Metabolomics/Metabonomics Literature Roundup 2006

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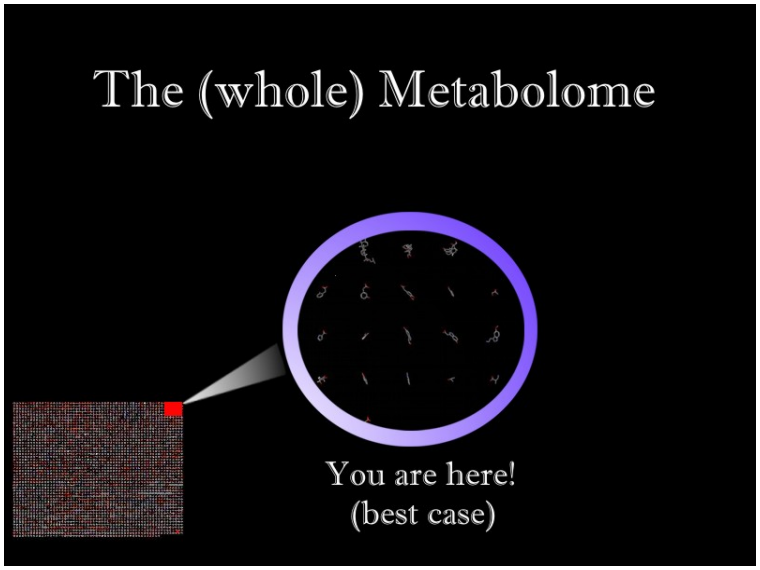
Report December 2006, 17 pages

Introduction

Metabolomics and Metabonomics try to analyze all metabolic responses in all life forms in a comprehensive manner (www.metabolomicssociety.org). Metabolites are the intermediates and products of metabolism (http://en.wikipedia.org/wiki/Metabolite) and usually defined as small molecules with a molecular mass up to 2000 Dalton. Qualitative, quantitative and time course experiments are done with the help of complex analytical techniques like NMR, GC-MS, LC-MS, UV or FT-IR. Metabolomics is part of the life science tree: Genomics (gene level), Transcriptomics (mRNA level) and Proteomics (protein level). Bioinformatics and Cheminformatics help to solve the complex mathematical and statistical problems of Metabolomics. Both terms (Metabonomics and Metabolomics) are defined in a different way by different groups which led to a fancy "war of the words". The author personally beliefs that both terms have the same intention: "Solving the metabolome". The Metabolomics Society recently released the correct definitions and terms for proper use.

This report gives an in-depth analysis of the literature in the field of Metabolomics/Metabonomics from **first citations up to the year 2006**. The field of "metabolomics" itself is probably older than 3000 years[1]. The renaissance started with modern analytical techniques in the 70s of the last century. Both terms were used more frequently during the year 2000.



[1] *Clinical features similar to diabetes mellitus were described 3000 years ago by the ancient Egyptians. The term "diabetes" was first coined by Araetus of Cappodocia (81-133AD). Later, the word mellitus (honey sweet) was added by Thomas Willis (Britain) in 1675 after rediscovering the sweetness of urine and blood of patients (first noticed by the ancient Indians).* History of diabetes mellitus. Ahmed AM, Saudi Med J. 2002 Apr;23(4):373-8.

1) General Numbers

The following portals were used for analysis:

Web of Science (WOS) (http://portal.isiknowledge.com/)

Google Scholar (Google) (http://scholar.google.com/)

CAS Scifinder (CAS) (https://scifinder.cas.org/)

The results here usually refer to the number of publications. Due to duplications or reference problems in the databases certain results may overlap. Author names or institute names were sometimes misspelled. In these cases results were adjusted to the best knowledge, without bias.

Web Of Science
Metabonomics: 360 records. TS=(metabonomics)
Metabolomics: 651 records. TS=(metabolomics)

Google Scholar
Results: 1,420 for metabonomics
Results: 3,920 for metabolomics
Results: 458 for metabonomics AND metabolomics

CAS Scifinder (only CAPLUS to exactly remove duplicates)
Metabonomics and Metabolomics: 1393 results (do not compare to 2005 roundup)
Single authors involved: 3653
Single molecules involved: ~1393 (~9000 sequences excl.) (compared to KEGG ~20.000)

Metabonomics: 281 references as entered; 1393 concept records

Using "Metabonomics" as entered:

- 332 different molecules involved in research, which contain calculated properties (excluding sequences)
- 186 molecules involved in analytical studies

Metabolomics: 636 references as entered; 1393 concept records

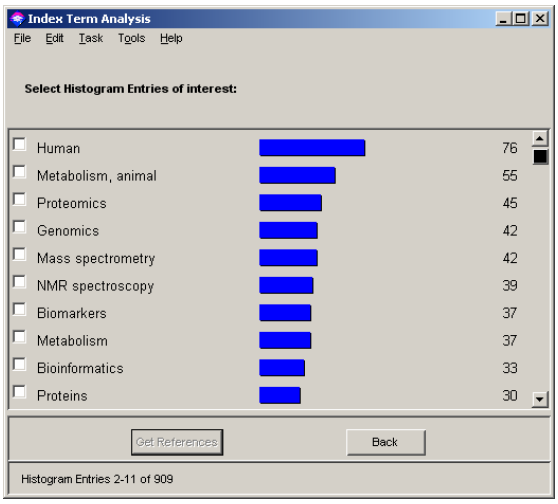
Using "Metabolomics" as entered:

- 936 different molecules involved in research, which contain calculated properties (excluding sequences)
- 615 molecules involved in analytical studies

2) Hot authors and topics 2006

A total of 405 new references (76 for metabonomics, 226 for metabolomics, rest overlap) were found in CAS for the year 2006.

The 10 hottest topics 2006:



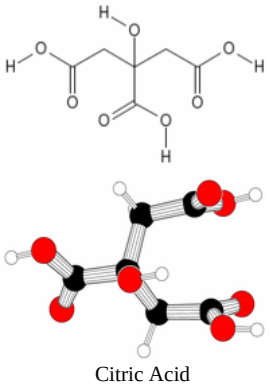
1. Humans
2. Metabolism, animal
3. Proteomics
4. Genomics
5. Mass spectrometry
6. NMR spectroscopy
7. Biomarkers
8. Metabolism
9. Bioinformatics
10. Proteins

The 12 most diligent authors 2006 (blue web links):

1. Nicholson Jeremy K – 16 refs	– 1x first author	– 9x last author
2. Holmes Elaine – 14 refs	– 2x first author	– 2x last author
3. Lindon John C – 10 refs	– 1x first author	– 2x last author
4. Griffin Julian L – 8 refs	– 6x first author	– 1x last author
5. Fiehn Oliver – 6 refs	– 2x first author	– 1x last author
6. Cloarec Olivier – 5 refs	– 0x first author	– 0x last author
7. Cravatt Benjamin F – 5 refs	– 3x first author	– 2x last author
8. Fukusaki Eiichiro – 5 refs	– 2x first author	– 1x last author
9. Goodacre Royston – 5 refs	– 0x first author	– 3x last author
10. Kochhar Sunil – 5 refs	– 1x first author	– 0x last author
11. Rockett John – 5 refs	– 0x first author	– 1x last author
12. Tjeerdema Ronald S – 5 refs	– 0x first author	– 3x last author

The most analyzed molecules 2006:

1. Citric Acid – 34 refs
2. D-Glucose – 32 refs
3. Lactic Acid – 31 refs
4. L-Alanine – 28 refs
5. L-Valine – 24 refs
6. L-Glutamine – 23 refs
7. Taurine – 22 refs
8. L-Phenylalanine – 21 refs
9. Succinic Acid – 21 refs
10. L-Tyrosine – 20 refs



Citric Acid
(Wikipedia)

Social Network Analysis of the 12 most diligent authors only for 2006 (blue web links) using analysis of cited references and citing references (top 3 hits only)

1. Nicholson Jeremy K – 16 refs
…cited the works of: Nicholson Jeremy K, Holmes Elaine, Lindon John C
…was cited by: Lindon John C, Holmes Elaine, Nicholson Jeremy K

2. Holmes Elaine – 14 refs
… cited the works of: Nicholson Jeremy K, Holmes Elaine, Lindon John C
…was cited by: Lindon John C, Holmes Elaine, Nicholson Jeremy K

3. Lindon John C – 10 refs
…cited the works of: Nicholson Jeremy K, Holmes Elaine, Lindon John C
…was cited by: Holmes Elaine, Lindon John C, Nicholson Jeremy K

4. Griffin Julian L – 8 refs
…cited the works of: Nicholson Jeremy K, Holmes Elaine, Griffin Julian L
…was cited by: Ala Korpela Mika, Bach Knudsen Knud E, Bertram Hanne C

5. Fiehn Oliver – 6 refs
…cited the works of: Tjeerdema Ronald S, Fiehn Oliver, Nicholson Jeremy K
…was cited by: Shulaev Vladimir

6. Cloarec Olivier – 5 refs
…cited the works of: Nicholson Jeremy K, Holmes Elaine, Lindon John C
…was cited by: Holmes Elaine, Barton Richard H, Beltrami Laura

7. Cravatt Benjamin F – 5 refs
…cited the works of: Cravatt Benjamin F, Lichtman Aron H, Giang Dan K
…was cited by: Herman Ariel G, Stockwell Brent R,

8. Fukusaki Eiichiro – 5 refs
…cited the works of: Fiehn Oliver, Kobayashi Akio, Soga Tomoyoshi

9. Goodacre Royston – 5 refs
…cited the works of: Goodacre Royston, Kell Douglas B, Fiehn Oliver
…was cited by: Griffin Julian L, Brison Daniel R, Ellis David I

10. Kochhar Sunil – 5 refs
…cited the works of: Nicholson Jeremy K, Holmes Elaine, Lindon John C
…was cited by: Bijlsma Sabina, Bobeldijk Ivana, Brison Daniel R

11. Rockett John – 5 refs
…cited the works of: Nicholson Jeremy K, Holmes Elaine, Lindon John C

12. Tjeerdema Ronald S – 5 refs
…cited the works of: Tjeerdema Ronald S, Nicholson Jeremy K, Nicholson J K
…was cited by: Tjeerdema Ronald S, Viant Mark R, Charlton Adrian J

3) Country Analysis

According to Web of Science the leading (publishing) countries in the field of **metabolomics OR metabonomics** are:

Country	Publications	Percentage
USA	363	39.49 %
ENGLAND	251	27.31 %
GERMANY	87	9.46 %
NETHERLANDS	65	7.07 %
JAPAN	63	6.85 %
SWITZERLAND	42	4.57 %
CANADA	38	4.13 %
PEOPLES R CHINA	30	3.26 %

According to Web of Science the leading (publishing) countries in the field of **metabonomics:**

Country	Publications	Percentage
England	163	45.27 %
USA	145	40.27 %
PEOPLES R CHINA	23	6.38 %
SWITZERLAND	22	6.11 %
GERMANY	20	5.55 %
SWEDEN	15	4.16 %
NETHERLANDS	11	3.05 %
CANADA	9	2.50 %

According to Web of Science the leading (publishing) countries in the field of **metabolomics**

Country	Publications	Percentage
USA	255	39.17 %
ENGLAND	125	19.20 %
GERMANY	73	11.21 %
NETHERLANDS	60	9.21 %
JAPAN	58	8.90 %
CANADA	31	4.76 %
SWITZERLAND	28	4.30 %
AUSTRALIA	23	3.53 %

4) Institute Analysis

According to WOS the leading institutions in the field of **metabolomics/metabonomics** are:

Name	Publications
Univ London Imperial Coll Sci Technol	101
UNIV CALIF ALL	49
Univ Calif Davis	37
AstraZeneca	34
Max Planck Inst Mol Plant Physiol	33
Univ Cambridge	29
TNO	28
Univ Manchester	24
NESTLE RES CTR	22
Waters Corp	20
Chiba Univ	18
CHINESE ACAD SCI	17
Duke UNIV	14
Univ Wageningen & Res Ctr	14
UNIV BIRMINGHAM	13
UNIV OXFORD	13

According to Web of Science the top 5 leading institutions (**metabonomics**) are the Imperial College, Astra Zeneca (drug company) and Waters (analytical devices). 360 records analyzed.

Name	Publications
Imperial College (UK)	97
Astra Zeneca	35
Waters Corp	22
UNIV CAMBRIDGE	18
UNIV CALIF ALL	16

According to Web of Science the top 5 leading institutions (**metabolomics**) are the Max Planck Institute for Molecular Plant Physiology in Golm, the UC Davis, the Chiba University (Japan) and the University of Cambridge. 651 records analyzed.

Name	Publications
UNIV CALIF ALL	46
UNIV CALIF DAVIS	35
Max Planck (MPIMP) Golm (Germany)	33
TNO (Netherlands)	29
Univ Cambridge (UK)	24

5) Journal Names WOS 2006

According to Web of Science most of the **metabonomics** studies were published in

Journal Name	Publications	Percentage
ANALYTICAL CHEMISTRY	22	6.11%
JOURNAL OF PROTEOME RESEARCH	17	4.72 %
JOURNAL OF PHARMACEUTICAL AND BIOMEDICAL ANALYSIS	11	3.05 %
ABSTRACTS OF PAPERS OF THE ACS	8	2.22 %
ANALYTICAL BIOCHEMISTRY	8	2.22 %
BIOMARKERS	8	2.22 %
CHEMICAL RESEARCH IN TOXICOLOGY	8	2.22 %
CURRENT OPINION IN CHEMICAL BIOLOGY	8	2.22 %
JOURNAL OF CHROMATOGRAPHY B	7	1.94 %
RAPID COMMUNICATIONS IN MASS SPECTROMETRY	7	1.94%

According to Web of Science most of the **metabolomics** studies were published in:

Journal Name	Publications	Percentage
ANALYTICAL CHEMISTRY	28	4.30%
JOURNAL OF NUTRITION	19	2.91 %
BIOINFORMATICS	13	1.99 %
PHYTOCHEMISTRY	13	1.99 %
PLANT AND CELL PHYSIOLOGY	13	1.99 %
ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY	12	1.84 %
JOURNAL OF CHROMATOGRAPHY A	12	1.84 %
JOURNAL OF EXPERIMENTAL BOTANY	11	1.68 %
ANALYTICAL BIOCHEMISTRY	10	1.53 %
PLANT PHYSIOLOGY	10	1.53 %

The new Metabolomics journal (est. 2005) from Springer is not listed here, but in the following CAS analysis page. In 2006 around 24 papers were published there.

6) Journal Names CAS 2006

According to CAS most of the **metabonomics** studies (direct term) were published in

Journal Name	Publications
Analytical Chemistry	16
Journal of Proteome Research	15
Analyst (Cambridge, United Kingdom)	7
Journal of Pharmaceutical and Biomedical Analysis	7
Analytical Biochemistry	6
Chemical Research in Toxicology	6
Current Opinion in Drug Discovery & Development	5
Journal of Chromatography, B	5
Metabonomics in Toxicity Assessment	5
Toxicology and Applied Pharmacology	5

According to CAS most of the **metabolomics** studies (direct term) were published in

Journal Name	Publications
Analytical Chemistry	29
Metabolomics (Springer) (*est. 2005*)	23
Journal of Nutrition	13
Biotechnology in Agriculture and Forestry	12
Bioinformatics	10
Methods in Molecular Biology	10
Phytochemistry (Elsevier)	10
U.S. Pat. Appl. Publ.	10
Journal of Proteome Research	9
PCT Int. Appl.	9

The new Metabolomics journal (est. 2005) from Springer is the official organ of the Metabolomics Society and has more than 56 articles published since 2005. Unfortunately articles are not found in the popular PubMed search engine. However the Google Scholar search engine finds these publications, but citations are usually less accurate than in CAS SciFinder. Currently no impact factor has been assigned by ISI but the Editorial Board and reviewers are highly specialized for the field of Metabolomics.

7) Fields of Interest

According to CAS the following fields of interest (index terms) were covered by **metabonomics and metabolomics**:

Field of Interest	Count
Human	235
Metabolism	182
Mass spectrometry	162
NMR spectroscopy	161
Metabolism, animal	142
Proteins	126
Bioinformatics	125
Biomarkers	109
Proteomics	102
Simulation and Modeling	101
Genomics	100
Urine analysis	100
Genome	92
Principal component analysis	91
Proteome	83
NMR (nuclear magnetic resonance)	78
Metabolism, plant	77
Metabolic pathways	71
Liquid chromatography	69
Databases	67
Urine	66
Data processing	64
Liver	63
Diagnosis	62
Blood analysis	58
Transcriptome	57
Metabolism, microbial	55
High throughput screening	54
Computer program	50
Embryophyta	50
Plants	48
Amino acids, biological studies	47
Gas chromatography	47
Information systems	47
Nutrition, animal	47
HPLC	46
Drug discovery	45
Electrospray ionization mass spectrometry	45
Genetics	44
Pattern recognition	43

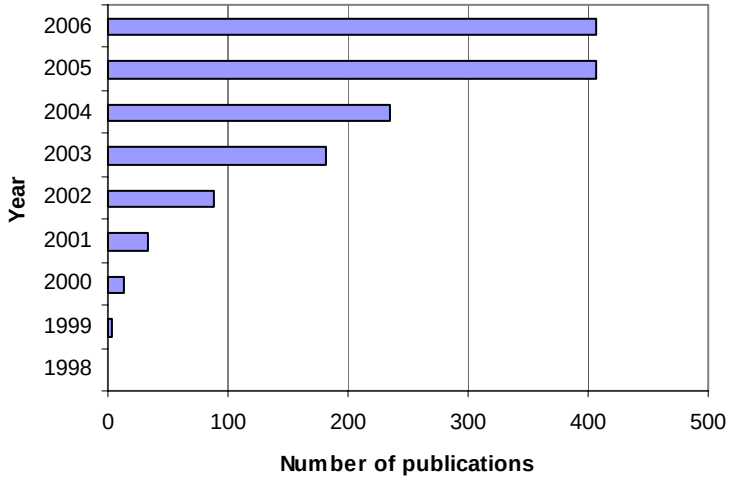
8) Top Terms 2006

The associated top terms in 2006 according to CAS are:

Metabonomics 2006 (from 74 references)	**Metabolomics 2006 (from 226 references)**
Human	Human
Metabolism, animal	Proteomics
NMR spectroscopy	Genomics
Urine analysis	Mass spectrometry
Biomarkers	Metabolism, animal
Blood analysis	Bioinformatics
Urine	Metabolism
Data processing	Simulation and Modeling
Principal component analysis	Data processing

9) Publications per Year

The number of publications per year in the field of **metabonomics and metabolomics** according to CAS (CAPlus database only) are listed here. It was falsely predicted last year that using a conservative factor of 1.5 the number of publications can double up to 1000 in the year 2007. However this regression estimation was too optimistic. The number of publications stagnated from 407 in 2005 to 406 in 2006. Nevertheless the number of authors jumped from 2521 to 3615 – a 40% increase. The database may be updated during the year 2007.



According to Web of Science and CAS the following numbers of publications have been written. The CAPlus database (direct terms only) was used – numbers are different to the last year table. If the term is not directly mentioned it will give no hit. The term "metabolome" is found already twice in 1998.

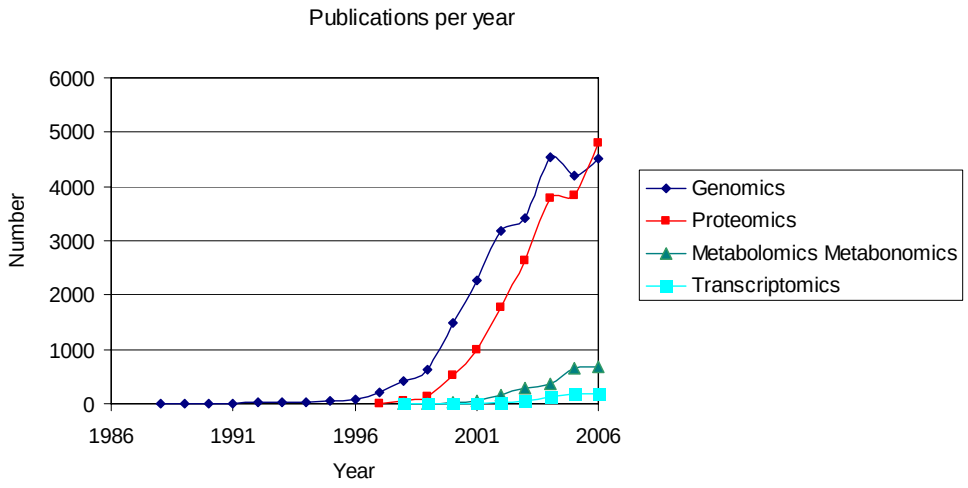
Year	Metabonomics (WoS)	Metabolomics (WoS)	Metabonomics (CAS)	Metabolomics (CAS)
2006	109	243	74	226
2005	96	194	81	191
2004	71	112	56	97
2003	47	63	35	64
2002	21	28	21	31
2001	9	10	4	9
2000	6	1	6	0
1999	1	0	1	0

10) Metabolomics compared to other Life Science Fields

Metabolomics is an emerging field. Where genomics almost reached a plateau in number of publications, metabolomics unfortunately also reached a plateau in publications this year. This may be due to an increased quality of papers or the increased number of research cooperations.

Number of publications CAS+Medline	**2005**	**2006**	**increase %**
Genomics	4206	4516	6.86
Transcriptomics	175	191	8.38
Proteomics	3831	4797	20.14
Metabolomics and Metabonomics	648	687	5.68

The plateau could also be reached because of the number of real world problems, which can't be solved like in proteomics. Proteomics publications were higher than in genomics for the first time.



Metbolites for instance, can not be sequenced like proteins or peptides. Metabolites can not be BLASTed against databases which contain biological functions, although databases like KEGG or PubChem exist but they are much smaller and contain less information. Most of the metadata of small molecules is not freely accessible, due to the ancient publication manners of many scientists and journals (adverse to Open Content). Mass spectra of small molecules are very diverse, if not diverse-diverse. This makes structure elucidation very complex and cumbersome. NMR which could be used for massive structure elucidation has not enough resolving power and a lack of sensitivity. A simple increase in number of machines (NMR, MS, computers) or any other technology will not solve that problem, like it was solved by Craig Venter's ShotGun Genomics (installing hundreds of sequencers in one room and let automates do the job). Instead new technologies are needed and real jumps in innovation (Orbitrap, UPLC, DART) or even more important - better software technologies and curated and unified open access databases.

11) Single Author Analysis

According to WOS* the most publications in the field of **metabolomics** (out of more than 1895 different authors) were written by:

Author	Publications
GRIFFIN, JL	23
GERMAN, JB	22
FIEHN, O	21
KELL, DB	17
SAITO, K	17
VAN DER GREEF, J	15
WATKINS, SM	15
GOODACRE, R	15
MENDES, P	13
NICHOLSON, JK	12
VIANT, MR	10
WECKWERTH, W	10

According to WOS* the most publications in the field of **metabonomics** (out of more than 1055 different authors) were written by:

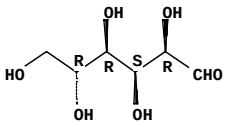
Author	Publications
NICHOLSON, JK	74
HOLMES, E	61
LINDON, JC	43
WILSON, ID	26
ANTTI, H	17
GRIFFIN, JL	17
BOLLARD, ME	12
LENZ, EM	11
PLUMB, RS	11
BECKONERT, O	10

(*)The WOS data is much more conservative, so there may be a loss of numbers, but the abbreviation of names is more accurate than CAS. This will explain the differences to last year's literature roundup.

12) Most Analyzed Molecules - Top 10

According to CAS the top 10 of the most cited compounds (out of ~1000) for the field of **metabolomics and metabonomics** are listed in the table. Interesting to know is that the KEGG database, which is an acknowledged database for metabolomics, contains more than 16000 molecules. That means the "metabolic sciences" itself were existing long before the "omics" era started.

Name	References
D-Glucose	132
Citric acid	100
Lactic acid	82
Succinic acid	75
L-Alanine	72
Taurine	71
Glutamic acid	65
L-Valine	65
L-Glutamine	58



Glucose is one of the most analyzed molecules in the world (not only in metabolomics).
This is why certain journals do not accept any "new" technology for glucose analysis.

13) Most Cited Publications for Metabonomics

According to Web of Science the most cited papers for metabonomics are:

Nicholson JK, Lindon JC, Holmes E
'**Metabonomics**': understanding the metabolic responses of living systems to pathophysiological stimuli via multivariate statistical analysis of biological NMR spectroscopic data
XENOBIOTICA 29 (11): 1181-1189 NOV 1999
Times Cited: 283

2. Nicholson JK, Connelly J, Lindon JC, et al.
Metabonomics: a platform for studying drug toxicity and gene function
NATURE REVIEWS DRUG DISCOVERY 1 (2): 153-161 FEB 2002
Times Cited: 234

3. Brindle JT, Antti H, Holmes E, et al.
Rapid and noninvasive diagnosis of the presence and severity of coronary heart disease using H-1-NMR-based **metabonomics**
NATURE MEDICINE 8 (12): 1439-1444 DEC 2002
Times Cited: 151

4. Gavaghan CL, Holmes E, Lenz E, et al.
An NMR-based metabonomic approach to investigate the biochemical consequences of genetic strain differences: application to the C57BL10J and Alpk : ApfCD mouse
FEBS LETTERS 484 (3): 169-174 NOV 10 2000
Times Cited: 97

5. Nicholson JK, Wilson ID
Understanding 'global' systems biology: **Metabonomics** and the continuum of metabolism
NATURE REVIEWS DRUG DISCOVERY 2 (8): 668-676 AUG 2003
Times Cited: 86

6. Lindon JC, Nicholson JK, Holmes E, et al.
Metabonomics: Metabolic processes studied by NMR spectroscopy of biofluids
CONCEPTS IN MAGNETIC RESONANCE 12 (5): 289-320 2000
Times Cited: 82

7. Lindon JC, Nicholson JK, Holmes E, et al.
Contemporary issues in toxicology - The role of **metabonomics** in toxicology and its evaluation by the COMET project
TOXICOLOGY AND APPLIED PHARMACOLOGY 187 (3): 137-146 MAR 15 2003
Times Cited: 76

8. Holmes E, Nicholls AW, Lindon JC, et al.
Chemometric models for toxicity classification based on NMR spectra of biofluids
CHEMICAL RESEARCH IN TOXICOLOGY 13 (6): 471-478 JUN 2000
Times Cited: 72

9. Goodacre R, Vaidyanathan S, Dunn WB, et al.
Metabolomics by numbers: acquiring and understanding global metabolite data
TRENDS IN BIOTECHNOLOGY 22 (5): 245-252 MAY 2004
Times Cited: 71

10. Aardema MJ, MacGregor JT
Toxicology and genetic toxicology in the new era of "toxicogenomics": impact of "-omics" technologies
MUTATION RESEARCH-FUNDAMENTAL AND MOLECULAR MECHANISMS OF MUTAGENESIS 499 (1): 13-25 JAN 29 2002
Times Cited: 68

14) Most Cited Publications for Metabolomics

According to Web of Science the most cited papers for metabolomics are:

1. Fiehn O, Kopka J, Dormann P, et al.
Metabolite profiling for plant functional genomics
NATURE BIOTECHNOLOGY 18 (11): 1157-1161 NOV 2000
Times Cited: 323

2. Raamsdonk LM, Teusink B, Broadhurst D, et al.
A functional genomics strategy that uses metabolome data to reveal the phenotype of silent mutations
NATURE BIOTECHNOLOGY 19 (1): 45-50 JAN 2001
Times Cited: 259

3. Fiehn O
Metabolomics - the link between genotypes and phenotypes
PLANT MOLECULAR BIOLOGY 48 (1-2): 155-171 JAN 2002
Times Cited: 251

4. Sumner LW, Mendes P, Dixon RA
Plant **metabolomics**: large-scale phytochemistry in the functional genomics era
PHYTOCHEMISTRY 62 (6): 817-836 MAR 2003
Times Cited: 130

5. Kuiper HA, Kleter GA, Noteborn HPJM, et al.
Assessment of the food safety issues related to genetically modified foods
PLANT JOURNAL 27 (6): 503-528 SEP 2001
Times Cited: 90

6. Tolstikov VV, Fiehn O
Analysis of highly polar compounds of plant origin: Combination of hydrophilic interaction chromatography and electrospray ion trap mass spectrometry
ANALYTICAL BIOCHEMISTRY 301 (2): 298-307 FEB 15 2002
Times Cited: 85

7. Weckwerth W
Metabolomics in systems biology
ANNUAL REVIEW OF PLANT BIOLOGY 54: 669-689 2003
Times Cited: 75

8. Hirai MY, Yano M, Goodenowe DB, et al.
Integration of transcriptomics and **metabolomics** for understanding of global responses to nutritional stresses in Arabidopsis thaliana
PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA 101 (27): 10205-10210 JUL 6 2004
Times Cited: 72

9. Goodacre R, Vaidyanathan S, Dunn WB, et al.
Metabolomics by numbers: acquiring and understanding global metabolite data
TRENDS IN BIOTECHNOLOGY 22 (5): 245-252 MAY 2004
Times Cited: 71

10. Bino RJ, Hall RD, Fiehn O, et al.
Potential of **metabolomics** as a functional genomics tool
TRENDS IN PLANT SCIENCE 9 (9): 418-425 SEP 2004
Times Cited: 69