Metabolomic Applications in Translation and Biomedical Research

UAB 2012

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SOLVAY CONFERENCE 1927

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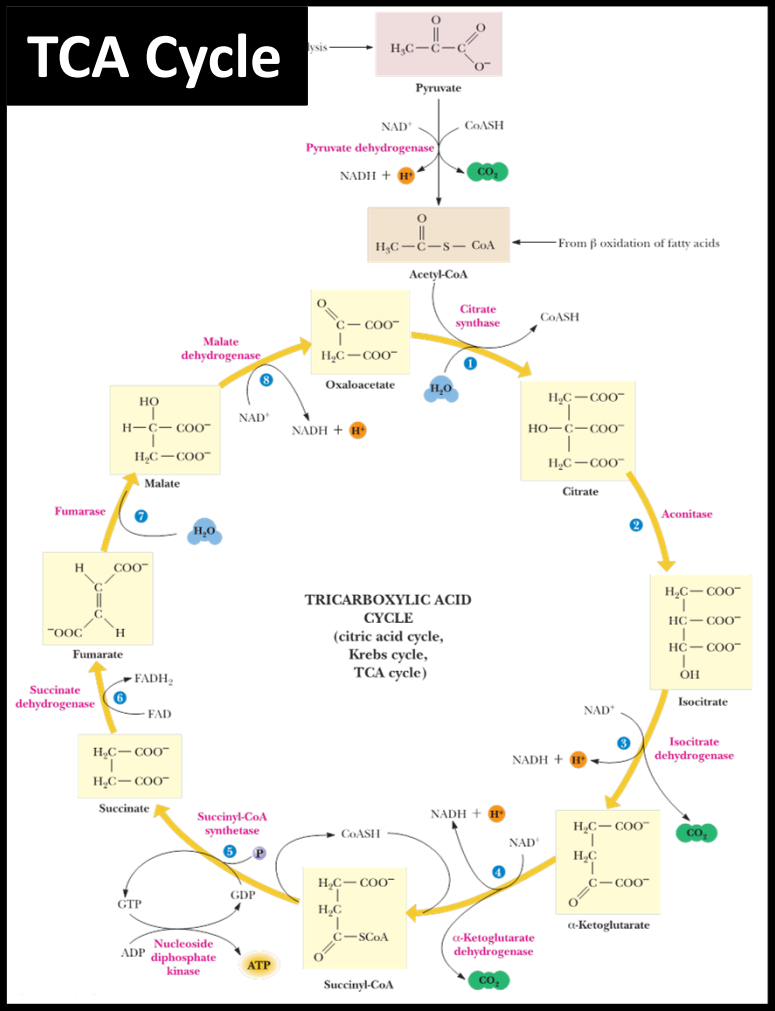
Absents : Sir W.H. BRAGG, H. DESLANDRES et E. VAN AUBEL

TCA Cycle

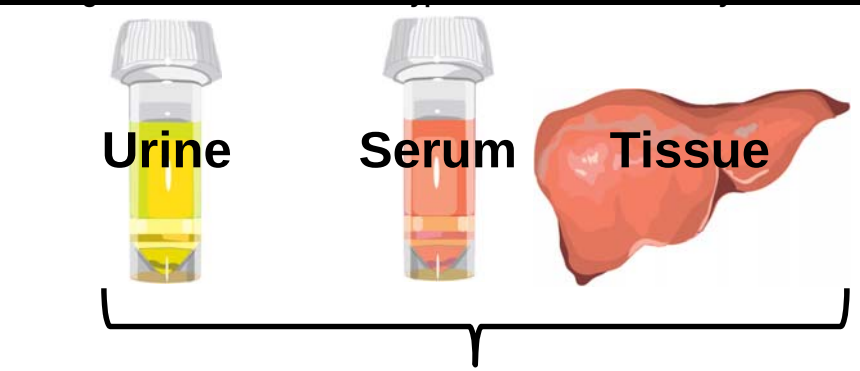


Biochemistry 5th Ed

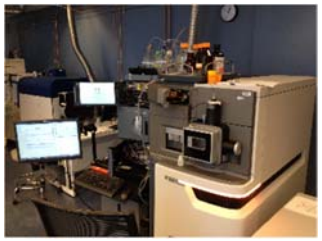
Flux Analysis

- HMDB
- METLIN
- MASSBANK
- MZEDDB
- NIST

Metabolite Identification, Annotation, Characterization



Extraction



UPLC-ESI-QTOFMS

Data Acquisition

GC-MS

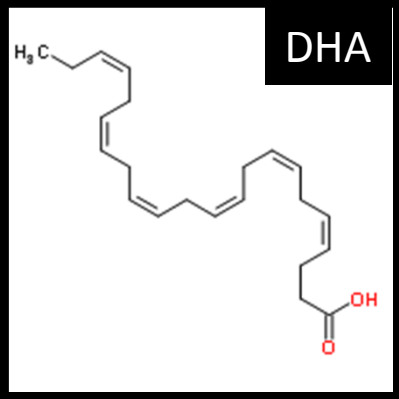
Peak Alignment, Normalization

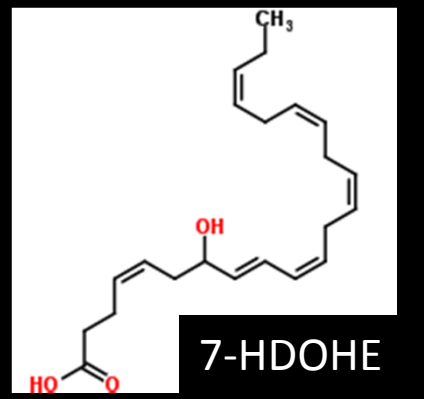
(XCMS, MZMine, MarkerLynx, MarkerView, MassProfiler)

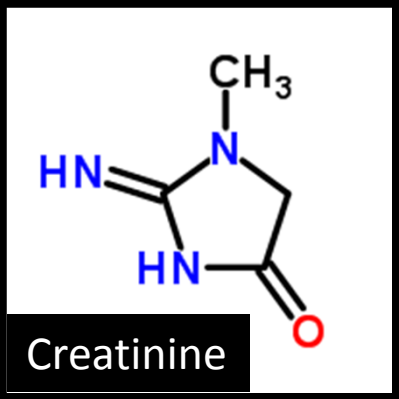
Multivariate Data Analysis

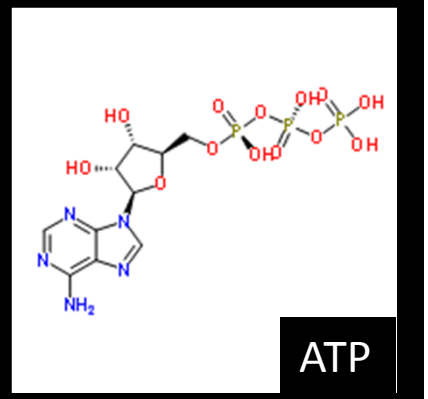
(PCA, OPLS, Random Forests)

Metabolite(s)





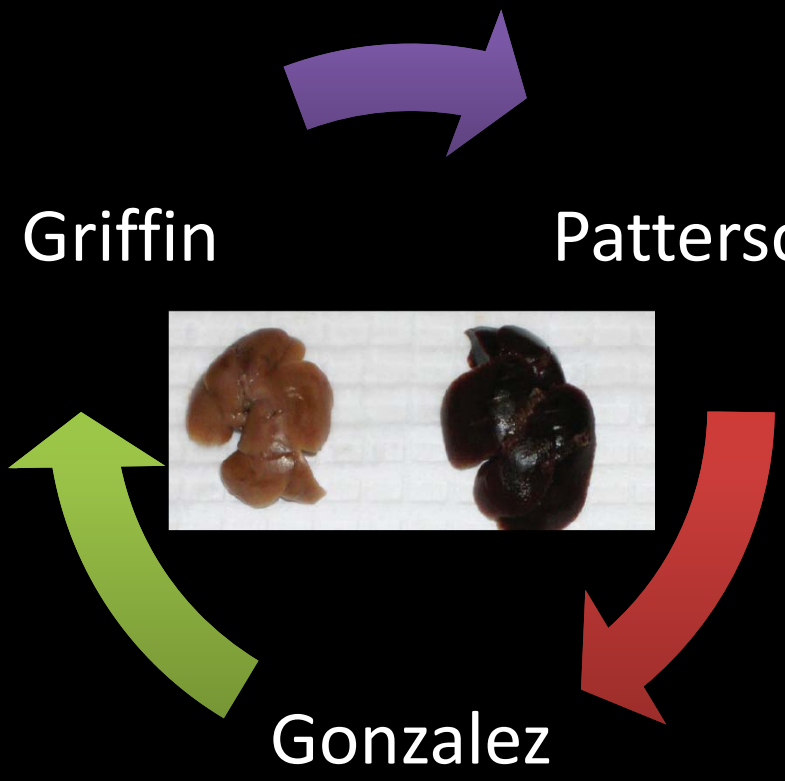




"Why can't you just inject it into your instrument thingy?"

TOX PATH 2012

Optimized Metabolite Extraction, Separation, and Identification for Metabolomics (NIH Common Fund)



- Extraction
- Chromatography
- Open format
- Encourage public comment to build consensus
- Protocol repository

Table 3

Summary of Common Important Variables from Random Forests Analysis of Day 0, Day 7, and Day 14

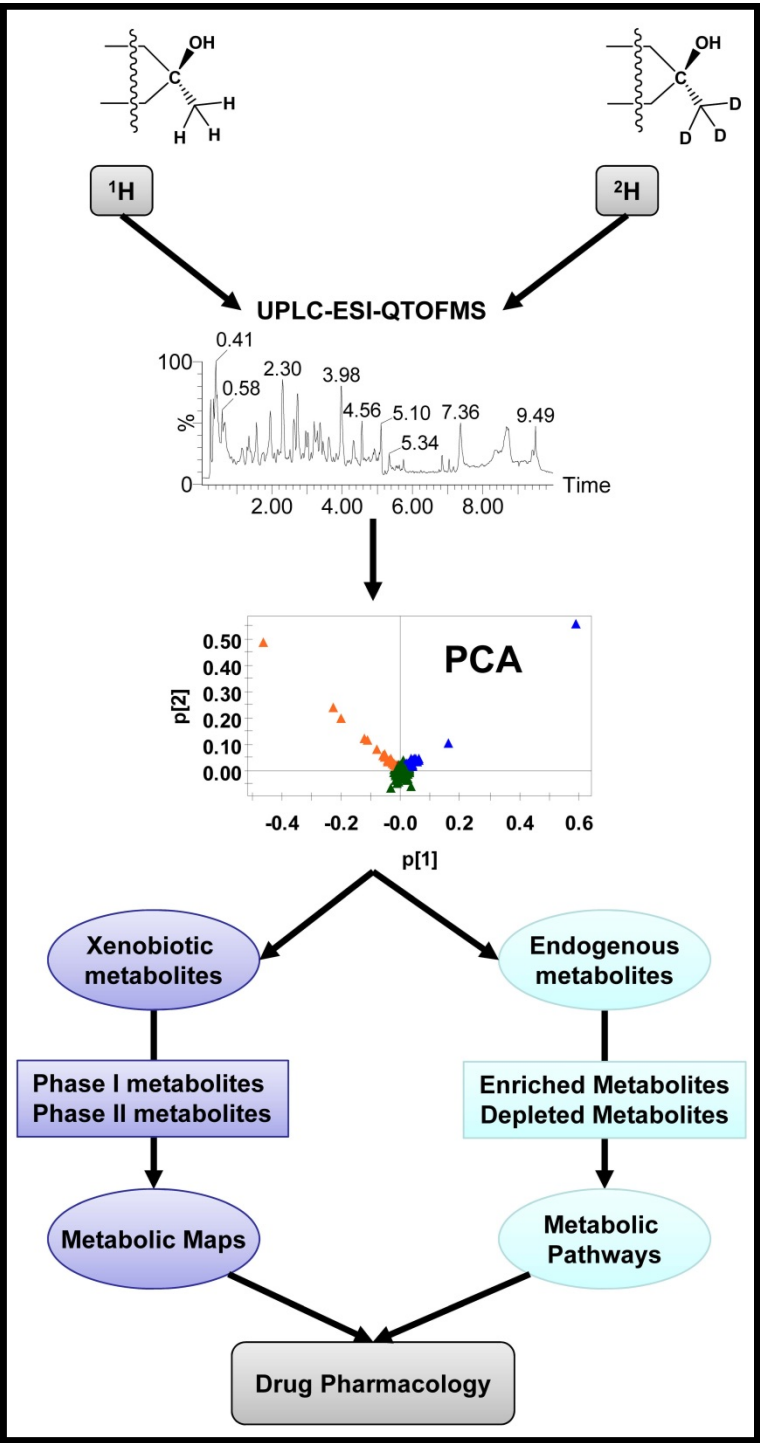
Identity	m/z (ESI+)	Retention Time (min)	Empirical Formula	Mass Error (ppm)	Day 0 vs. Day 7 Mean Rank (95% CI)	Day 0 vs. Day 14 Mean Rank (95% CI)
Common Biomarkers (and adducts) Spanning 2 Week Study						
Pantothenic Acid[†] a	242.1003$^+$	2.07	C9H17NO5Na$^+$	-0.4	1.32 (1.16-1.52)	1.56 (1.2-1.9)
b	220.1179$^+$	2.07	C9H18NO5$^+$	-2.7	1.68 (1.48-1.84)	3.24 (2.5-4.0)
c	202.1063$^+$	2.06	C9H16NO4$^+$	-7.9	4.28 (3.95-4.56)	7.6 (6.8-8.2)
Acetylcarnitine	204.1233$^+$	0.37	C9H18NO4$^+$	-1.5	4.36 (4.12-4.6)	3.04 (2.4-3.7)
Serum Uric Acid[*]	na	na	na	na	6.6 (6.4-6.8)	11.4 (10.8-12.0)
unknown	308.1831$^+$	4.73	na	na	10.4 (9.92-10.9)	5.8 (5.0-6.5)
unknown	319.1658$^+$	3.45	na	na	13.5 (12.7-14.2)	5.2 (4.4-5.9)
Other Notable Biomarkers						
Serum Cholesterol[*]	na	na	na	na	26.2 (24.8-27.8)	15.1 (13.9-16.4)
Carnitine	162.1133$^+$	0.32	C7H16NO3$^+$	1.9	28.2 (26.2-30.9)	11.8 (10.6-13.1)
Isovalerylcarnitine	246.1693$^+$	2.83	C12H24NO4$^+$	-4.9	37.3 (33.8-41.3)	6.84 (6.2-7.5)
Isobutyrylcarnitine	232.1531$^+$	2.10	C11H22NO4$^+$	-7.8	911 (708-1110)	29.6 (28.5-30.6)

[*]indicates measurement obtained from serum clinical biochemistry analysis.

na, not applicable.

[†]a = [Na^+] adduct; b = [H^+] protonated molecular ion; c = [M-H_2O]$^+$ fragmention

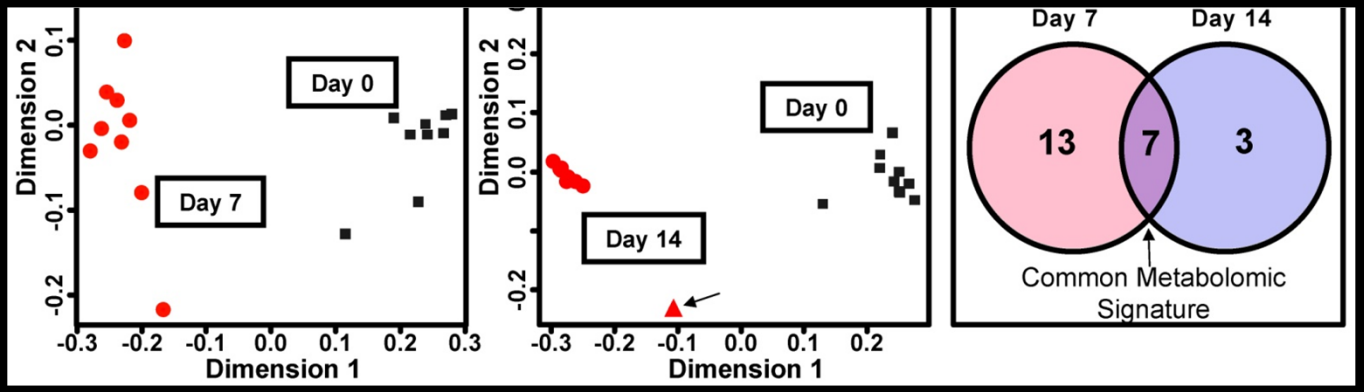
JPR 2009

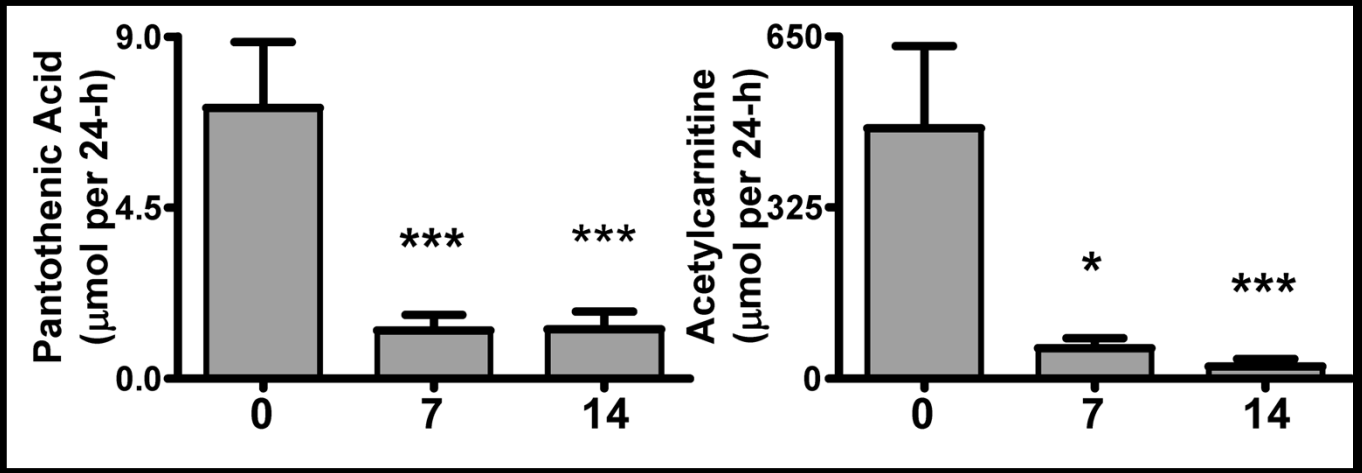

OH
C
H
H
H
OH
C
D
D
D
1H
2H
UPLC-ESI-QTOFMS
100
%
0
0.41
0.58
2.30
3.98
4.56
5.10
5.34
7.36
9.49
Time
2.00
4.00
6.00
8.00
PCA
0.50
0.40
0.30
0.20
0.10
0.00
p[2]
-0.4
-0.2
-0.0
0.2
0.4
0.6
p[1]
Xenobiotic metabolites
Endogenous metabolites
Phase I metabolites
Phase II metabolites
Enriched Metabolites
Depleted Metabolites
Metabolic Maps
Metabolic Pathways
Drug Pharmacology


30z
90CC — 90ML

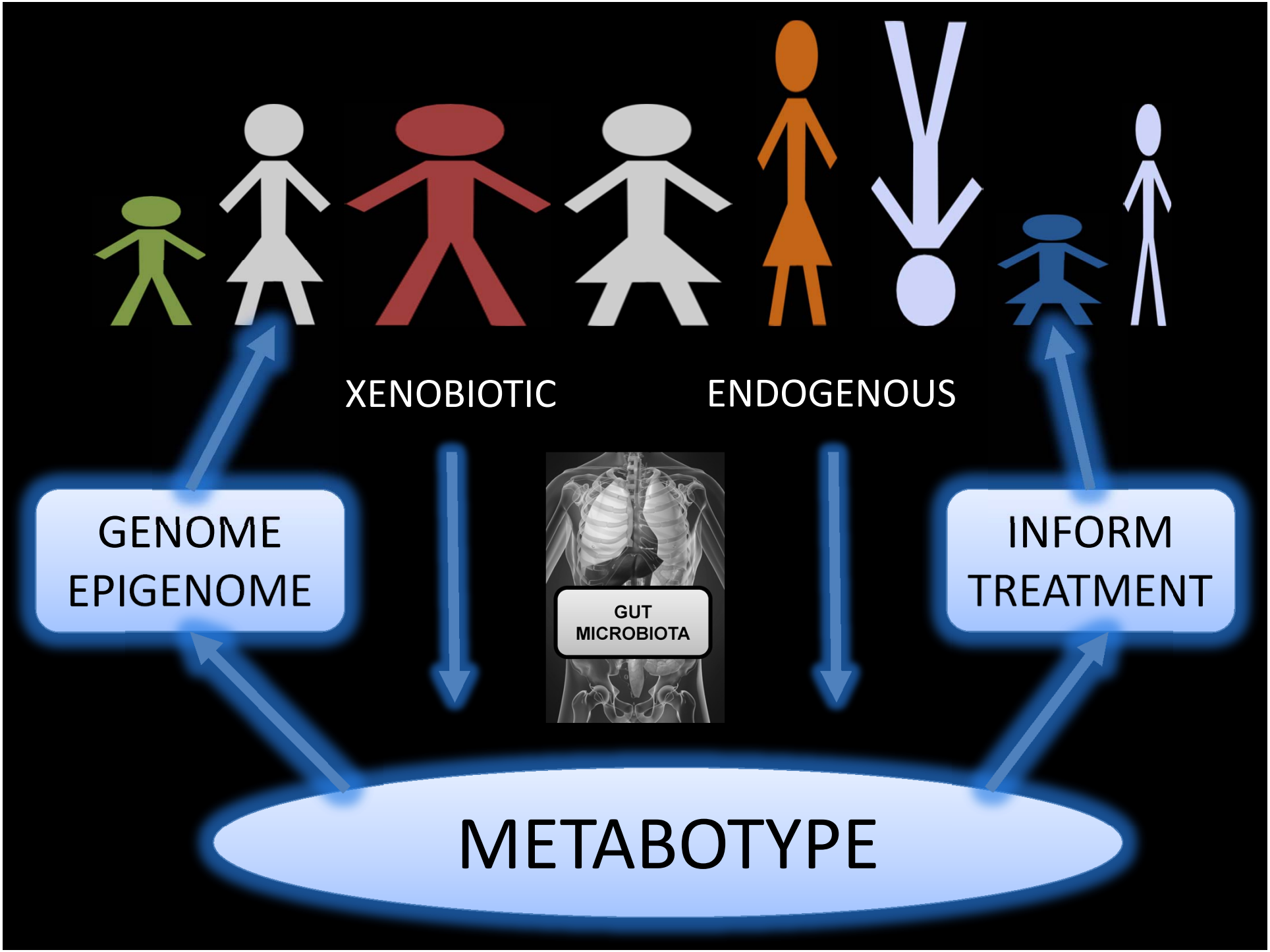
Drug Efficacy for Fenofibrate

1 WEEK 2 WEEK





JPR 2009


XENOBIOTIC
ENDOGENOUS
GENOME
EPIGENOME
GUT
MICROBIOTA
INFORM
TREATMENT
METABOTYPE

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