015eec26c8621b1View in MoNA []
	LC-MS/MS	LC-MS/MS Spectrum - LC-ESI-QTOF (UPLC Q-Tof Premier, Waters) 5V, Posit	ivesplash10-0udi-0009000000-ec1cab852ed9f9f78fa4 View in MoNA []
	LC-MS/MS	LC-MS/MS Spectrum - LC-ESI-QTOF (UPLC Q-Tof Premier, Waters) , Negativ	e splash10-0udi-1907000000-6f36df2733dadae380c2 View in MoNA 🗹
	LC-MS/MS	LC-MS/MS Spectrum - LC-ESI-QTOF (UPLC Q-Tof Premier, Waters) , Negativ	e splash10-0udi-0309000000-976a99c106ceca16d73b View in MoNA 🗹
	LC-MS/MS	LC-MS/MS Spectrum - LC-ESI-QTOF (UPLC Q-Tof Premier, Waters) , Negativ	e splash10-0pi0-1900000000-b2e286366d41e47dd8fc View in MoNA 🗹
	LC-MS/MS	LC-MS/MS Spectrum - LC-ESI-QTOF (UPLC Q-Tof Premier, Waters) , Negativ	e splash10-0udi-0209000000-e891863ec110aeb660b0 View in MoNA 🗹
	LC-MS/MS	LC-MS/MS Spectrum - LC-ESI-QTOF (UPLC Q-Tof Premier, Waters) , Positive	splash10-0udi-0940000000-aa52db00c1defe3ccf75 View in MoNA []
	LC-MS/MS	LC-MS/MS Spectrum - LC-ESI-QTOF (UPLC Q-Tof Premier, Waters) , Positive	splash10-0udi-0219000000-5ef285c4b6bfd220b8b1 View in MoNA []
	LC-MS/MS	LC-MS/MS Spectrum - LC-ESI-QTOF (UPLC Q-Tof Premier, Waters) , Positive	splash10-0udi-0219000000-547c83bb70e7da007d6c View in MoNA []
	LC-MS/MS	LC-MS/MS Spectrum - LC-ESI-QTOF (UPLC Q-Tof Premier, Waters) , Negativ	e splash10-0udi-1907000000-a59602c09f66e9656068 View in MoNA 🕜
	LC-MS/MS	LC-MS/MS Spectrum - LC-ESI-ITTOF (LCMS-IT-TOF), Positive	splash10-0udi-0009000000-4416f39adf6c9b919bfa View in MoNA [7]
	LC-MS/MS	LC-MS/MS Spectrum - LC-ESI-ITTOF (LCMS-IT-TOF), Negative	splash10-0udi-0019000000-eb14ec62fc2fb2f1da88 View in MoNA []
	LC-MS/MS	LC-MS/MS Spectrum - LC-ESI-ITTOF (LCMS-IT-TOF), Negative	splash10-0ufr-0910000000-0730bca525c17aac75c5 View in MoNA [7]
	1D NMR	1H NMR Spectrum	Not Available
	2D NMR	[1H,13C] 2D NMR Spectrum	Not Available

☐ Predicted spectra (Quercetin 3-glucuronide)

Spectra		
Spectra	Spectrum Type Description	Splash Key
	Predicted LC-MS/MSPredicted LC-MS/MS Spectrum - 10V, Positive	Not Available
	Predicted LC-MS/MSPredicted LC-MS/MS Spectrum - 20V, Positive	Not Available
	Predicted LC-MS/MSPredicted LC-MS/MS Spectrum - 40V, Positive	Not Available
	Predicted LC-MS/MSPredicted LC-MS/MS Spectrum - 10V, Negative	Not Available
	Predicted LC-MS/MSPredicted LC-MS/MS Spectrum - 20V, Negative	Not Available
	Predicted LC-MS/MSPredicted LC-MS/MS Spectrum - 40V, Negative	Not Available

~5000 predicted MS/MS from CFM-ID

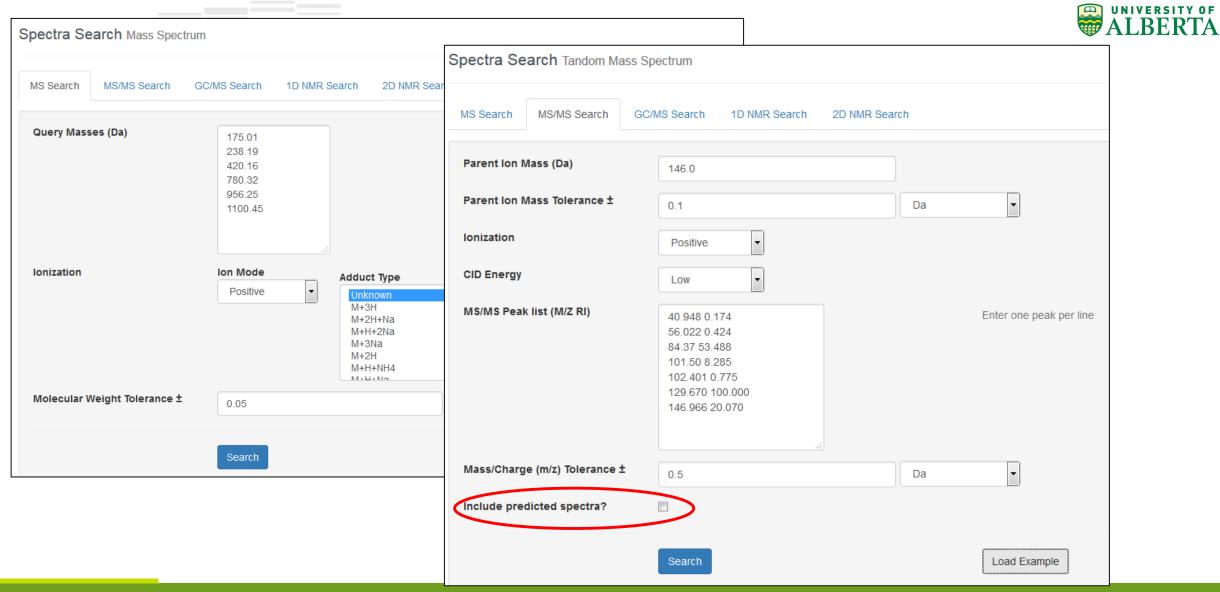
CFM-ID

Competitive Fragmentation Modeling for Metabolite Identification

http://cfmid.wishartlab.com/









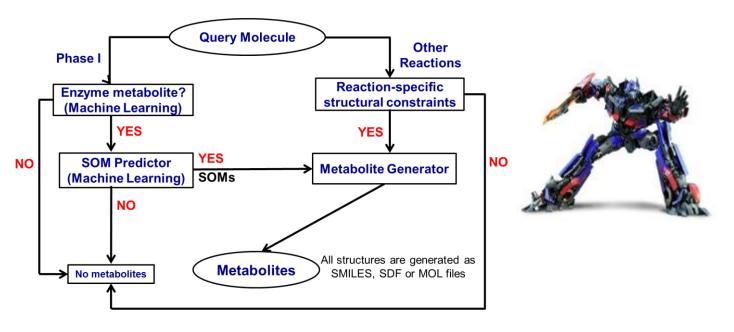
METABOLISM PREDICTION: BIOTRANSFORMER

- ☐ Many dietary biomarkers are expected to be metabolites of food constituents
- ☐ Information is largely missing on metabolites of many non-nutrients
- □ BioTransformer, an open-access software to predict metabolic by-products of a given compound

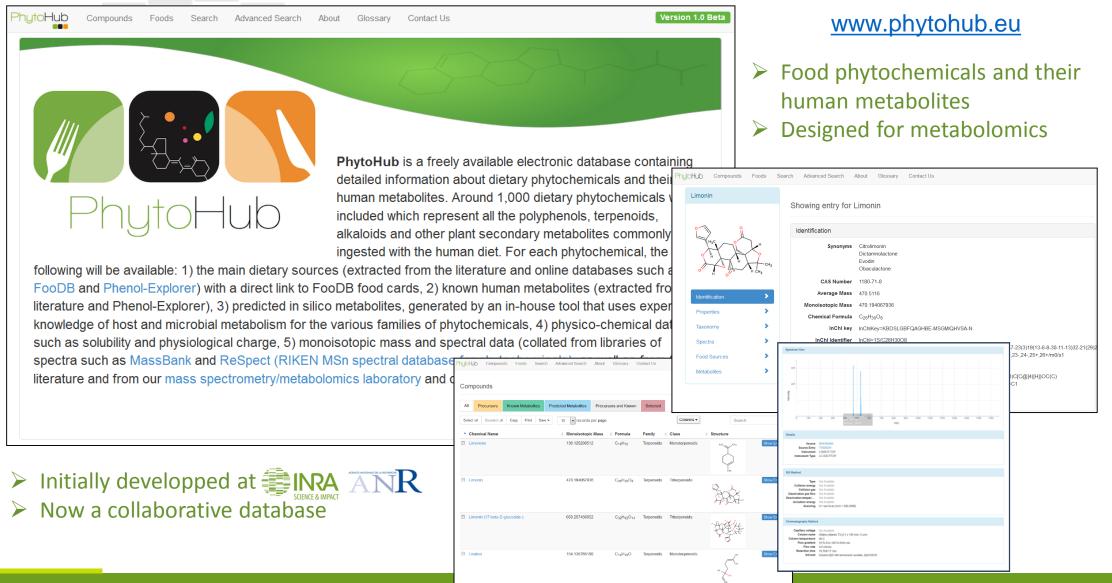


Computational metabolism

phase I metabolism (CYP450s) phase II metabolism (conjugation) microbial metabolism











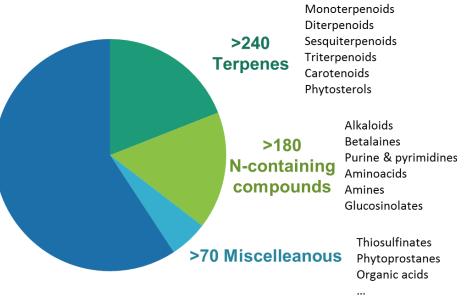
PHYTOHUB (www.phytohub.eu)

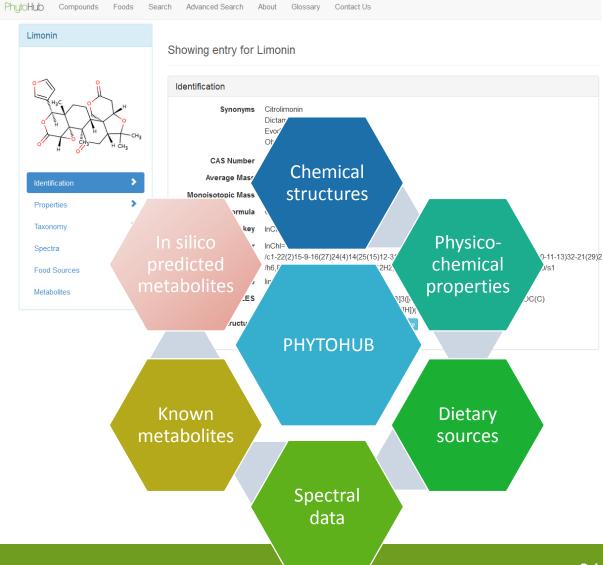
> 1230 dietary phytochemicals

> 660 Polyphenols

Anthocyanins Flavanols Flavanones Flavones, Flavonols Isoflavones Other flavonoids Hydroxybenzoic acids Hydroxycinnamic acids Other phenolic acids Ellagitannins Stilbenes Lignans

Coumarins









1- DATA ON PHYTOCHEMICAL METABOLITES: MANUAL EXTRACTION



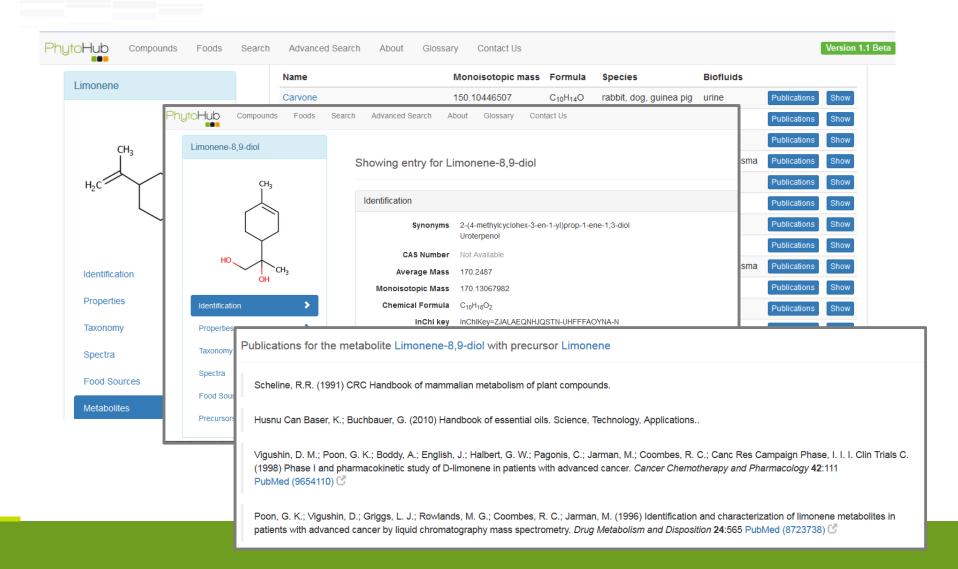
Data curation by experts of the different phytochemical families

Limonene		Name	Monoisotopic mass	Formula	Species	Biofluids		
Limonene		Carvone	150.10446507	C ₁₀ H ₁₄ O	rabbit, dog, guinea pig	urine	Publications	Show
		Carveol (trans-)	152.120115134	C ₁₀ H ₁₆ O	rabbit, rat	urine	Publications	Show
CH ₃		Limonene-1,2-diol	170.13067982	C ₁₀ H ₁₈ O ₂	human, rat	plasma	Publications	Show
]		Limonene-8,9-diol	170.13067982	C ₁₀ H ₁₈ O ₂	rat, rabbit, human, dog	urine, plasma	Publications	Show
H ₂ C		Limonene-8,9-diol glucuronide	346.162767808	C ₁₆ H ₂₆ O ₈	human, rabbit, dog, rat	urine	Publications	Show
		Limonene-10-ol	152.120115134	C ₁₀ H ₁₆ O	human, rabbit, dog, rat	urine	Publications	Show
CH	3	Limonene-10-ol-glucuronide	328.152203122	C ₁₆ H ₂₄ O ₇	human, rabbit, dog, rat	urine	Publications	Show
		Perillyl alcohol	152.120115134	C ₁₀ H ₁₆ O	rat, human	urine	Publications	Show
Identification	>	Perillic acid	166.099379692	C ₁₀ H ₁₄ O ₂	human, rabbit, dog, rat	urine, plasma	Publications	Show
		Perillic acid glucuronide	342.13146768	C ₁₆ H ₂₂ O ₈	human, rabbit, rat	urine	Publications	Show
Properties	>	Perillyl glycine	223.120843415	C ₁₂ H ₁₇ NO ₃	rat, rabbit, dog	urine	Publications	Show
Taxonomy	>	Perillic acid-8,9-diol	200.104859	C ₁₀ H ₁₆ O ₄	rat, rabbit, dog	urine	Publications	Show
Spectra	>	Dihydroperillic acid (trans-)	168.115029756	C ₁₀ H ₁₆ O ₂	rat, human	urine, plasma	Publications	Show
Food Sources	,	Dihydroperillic acid (cis-)	168.115029756	C ₁₀ H ₁₆ O ₂	rat, human	urine, plasma	Publications	Show
1 000 3001CES		Dihydroperillic acid glucuronide (trans-)	344.147117744	C ₁₆ H ₂₄ O ₈	human	urine	Publications	Show
Metabolites	>	Dihydroperillic acid glucuronide (cis-)	344.147117744	C ₁₆ H ₂₄ O ₈	human	urine	Publications	Show

1- DATA ON PHYTOCHEMICAL METABOLITES: MANUAL EXTRACTION



Data curation by experts of the different phytochemical families





Compound family	Experts	Affiliation				
Alkylresorcinols	Rikard Landberg	Swedish University of Agricultural Sciences, Uppsala, Sweden				
Anthocyanins	Wieslaw Wiczkowski	Institute of Animal Reproduction and Food Research of the Polish Academy of Sciences, Olsztyn, Poland				
Betalaines	Wieslaw Wiczkowski	Institute of Animal Reproduction and Food Research of the Polish Academy of Sciences, Olsztyn, Poland				
Carotenoids	Catherine Caris, Rachel Kopec	INRA Avignon, UMR408, France				
Ellagitannins	Paco Tomas-Barberan, Rocio Garcia-Villalba	CEBAS-CSIC, Murcia, Spain				
Flavanol metabolites	Peter Hollman	RIKILT Wageningen University, The Netherlands				
Flavanones metabolites	Claudine Manach	INRA Clermont-Ferrand, UMR1019, France				
Flavonol metabolites	Claudia Nunes dos Santos	ITQB-UNL/IBET, Oeiras, Portugal				
Hydroxycinnamic acids	Andreia Bento da Silva	Institute of Chemical and Biological Technology (ITQB), Oeiras, Lisbon, Portugal				
Miscellaneous phenolic acids	Andreia Bento da Silva	Institute of Chemical and Biological Technology (ITQB), Oeiras, Lisbon, Portugal				
Phytoprostanes	Cécile Gladine	INRA Clermont-Ferrand, UMR1019, France				
Phytosterols	Laura Nyström	Institute of Food, Nutrition and Health, ETH Zurich, Switzerland				
Procyanidin metabolites	Begoña Bartolomé Sualdea	Instituto de Investigación en Ciencias de la Alimentación (CIAL), CSIC-UAM, Madrid, Spain				
Stilbenes	Mireia Urpi-Sarda	University of Barcelona, Spain				
Terpenoids	Yoann Fillâtre	European Research Institute on Natural Ingredients, Grasse, France				

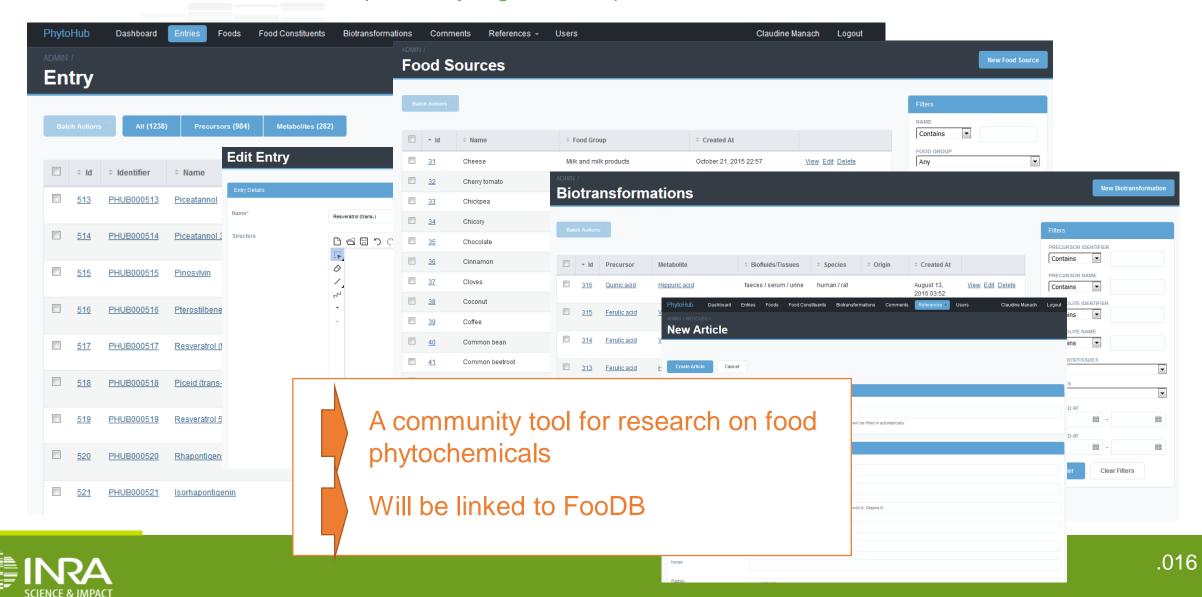
- ☐ Curators : min 1-2 experts for every family
 - ➤ Check PhytoHub data
 - ➤ Import new data from the literature (dietary sources, known metabolites, spectra...)
- □ Collaboration COST POSITIVe
 - > 77 research institutions with expertise on plant food bioactives

New curators are welcome!





☐ Back-end interface for online updates by registered experts



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2- A FOOD INTAKE BIOMARKERS DATABASI







http://exposome-explorer.iarc.fr/



« dedicated to biomarkers of exposure to environmental risk factors for diseases »

This information can be used by epidemiologists and clinicians to compare the performance and field of application of various biomarkers and specific biomarkers or panels of biomarkers most useful for biomonitoring or disease etiology studies.

Data collection was initiated with biomarkers for dietary and pollution exposures measured in the general population.

Exposome-Explorer contains so far data on 488 dietary and pollutant biomarkers extracted from 480 peer-reviewed publications. A total of 10508 concentration values measured in blood, urine and other biospecimens have been collected. It also contains 8034 correlation values between dietary biomarker levels and food intake and 536 values of biological reproducibility over time, precious indicators on the quality of a biomarker.

Exposome-Explorer has been developed at the International Agency for Research on Cancer (IARC) in collaboration with the University of Alberta, with the financial support of IARC, the European Commission (EXPOSOMICS, FP7-KBBE-2012, grant #308610; NutriTech FP7-KBBE-2011-5, grant #289511) and the Joint Programming Initiative FOODBALL (2014-17).



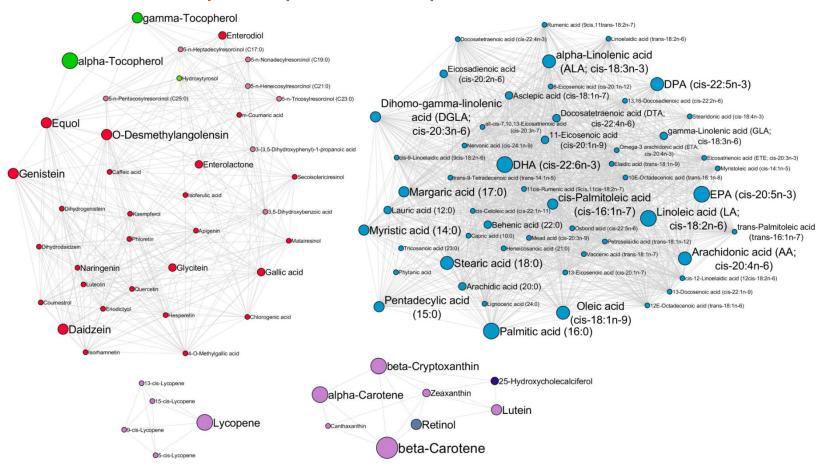
2- A FOOD INTAKE BIOMARKERS DATABASE







http://exposome-explorer.iarc.fr/



Statistics (June 2016)

All biomarkers

- 497 biomarkers
- 10,480 concentration values
- 480 publications analyzed

Dietary biomarkers

- 147 biomarkers
- 3,138 concentration values
- 220 publications analyzed
- Biomarkers
- Cohorts where measured
- Biospecimens
- Analytical methods
- Concentrations
- Correlations with exposures
- Reproducibility over time
- Confunding factors
- Linked to other databases



2- A FOOD INTAKE BIOMARKERS DATABASE







Correlation values

Search:	
---------	--

Show 10 rows Show/Hide columns Copy all rows

Showing 1 to 10 of 79 entries

Previous	1	2	3	4	5		8	Next
----------	---	---	---	---	---	--	---	------

Population	Intake 💠	Biological specimen	Biomarker	Correlation type •	Correlation value 🔻	Correlation p-value	Publication
Participants in the validation study of the MoBa cohort	Citrus fruits	Urine, 24-h	Flavanones	Pearson	0.66	< 0.01	Brantsaeter 2007
Participants in the validation study of the MoBa cohort	Citrus fruits	Urine, 24-h	Hesperetin	Pearson	0.66	< 0.01	Brantsaeter 2007
Participants in the validation study of the MoBa cohort	Citrus fruits	Urine, 24-h	Hesperetin	Pearson	0.64	< 0.01	Brantsaeter 2007
Participants in the validation study of the MoBa cohort	Citrus fruits	Urine, 24-h	Flavanones	Pearson	0.63	< 0.01	Brantsaeter 2007
Mothers in Maastricht with or without an increased fruit and vegetable diet intervention	Citrus fruits	Plasma, fasting	beta-Cryptoxanthin	Spearman	0.57	< 0.01	Bogers 2004
Adults living in the Parisian area	Citrus fruits	Urine, first morning spot	Naringenin	Spearman	0.56	< 0.0001	Mennen 2006
Participants in a dietary validation study	Citrus fruits	Plasma, fasting	Vitamin C	Spearman	0.53	< 0.001	Mohammadifard 201
Adults living in the Parisian area	Citrus fruits	Urine, first morning spot	Hesperetin	Spearman	0.52	< 0.0001	Mennen 2006
Adults living in the Parisian area	Citrus fruits	Urine, first morning spot	Naringenin	Spearman	0.48	= 0.0003	Mennen 2006
Adults living in the Parisian area	Citrus fruits	Urine, 24-h	Hesperetin	Spearman	0.46	= 0.0006	Mennen 2006

Showing 1 to 10 of 79 entries

Previous	1	2	3	4	5	 8	Next



2- A FOOD INTAKE BIOMARKERS DATABASE







Correlation values											
	Biomarkers ▼ Correlations ▼ Reproducib	ility Data search •	Publications About •								
Show 10 rows Show/Hide columns			Biomarl	er conce	ntration valu	ies					
Showing 1 to 10 of 79 entries										Search:	
showing I to 10 of 79 entries	Show 10 rows Show/Hide columns Copy all row	S									
	Showing 1 to 8 of 8 entries										
Population										Pre	evious 1 Nex
Participants in the validation study of the	Population	Biospecimen	Analytical method	Biomarker	Measurement	Arithmethic mean	Geometric mean	Median ▼	Unit 💠	Adjusted	Publication
Participants in the validation study of the	Employees at workplaces in Copenhagen area with or	Urine, 24-h	HPLC after enzymatic	Hesperetin	34	ilicali	Illeali	177.0	ug/day	JII	Krogholm 201
Participants in the validation study of the	without a free-fruit program intervention	Offic, 24 ff	hydrolysis	riespereuii	54			177.0	og/day		Riognourizo
Participants in the validation study of the	Participants in a dietary validation study	Urine, 24-h	LC-MS/MS after enzymatic hydrolysis	Hesperetin	85			98.0	ug/day		Carlsen 2011
Mothers in Maastricht with or without an	Employees at workplaces in Copenhagen area with or	Urine, 24-h	HPLC after enzymatic	Hesperetin	45			7.0	ug/day		Krogholm 201
Adults living in the Parisian area	without a free-fruit program intervention		hydrolysis	•					,		
Participants in a dietary validation study	Female university students	Plasma, fasting	HPLC after enzymatic hydrolysis	Hesperetin	47	22.16		5.75	nmol/L		Radtke 2002
Adults living in the Parisian area	Employees at workplaces in Copenhagen area with or	Urine, 24-h	HPLC after enzymatic	Hesperetin	45			5.0	ug/day		Krogholm 201
Adults living in the Parisian area	without a free-fruit program intervention		hydrolysis								
Adults living in the Parisian area	Employees at workplaces in Copenhagen area with or without a free-fruit program intervention	Urine, 24-h	HPLC after enzymatic hydrolysis	Hesperetin	34			5.0	ug/day		Krogholm 201
Showing 1 to 10 of 79 entries	Adults living in the Parisian area	Urine, 24-h	LC-MS/MS after enzymatic hydrolysis	Hesperetin	53	3.0			umol/day		Mennen 2006
	Adults living in the Parisian area	Urine, first morning spot	LC-MS/MS after enzymatic hydrolysis	Hesperetin	53	1.8			umol/L		Mennen 200

Next step will be to integrate dietary biomarkers identified in intervention studies (in link with literature reviews in FoodBAll WP3)



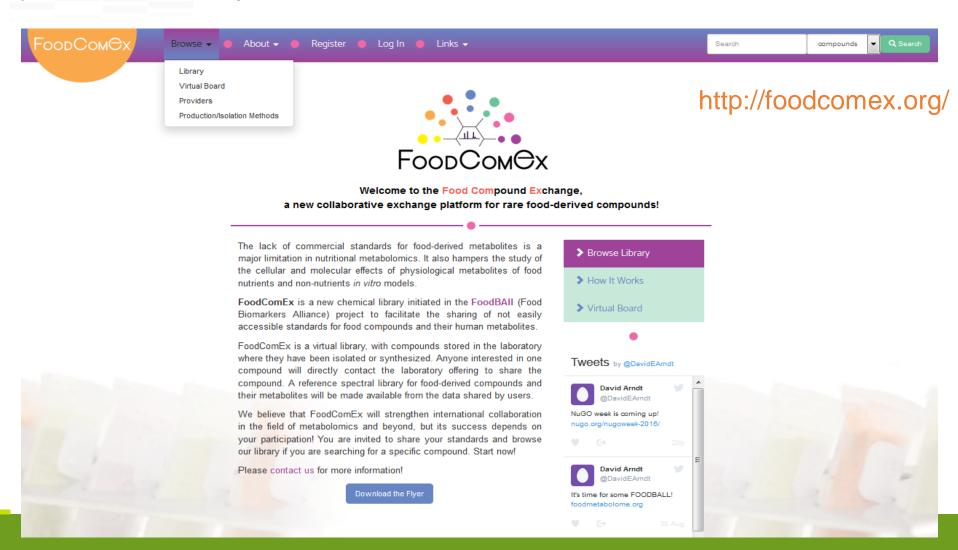


- Authentic standards are needed for validation of identifications in metabolomics studies
- ☐ Lack of commercial standards for many food-derived compounds : putative identifications
- ☐ Also hampers the development of quantitative methods of analysis for candidate biomarkers





☐ Many compounds have been synthetised or isolated in academic laboratories





Labo A



Labo B



Labo C



Information on available compounds & contact details





Chemical synthesis



Extraction-Purification from foods



 Biofluids from animals fed pure compounds or food extracts

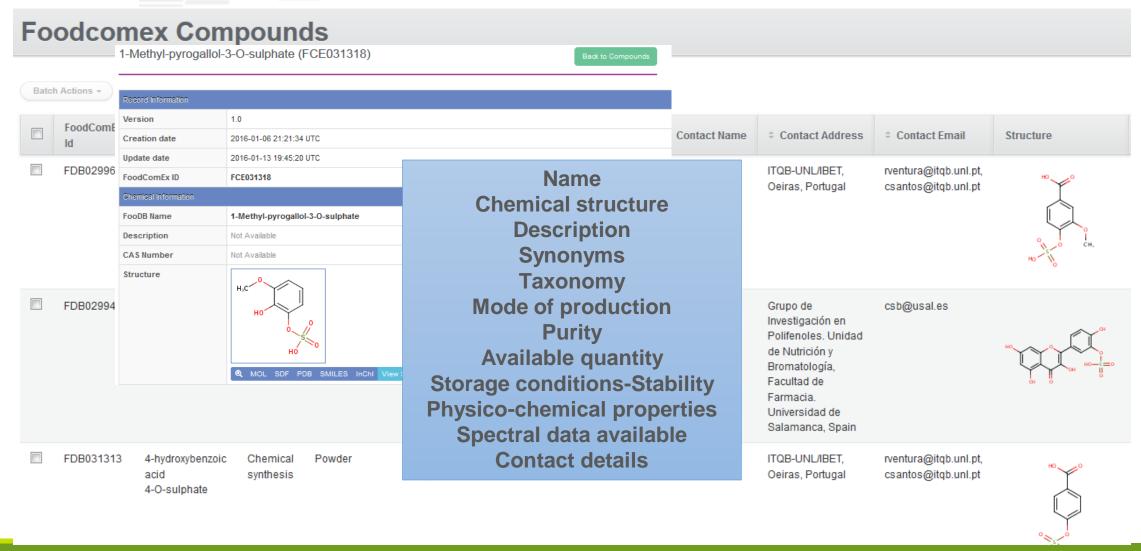


In vitro incubationsMicrosomes, isolated enzymes, microbiota



3- A RESOURCE TO FACILITATE SHARING OF STANDARDS : FOODCOME







3- A RESOURCE TO FACILITATE SHARING OF STANDARDS : FOODCOMEX



Foodcomex Compounds

Batcl	h Actions +									
	FoodComEx Id	Compound Name	Origin	Storage Form	Maximum Quantity	Storage Condition	Contact Name	Contact Address	Contact Email	Structure
	FDB029964	Vanillic acid 4-sulfate	Chemical synthesis	Powder	Production upon request		Rita Ventura, Claudia Santos	ITQB-UNL/IBET, Oeiras, Portugal	rventura@itqb.unl.pt, csantos@itqb.unl.pt	HO CH.
	FDB029941	Quercetin 3'-sulfate	Chemical synthesis	Freeze-dried	Milligram amounts when produced. Production upon	Room temperature in a dryer	Celestino Santos Buelga	Grupo de Investigación e Polifen	csb@usal.es	110
					Facultad de Farmacia. Universidad de Salamanca, Spain		OH 100-1=0			
	FDB031313	4-hydroxybenzoic acid 4-0-sulphate	(Cr	narter o	f good pr	actices o	nline)	ITQB-UNL/IBET, Oeiras, Portugal	rventura@itqb.unl.pt, csantos@itqb.unl.pt	но







- A virtual board to request unavailable compounds
- A providers directory to foster collaborations
- A repository of shared production methods

accessible standards for food compounds and their human metabolites.

FoodComEx is a virtual library, with compounds stored in the laboratory where they have been isolated or synthesized. Anyone interested in one compound will directly contact the laboratory offering to share the compound. A reference spectral library for food-derived compounds and their metabolites will be made available from the data shared by users.

We believe that FoodComEx will strengthen international collaboration in the field of metabolomics and beyond, but its success depends on your participation! You are invited to share your standards and browse our library if you are searching for a specific compound. Start now!

Please contact us for more information!

Download the Flyer





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4- A RESOURCE TO FACILITATE DATA SHARING AND EXCHANGES WITHIN THE

http://foodmetabolome.org



FOODBALL

FoodComEx

FooDB

Exposome Explorer

PhytoHub

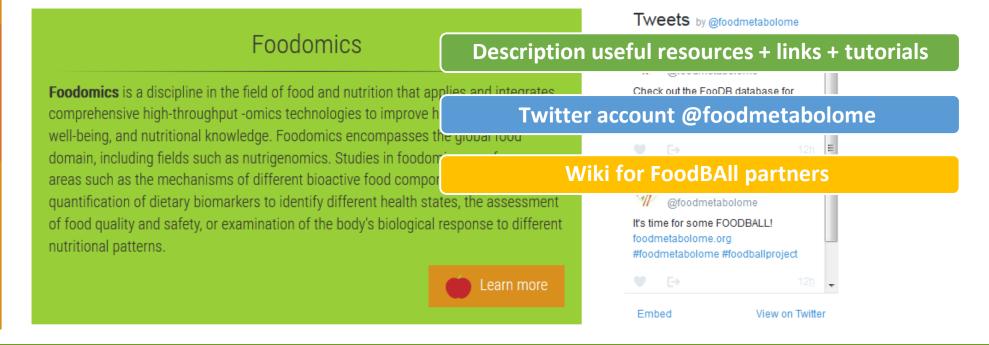
Tools and Resources

Wiki

About Us

Welcome to the **FOODBALL** Project

The **Food Biomarkers Alliance** (**FOODBALL**) is an initiative aimed at identifying and quantifying dietary biomarkers in order to improve the capabilities of nutritional assessment and research.





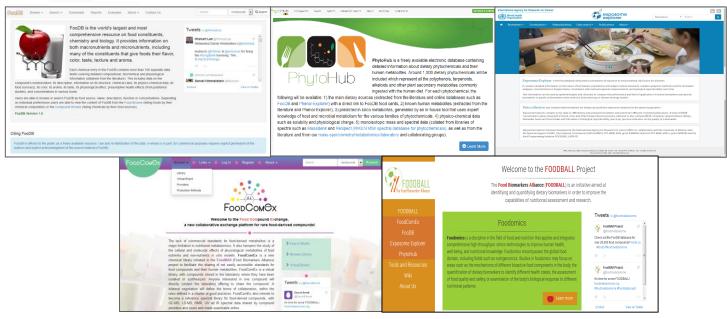
RESOURCES DEVELOPED IN FOODBALI



www.FooDB.ca

www.phytohub.eu

http://exposome-explorer.iarc.fr/



http://foodcomex.org/

http://foodmetabolome.org/

Please use these resources and give us your feedback!





Rosa Vazquez Fresno
Tanvir Sayed
David Arndt
Allison Pon
Albert remus Rosana
Yannick Djoumbou Feunang
David Wishart



Jarlei Fiamoncini
Franck Giacomoni Craig Knox
Balthazar Pavot
Estelle Pujos-Guillot
Christine Morand

International Agency for Research on Cancer



Joe Rothwell Vanessa Neveu Augustin Scalbert

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Mireia Urpi-Sarda Rafael Llorach



Marynka Ulaszewska

