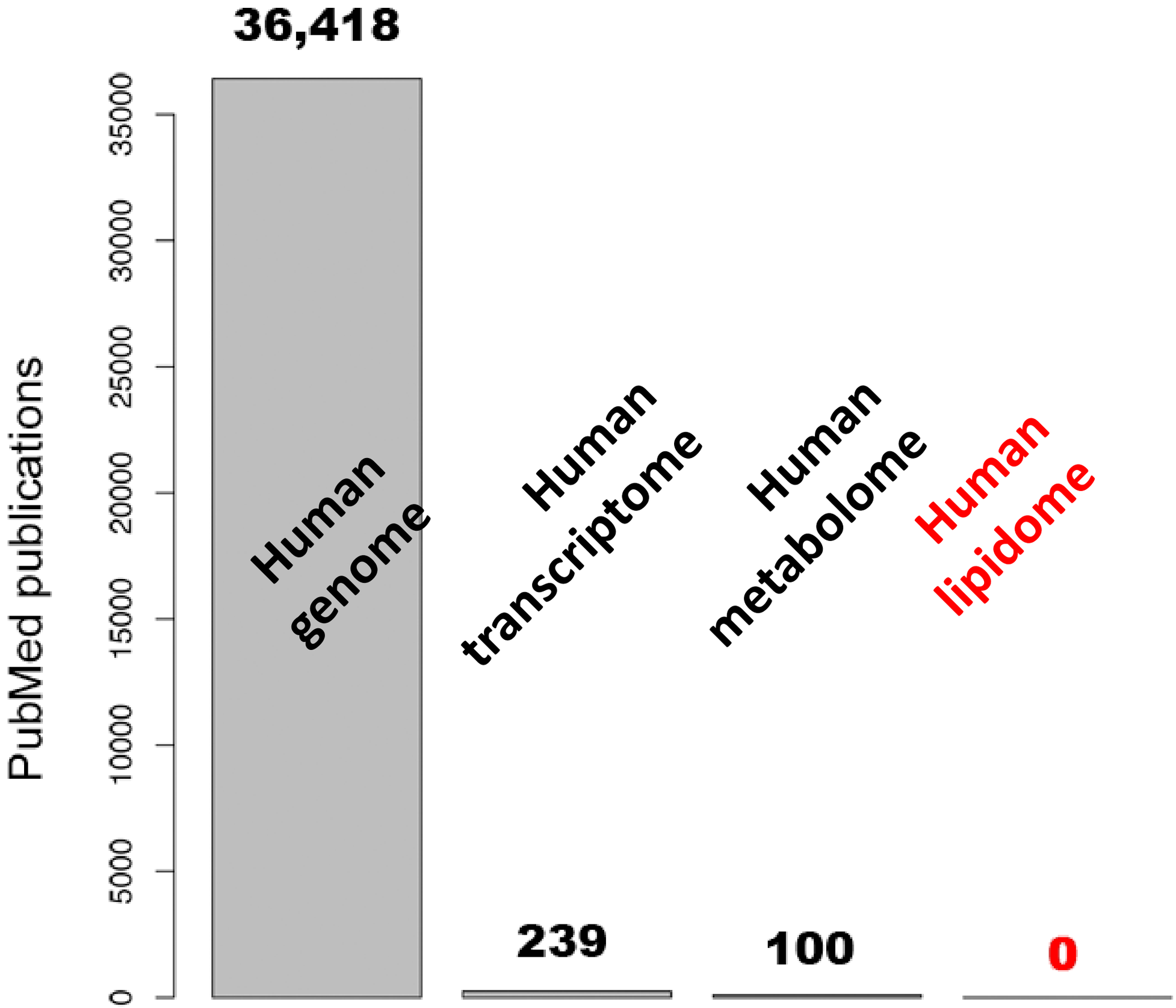
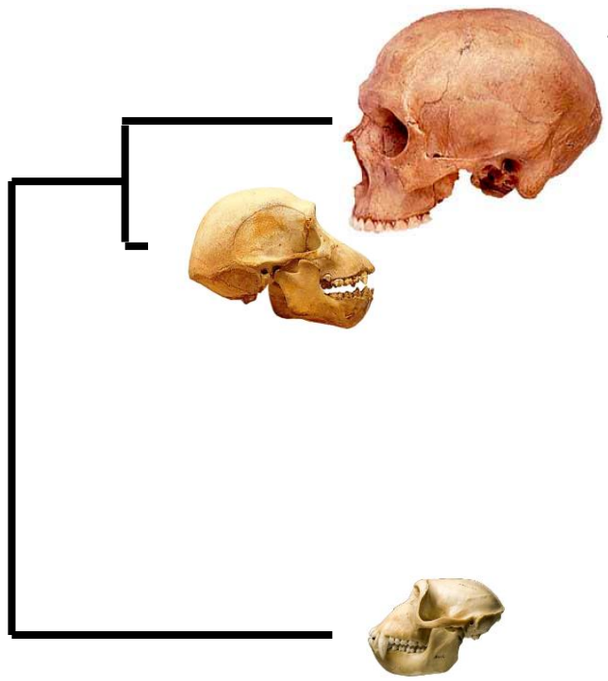
Системная липидомика в изучении биологии мозга человека

филипп хайтович


PubMed publications
0
5000
10000
15000
20000
25000
30000
35000
36,418
Human genome
239
Human transcriptome
100
Human metabolome
0
Human lipidome

Эволюция



Развитие

Данные

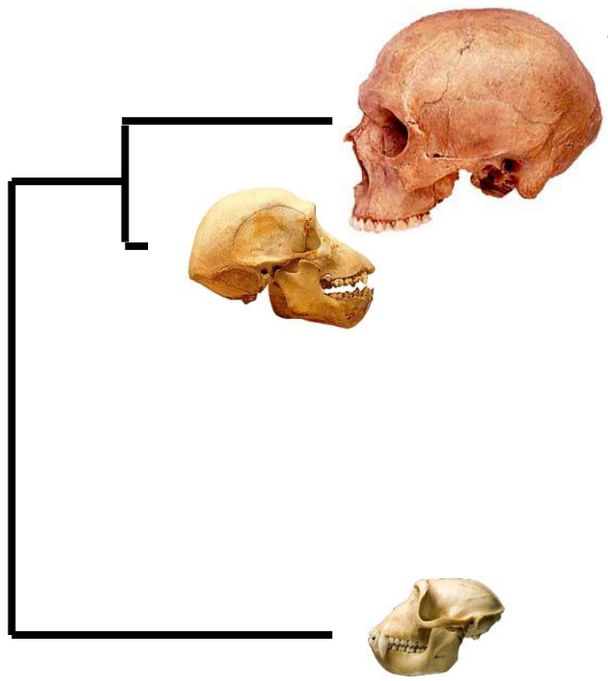
Метаболиты и Липиды

Белки

Экспрессия генов

Геном

Эволюция

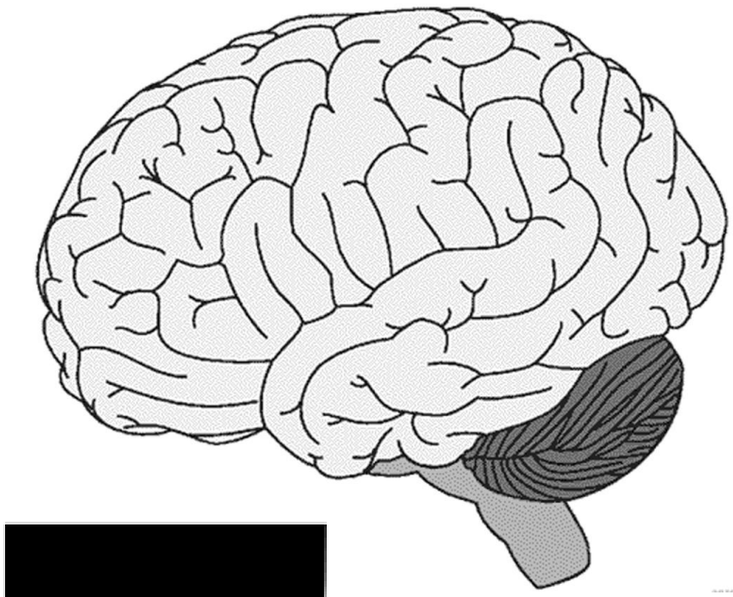


Развитие

Липиды

Данные

Imaging / Electrophysiology



Metabolome and Lipidome

Proteome

Transcriptome

Epigenome

Genome

Imaging / Electrophysiology

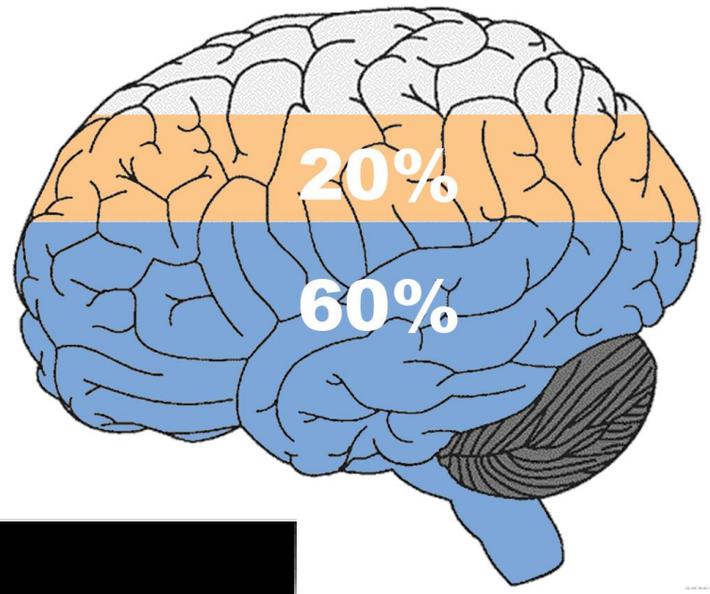
Metabolome and Lipidome

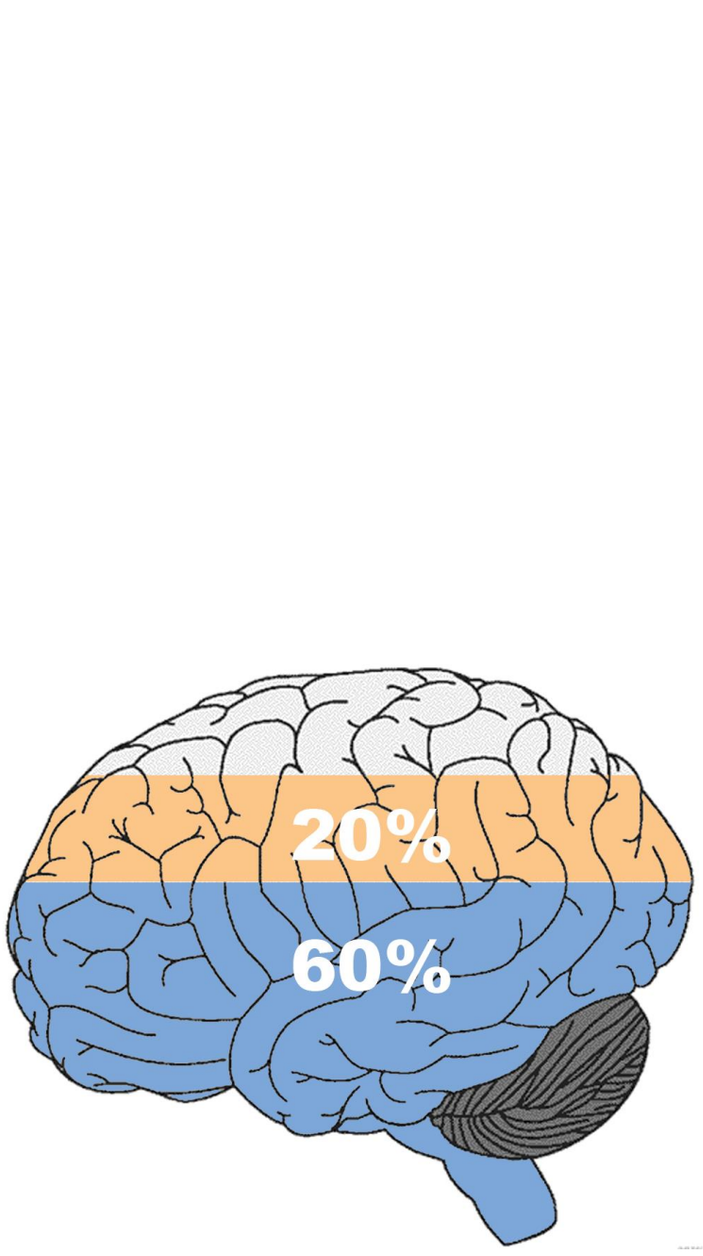
Proteome

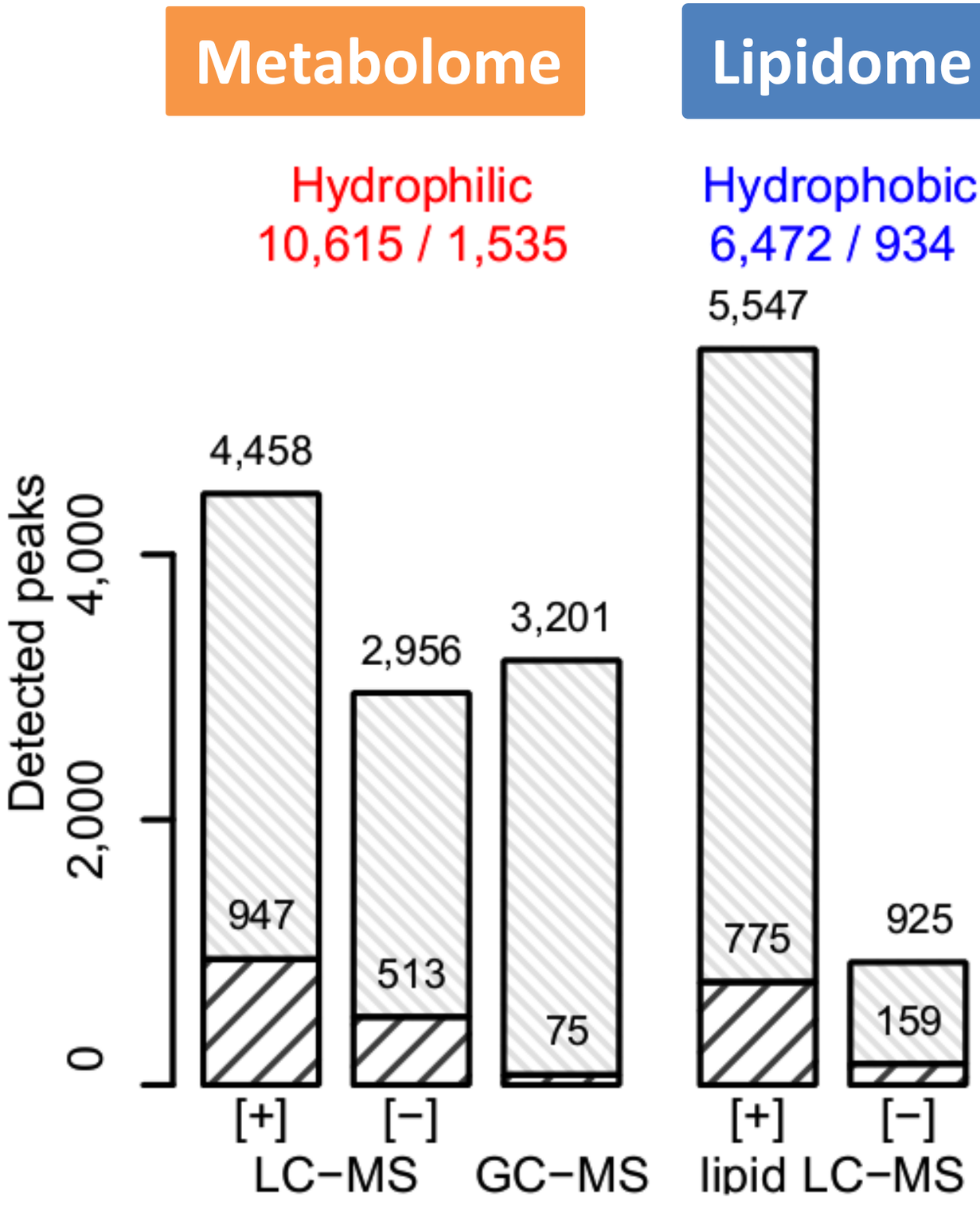
Transcriptome

Epigenome

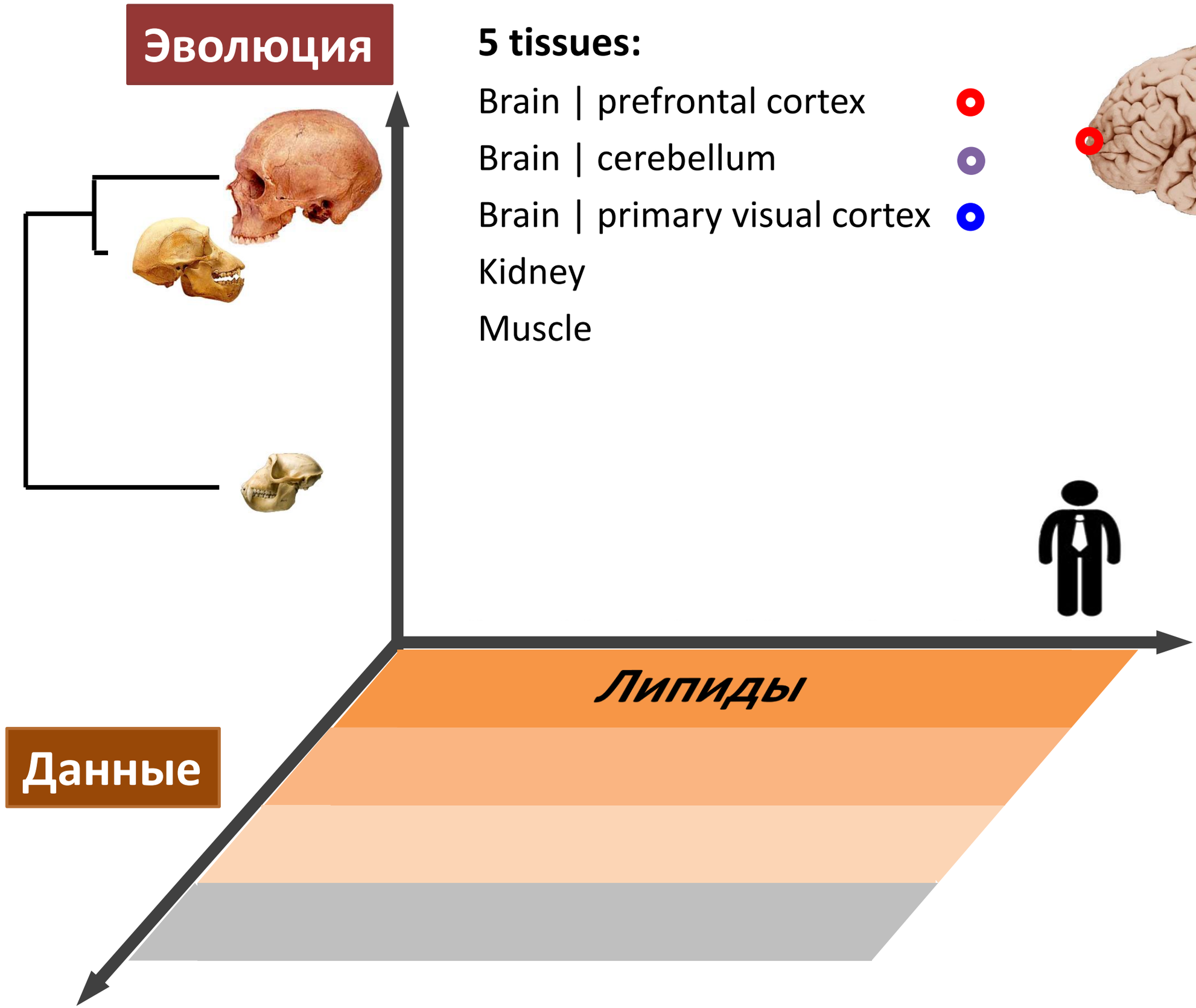
Genome




20%
60%


Metabolome
Lipidome
Hydrophilic
10,615 / 1,535
Hydrophobic
6,472 / 934
Detected peaks
4,000
2,000
0
4,458
2,956
3,201
5,547
947
513
75
775
925
159
[+]
[−]
[+]
[−]
LC−MS
GC−MS
lipid LC−MS

1. Системная липидомика тканей человека



5 tissues:

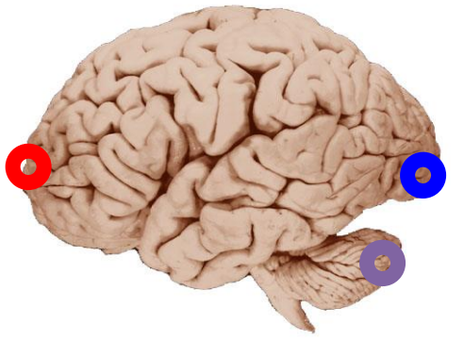
Brain | prefrontal cortex

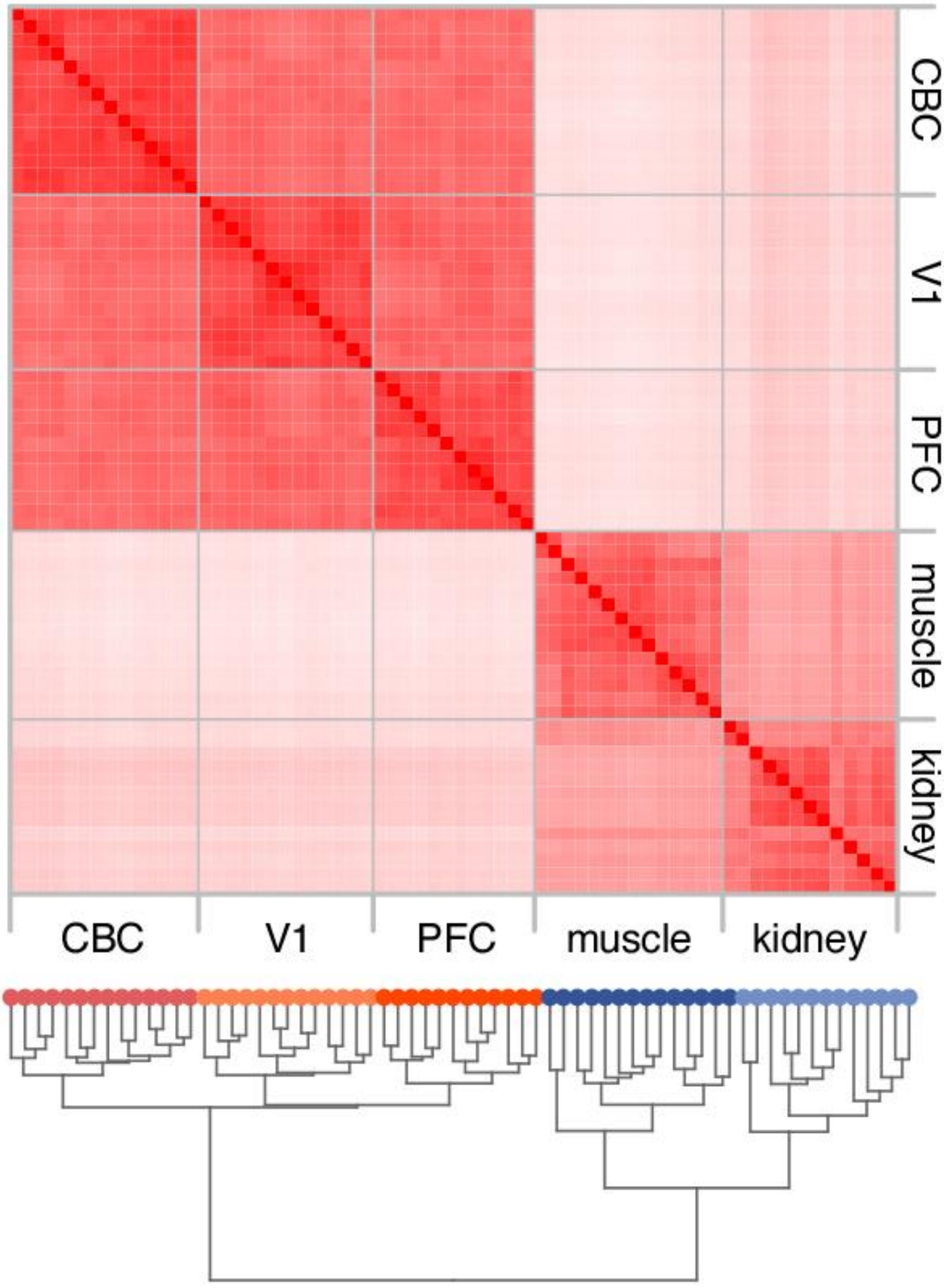
Brain | cerebellum

Brain | primary visual cortex

Kidney

Muscle




CBC
V1
PFC
muscle
kidney
CBC
V1
PFC
muscle
kidney

muscle
kidney
PFC
V1
CBC
cortex
brain

Tissue−specific compounds

0
500
1000
2000
3000

0
10
20
30
40
50
60 [%]

BE (1,498)

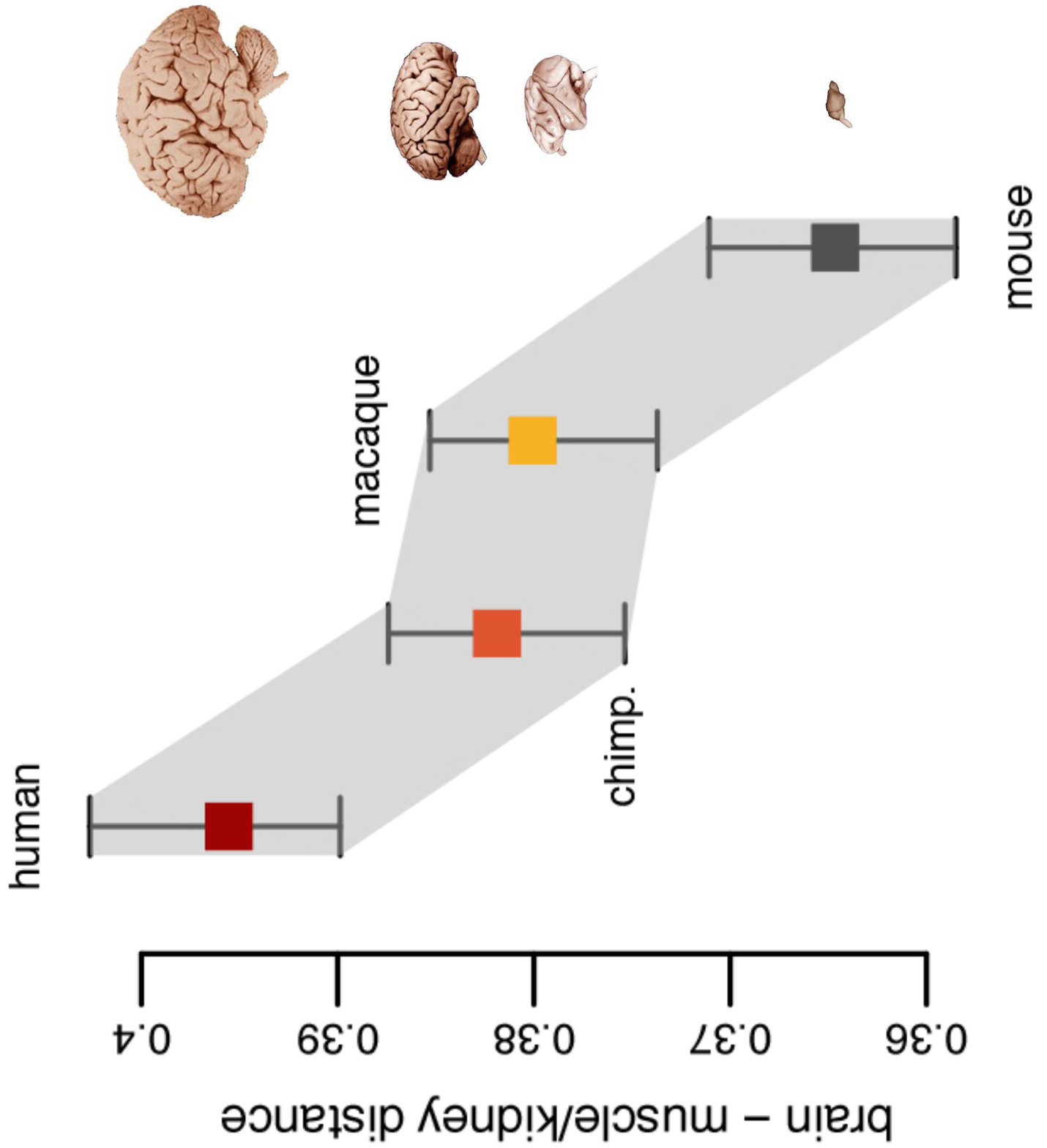
Concentration

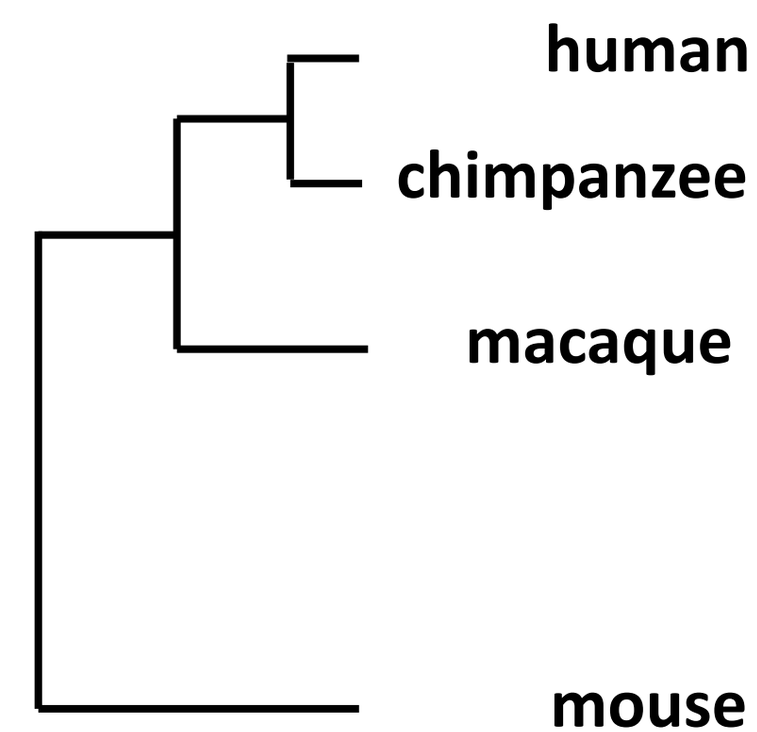
PFC
V1
CBC
kidney
muscle

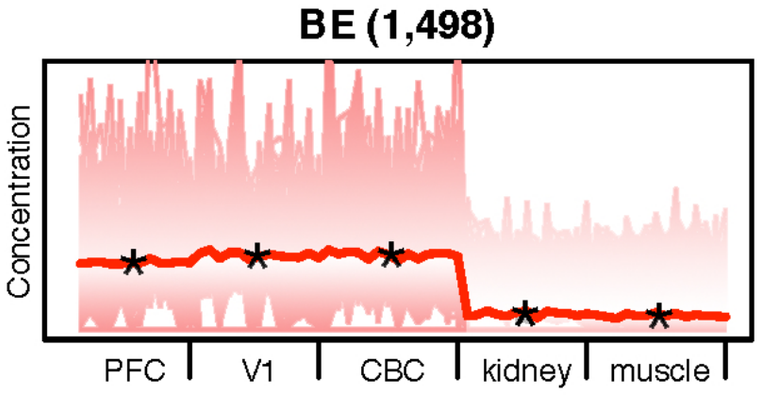
BD (2,840)

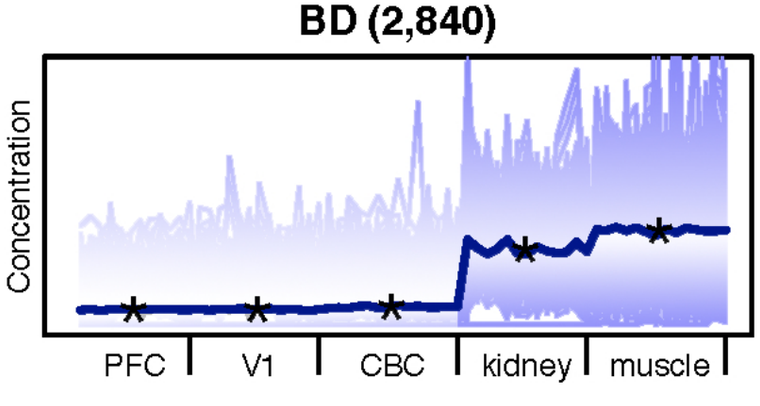
Concentration

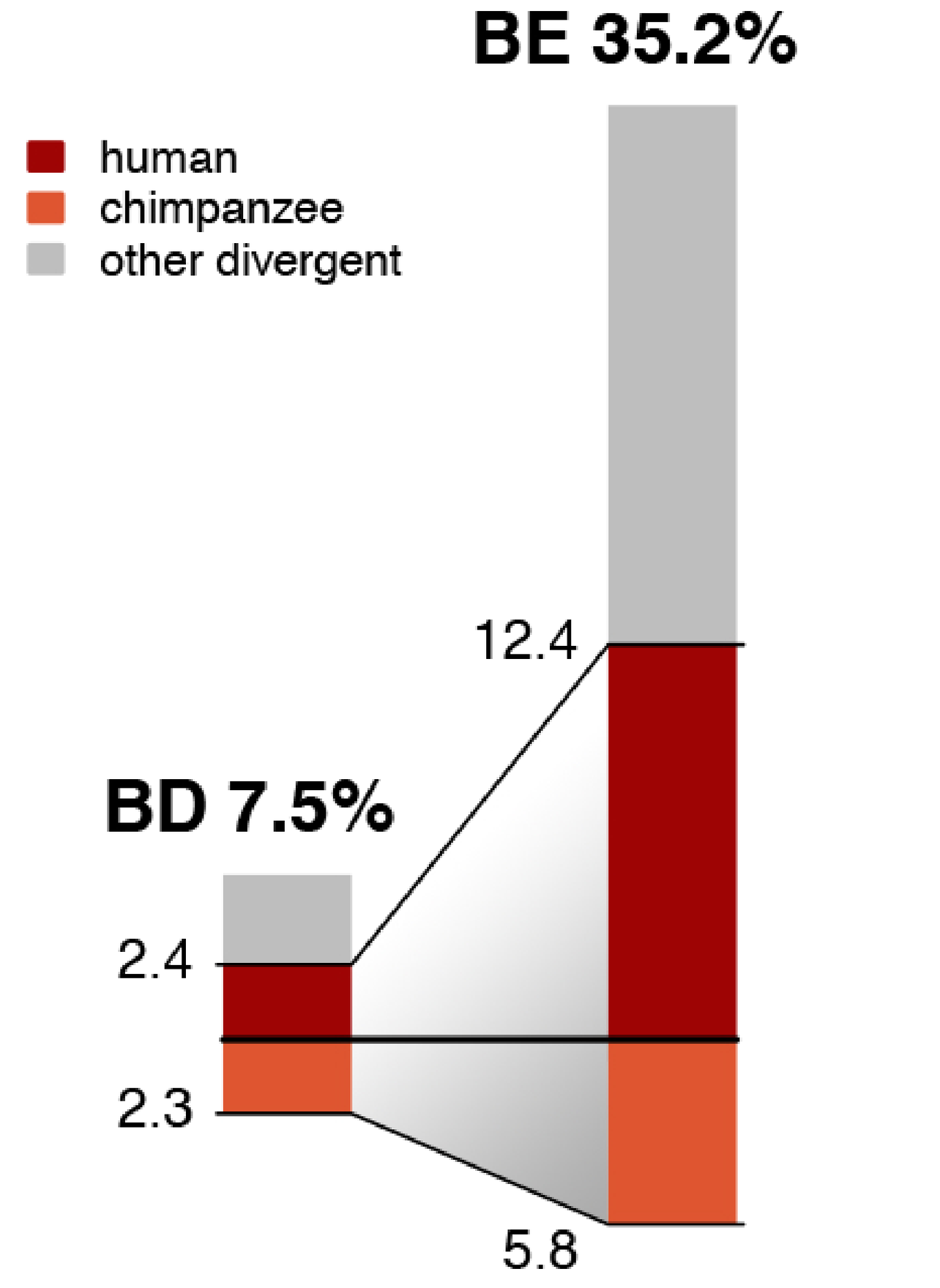
PFC
V1
CBC
kidney
muscle

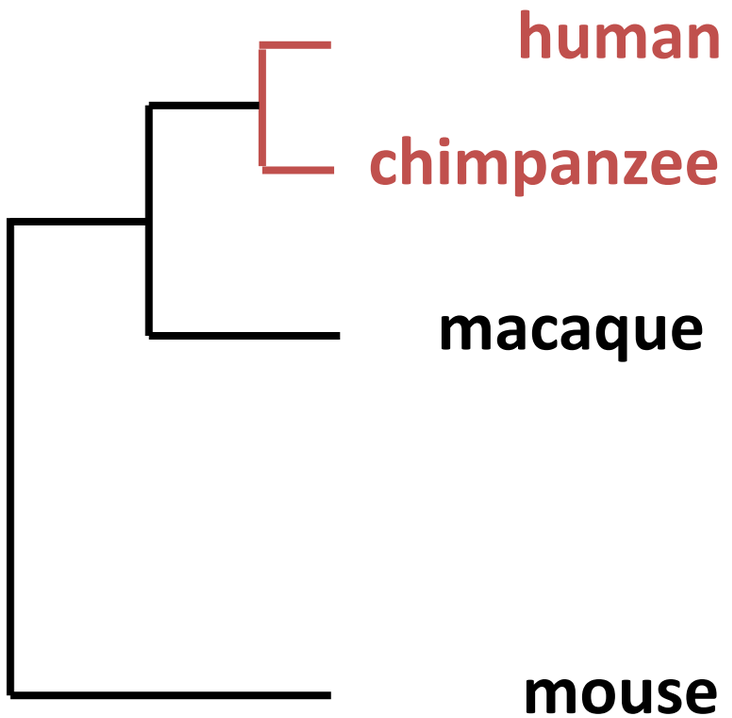

human
chimp.
macaque
mouse
brain – muscle/kidney distance
0.36
0.37
0.38
0.39
0.4
CBC
V1
PFC
muscle
kidney
CBC
V1
PFC
muscle
kidney

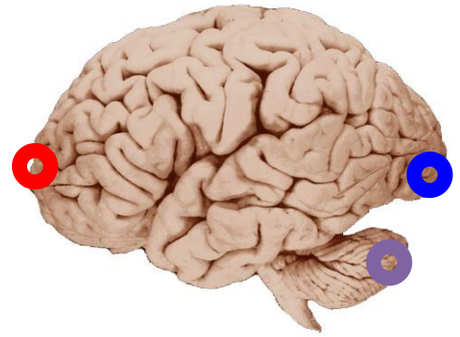

human
chimpanzee
macaque
mouse

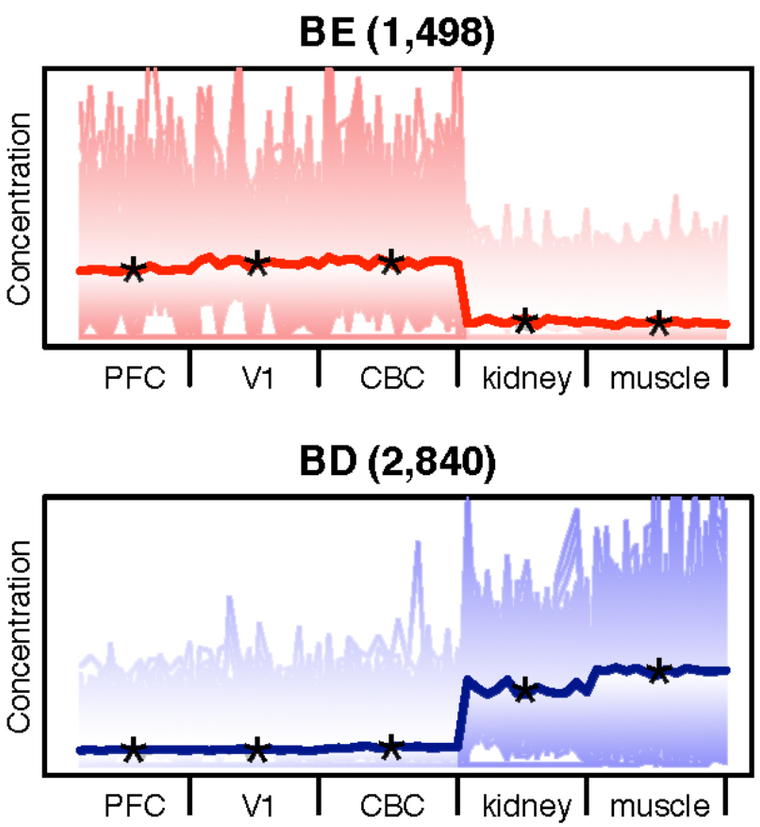

BE (1,498)
Concentration
PFC
V1
CBC
kidney
muscle

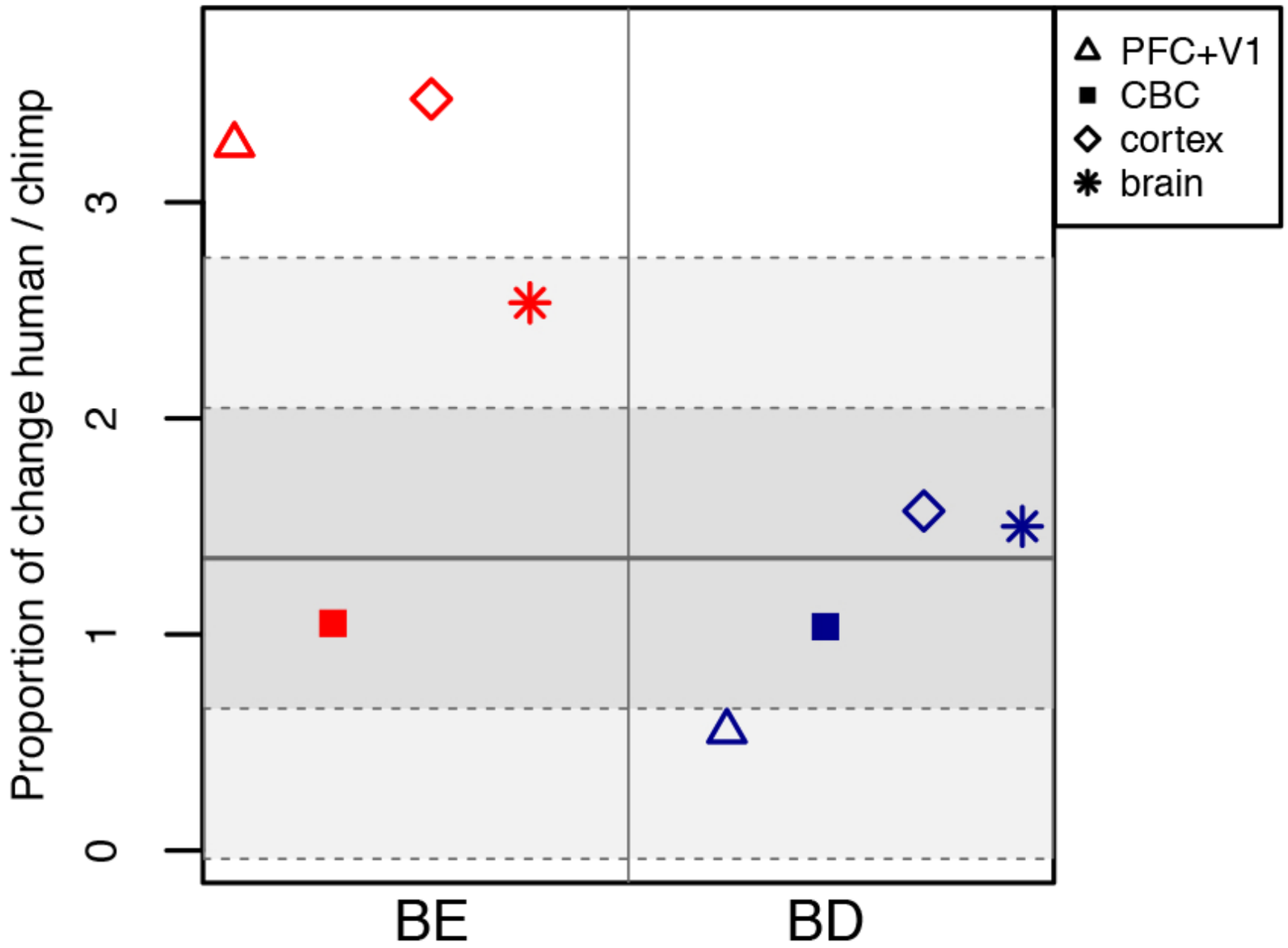

BD (2,840)
Concentration
PFC
V1
CBC
kidney
muscle


human
chimpanzee
other divergent
BE 35.2%
12.4
BD 7.5%
2.4
2.3
5.8


human
chimpanzee
macaque
mouse




BE (1,498)
Concentration
PFC
V1
CBC
kidney
muscle
BD (2,840)
Concentration
PFC
V1
CBC
kidney
muscle


Proportion of change human / chimp
0
1
2
3
BE
BD
PFC+V1
CBC
cortex
brain

Features unique to brain of:

mammals

primates

apes

human

Proportion of BE/BD features

0.9

0.8

0.2

0.1

0

Diacylglycerophosphocholines [GP0101]

Diacylglycero-phosphates [GP1001]
phosphoethanolamines [GP0201]
phosphoglycerols [GP0401]

metabolism of:
(alpha-)Linolenic acid
Arachidonic acid
Glycerophospholipid

Retrograde endocannabinoid signaling

Glycerophospho-glycerols [GP0401] [GP0402]

Diacylglycerols [GL0201]

Glycerophospho-cholines [GP0102], [GP0103], [GP0104]
ethanolamines [GP0202], [GP0203]

Diacylglycerophosphoinsitols [GP0601]

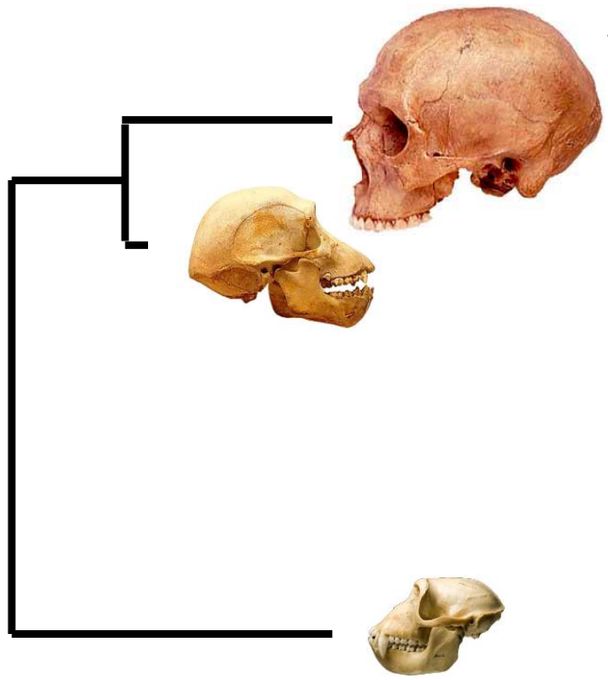
BE lipids
BD lipids

brain
cortex
CBC

Increasing brain complexity

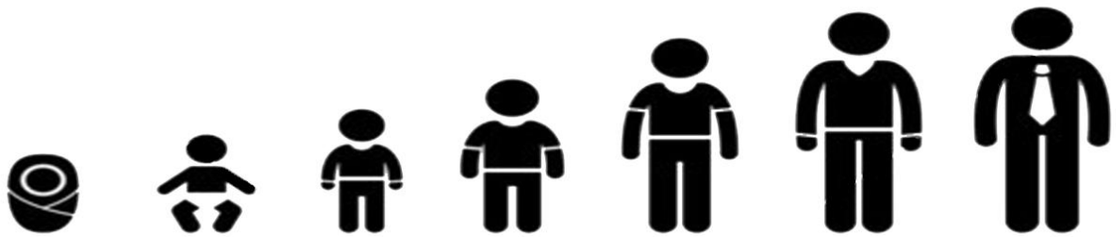
2. Системная липидомика развития мозга человека

Эволюция

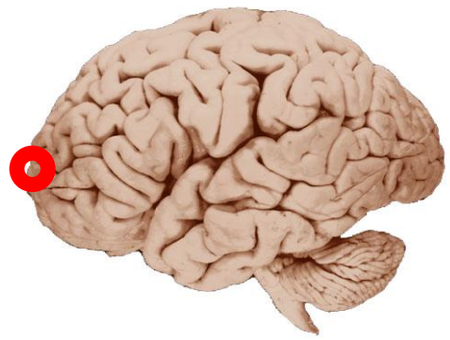


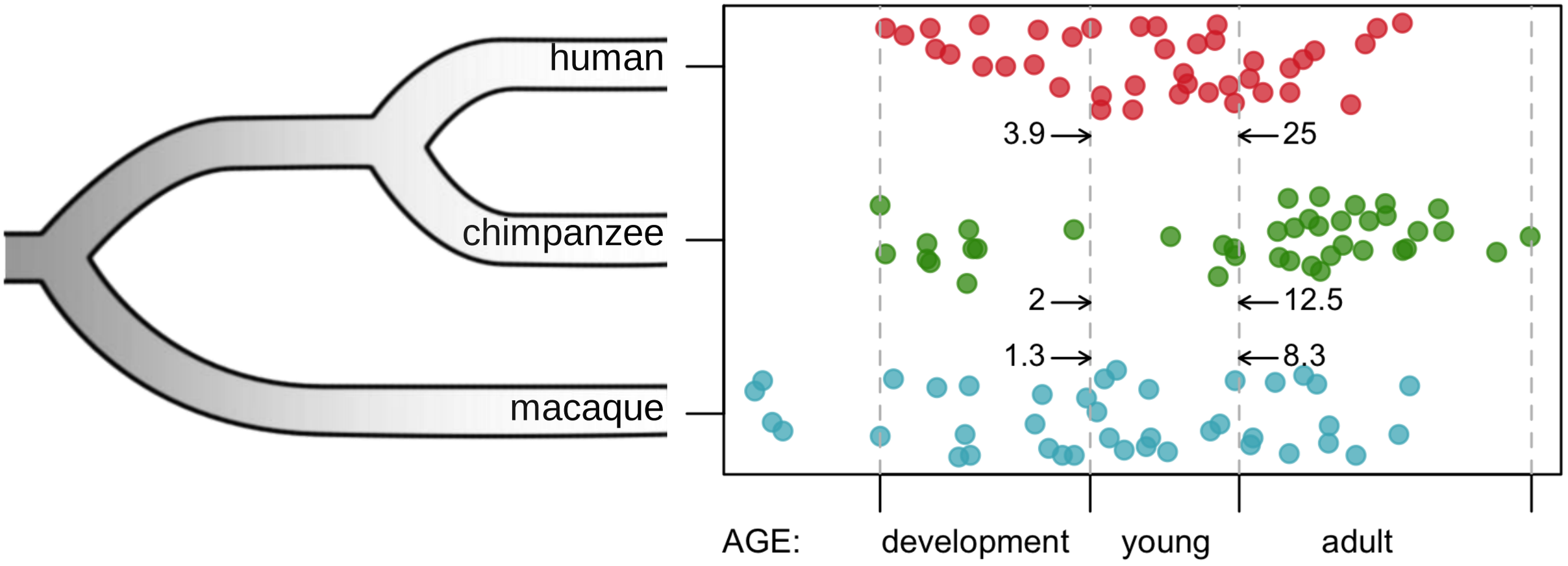
Данные

Метаболиты и Липиды

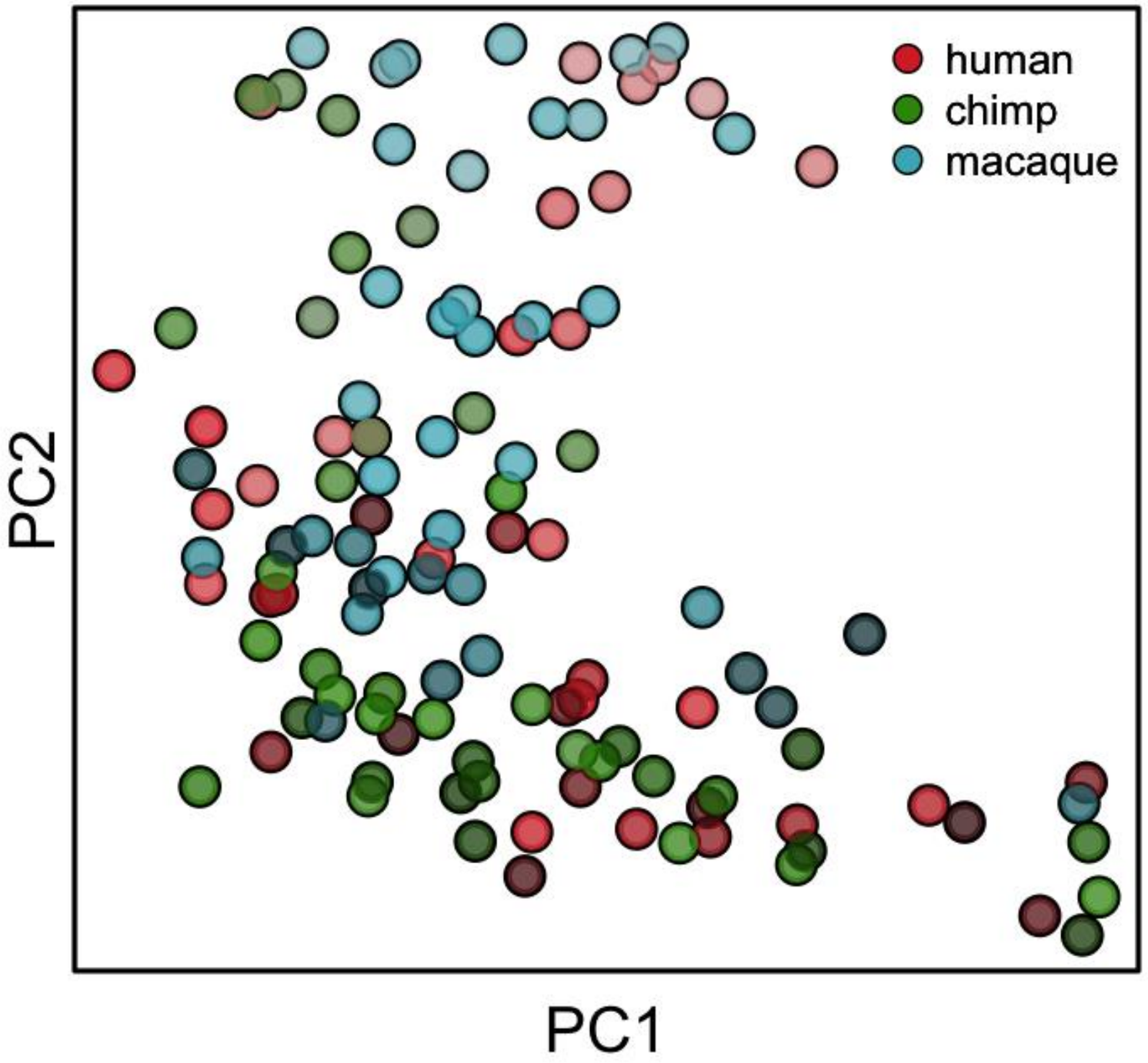


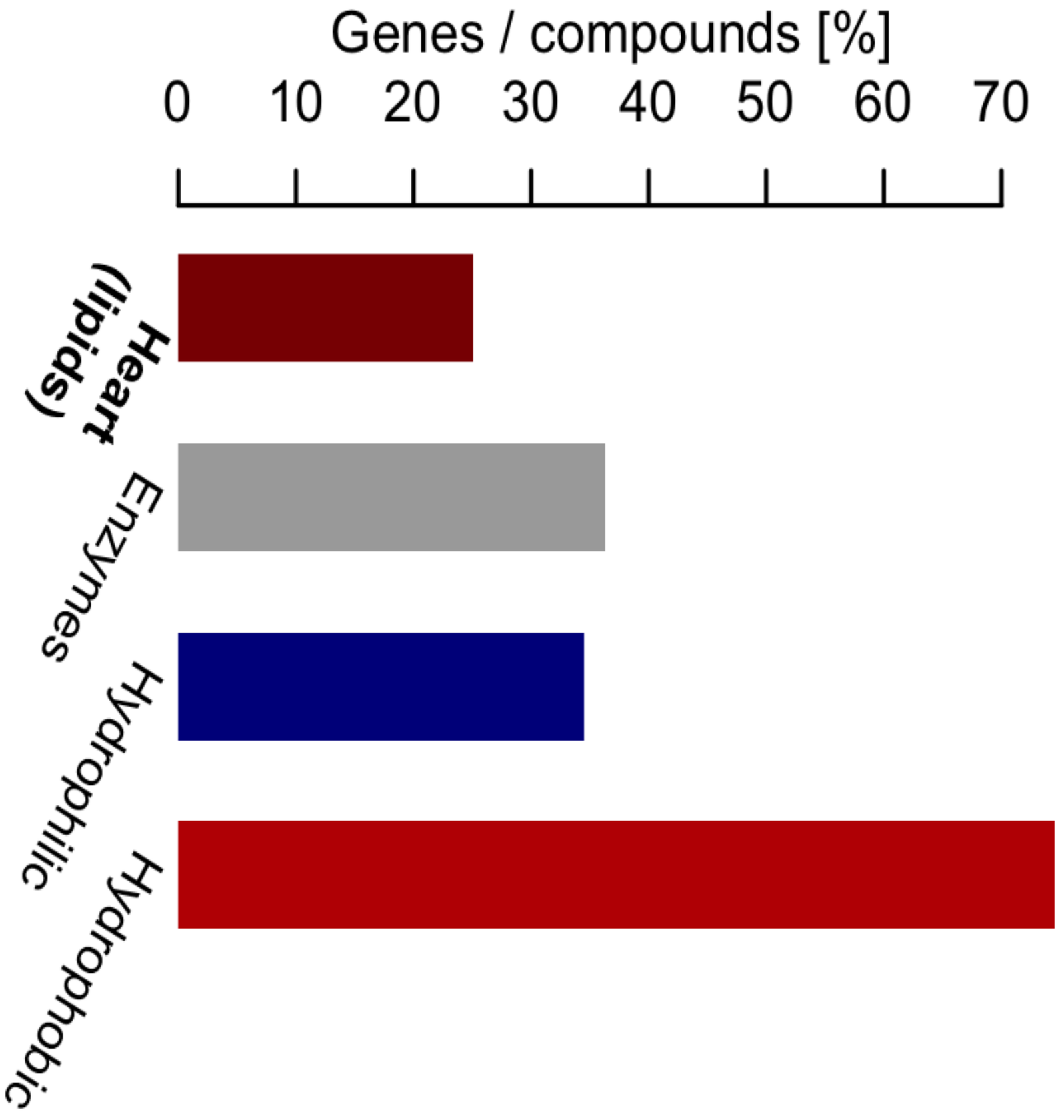
Brain | prefrontal cortex

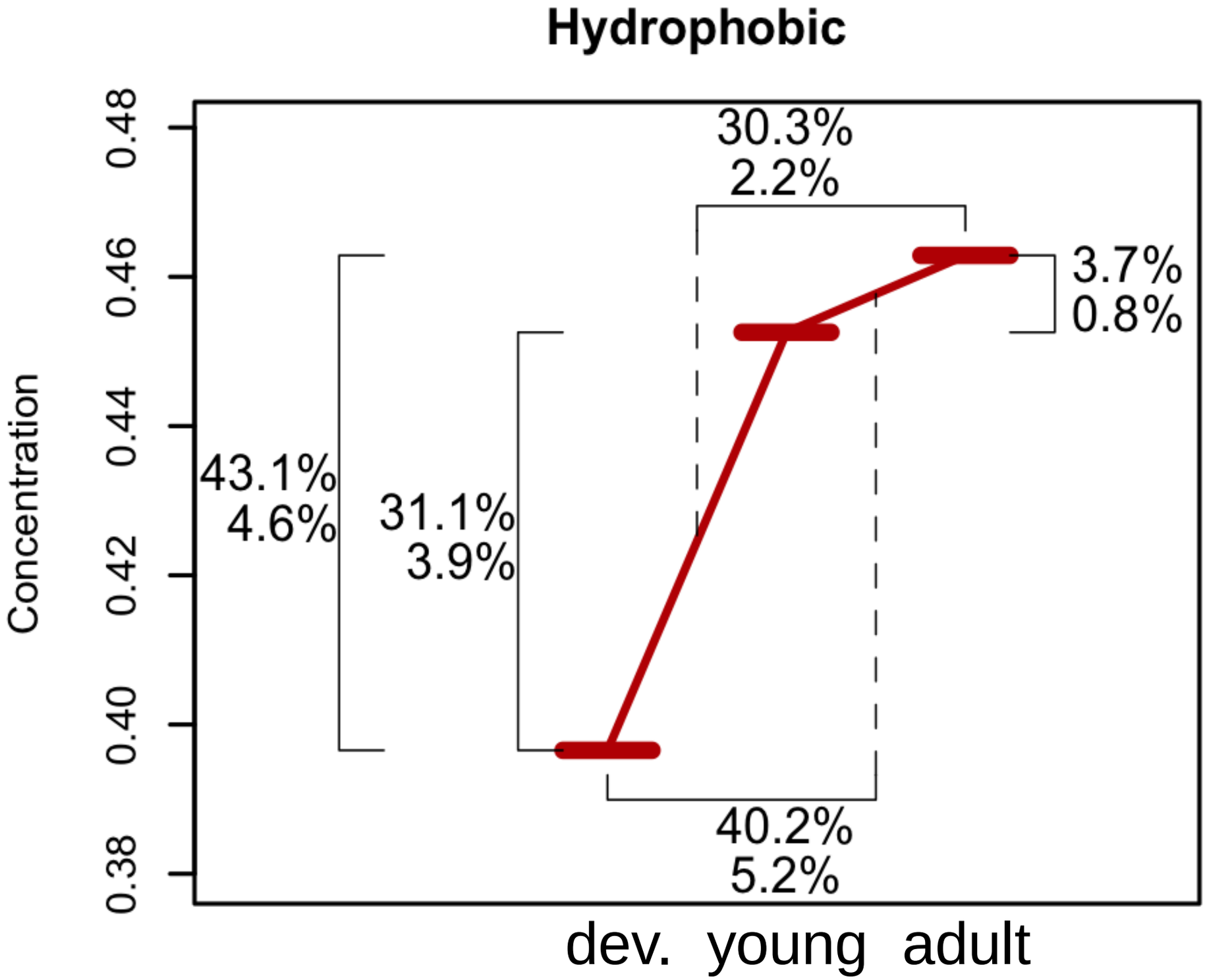


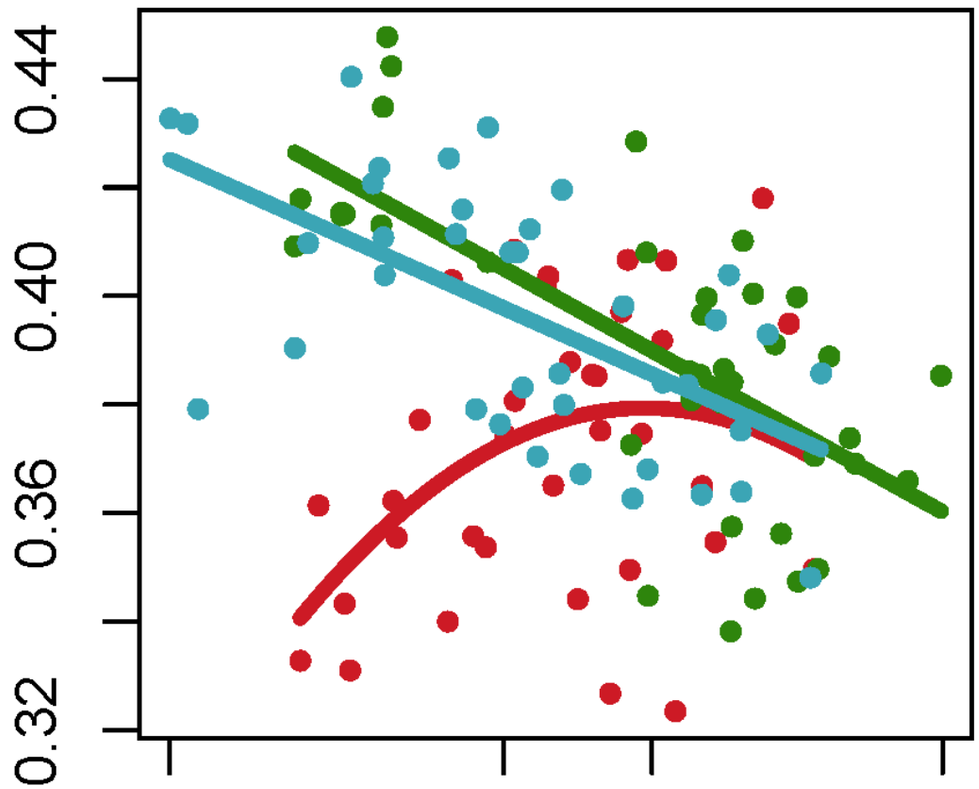

human
chimpanzee
macaque
3.9
25
2
12.5
1.3
8.3
AGE:
development
young
adult

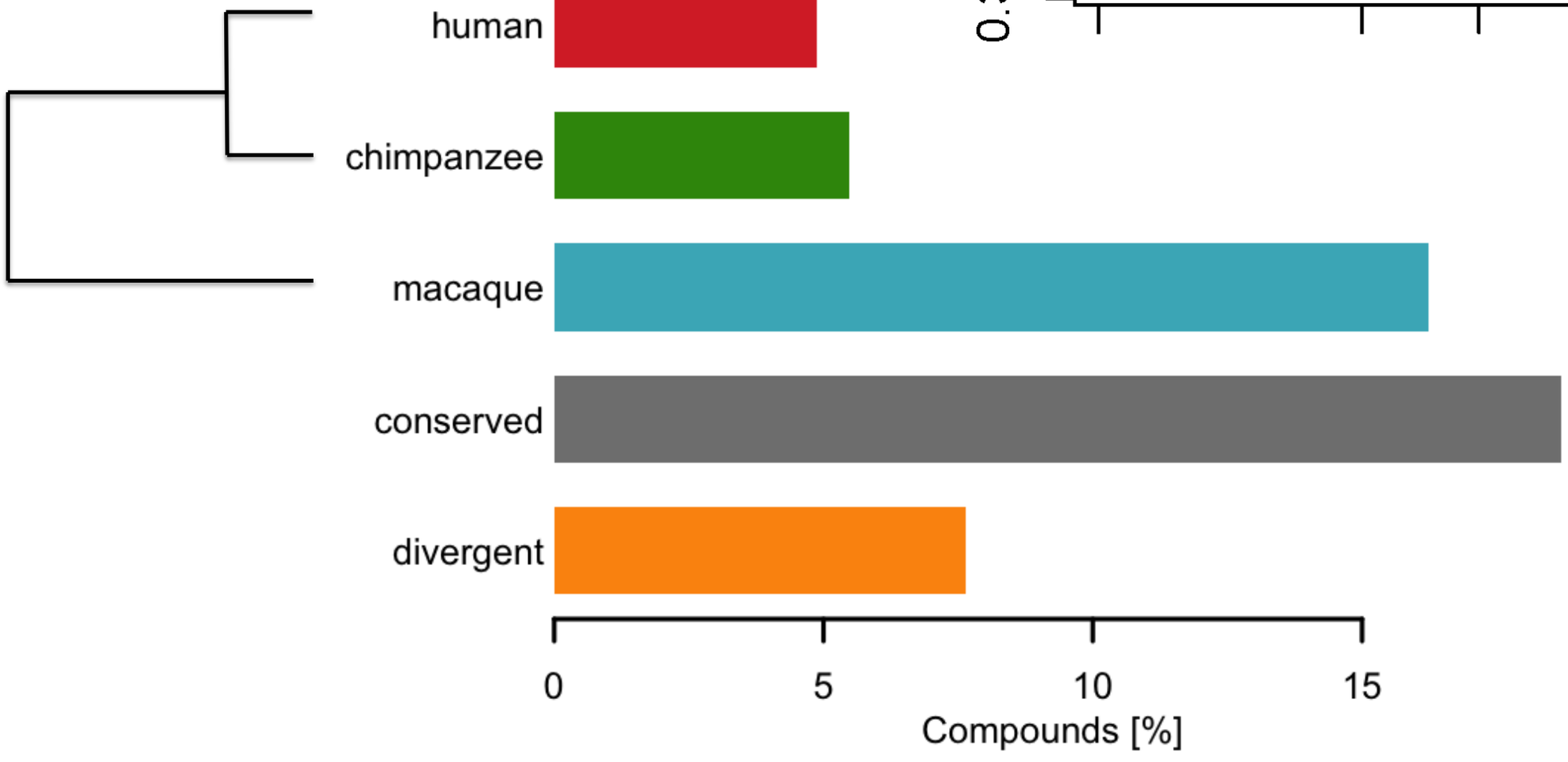
Hydrophobic



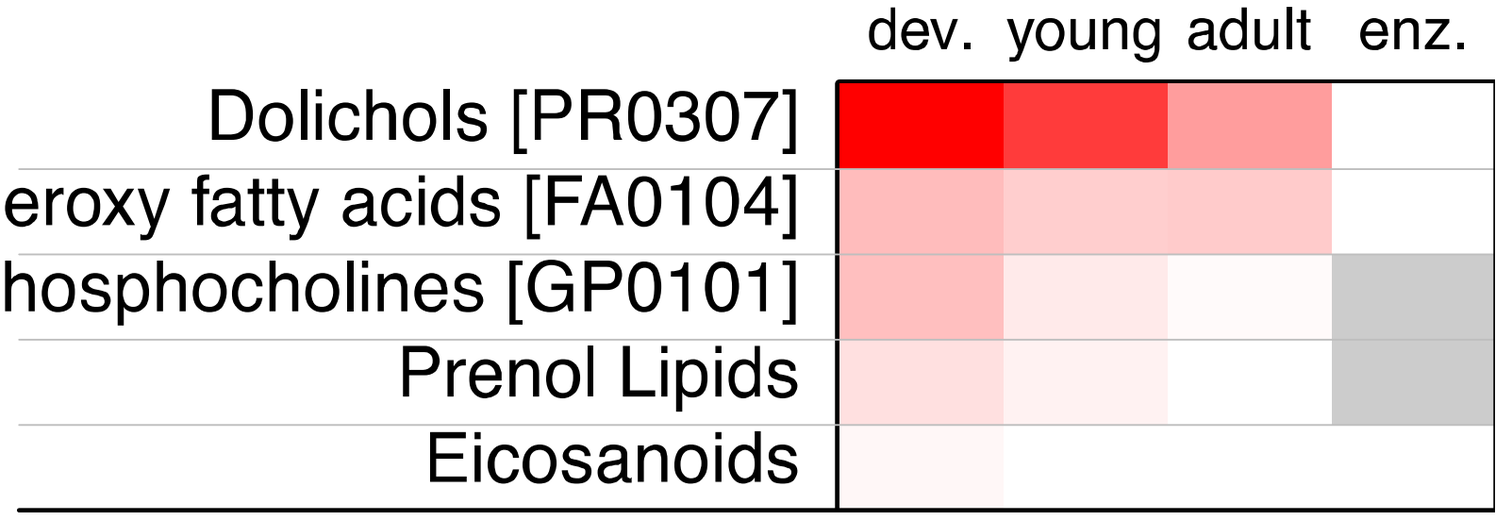

Genes / compounds [%]
0
10
20
30
40
50
60
70
Heart (lipids)
Enzymes
Hydrophilic
Hydrophobic


Hydrophobic
Concentration
0.48
0.46
0.44
0.42
0.40
0.38
43.1%
4.6%
31.1%
3.9%
30.3%
2.2%
3.7%
0.8%
40.2%
5.2%
dev.
young
adult

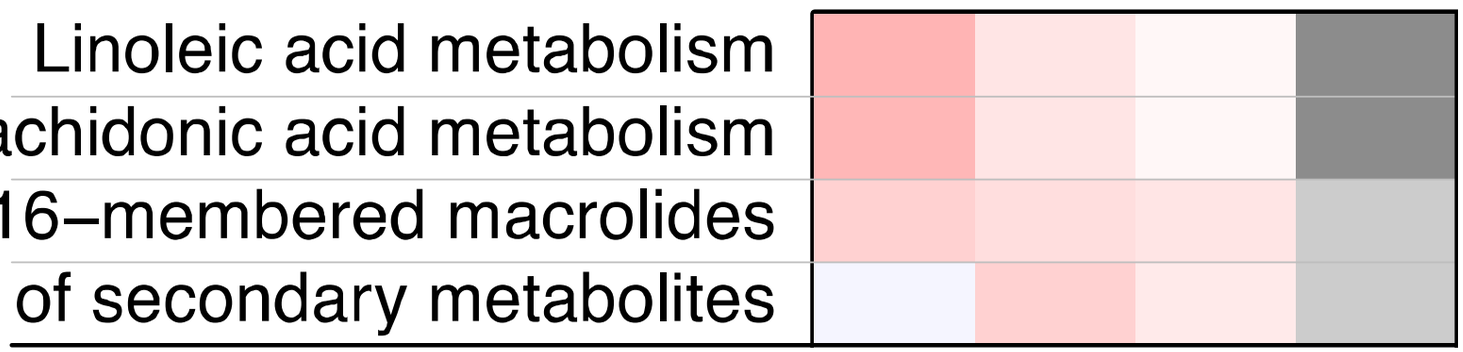

0.44
0.40
0.36
0.32


human
chimpanzee
macaque
conserved
divergent
0
5
10
15
Compounds [%]

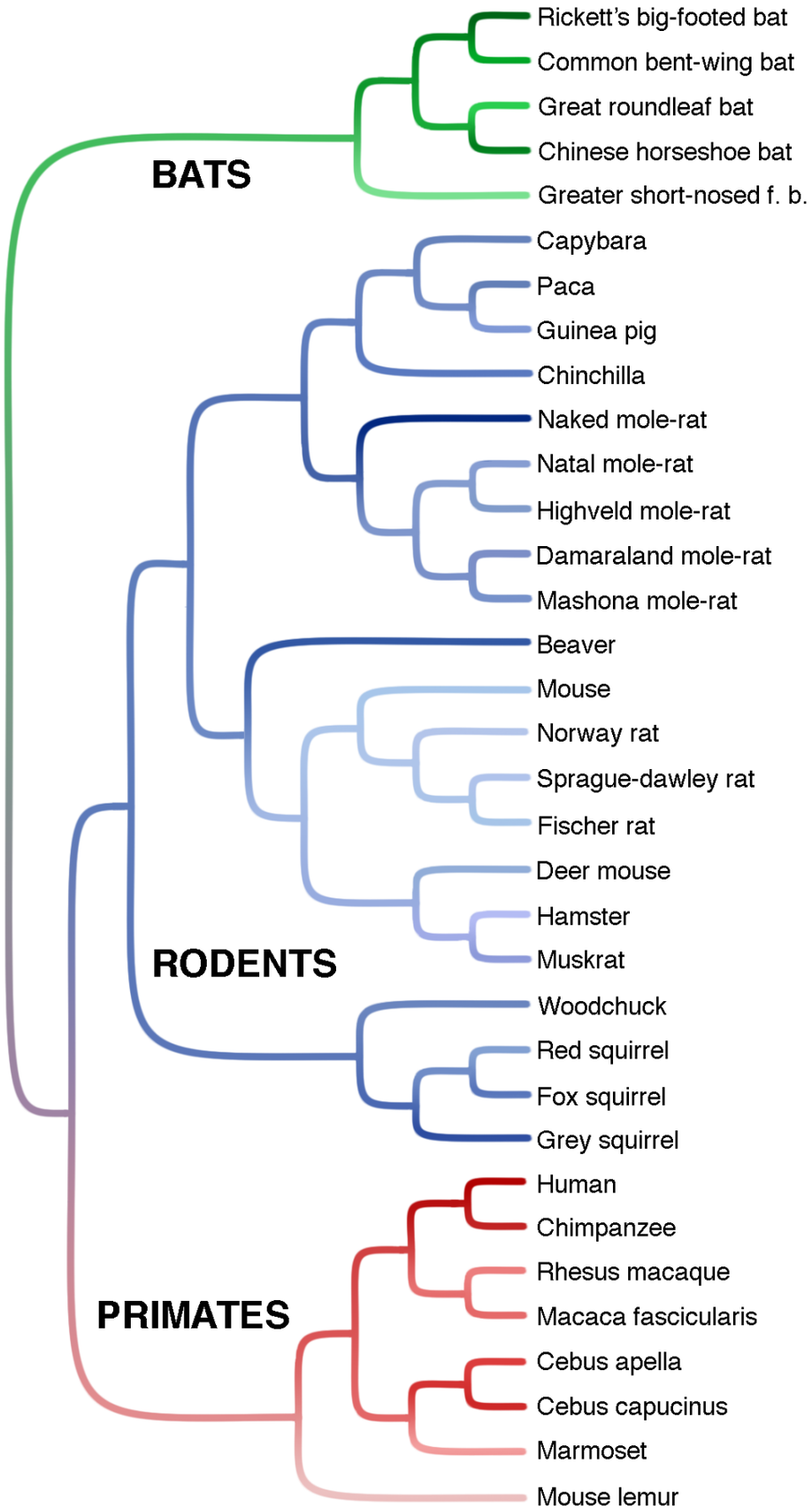
Lipid classes



Pathways



3. Системная липидомика долголетия



6 tissues:

Brain | prefrontal cortex

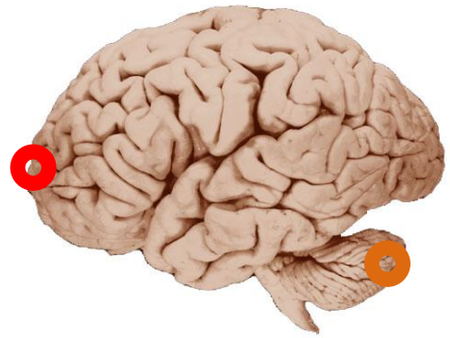
Brain | cerebellum

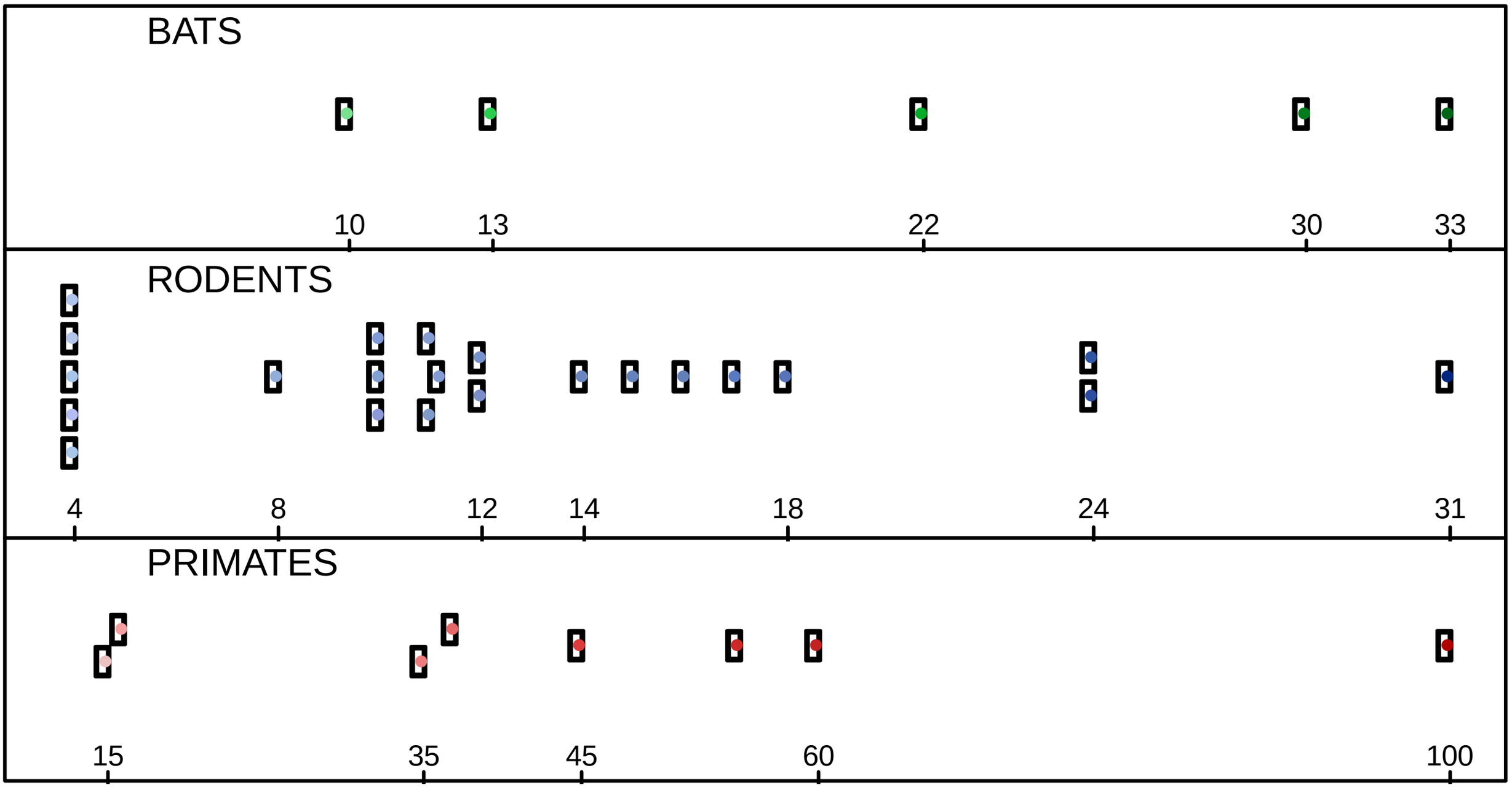
Kidney

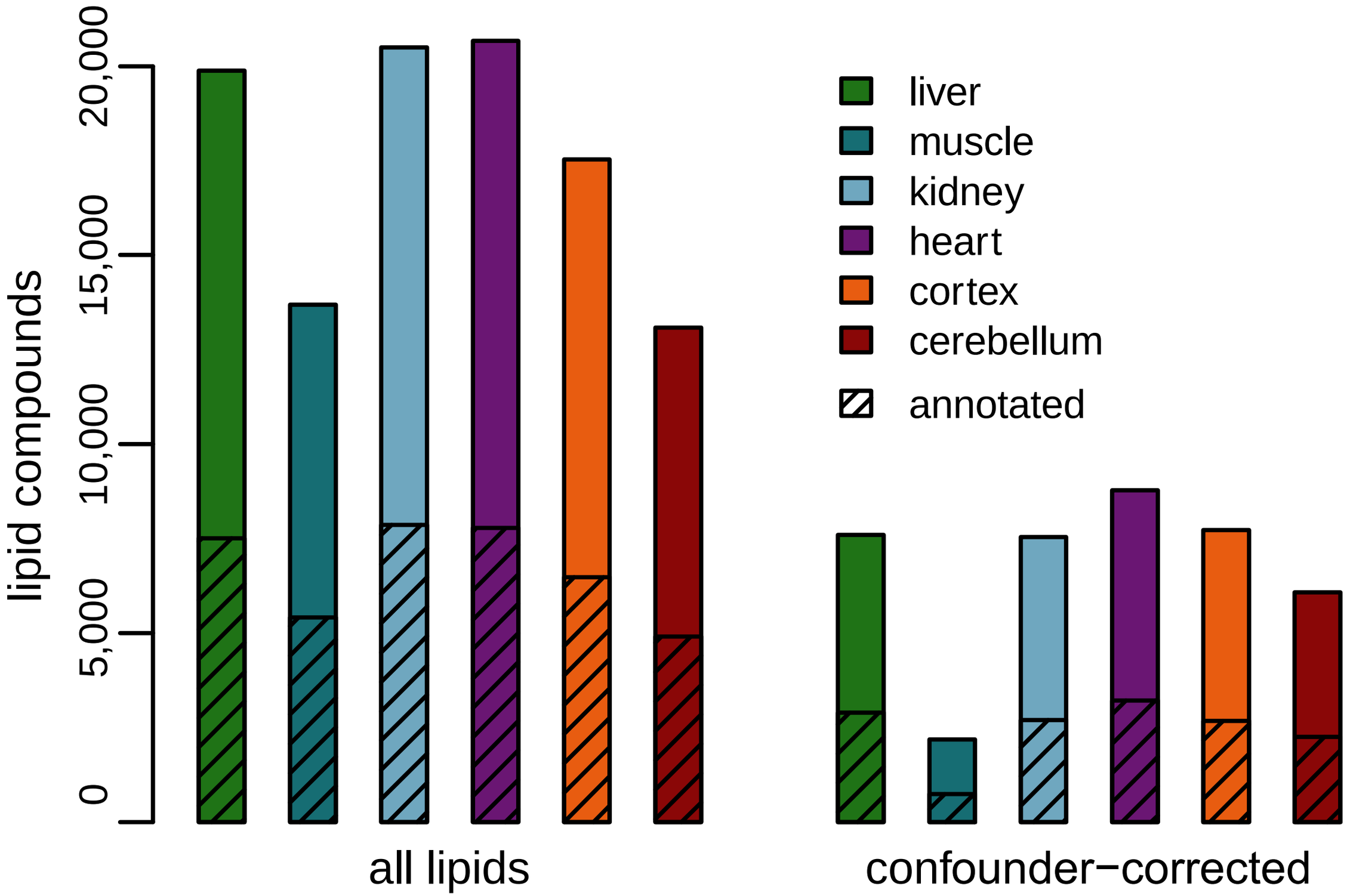
Muscle

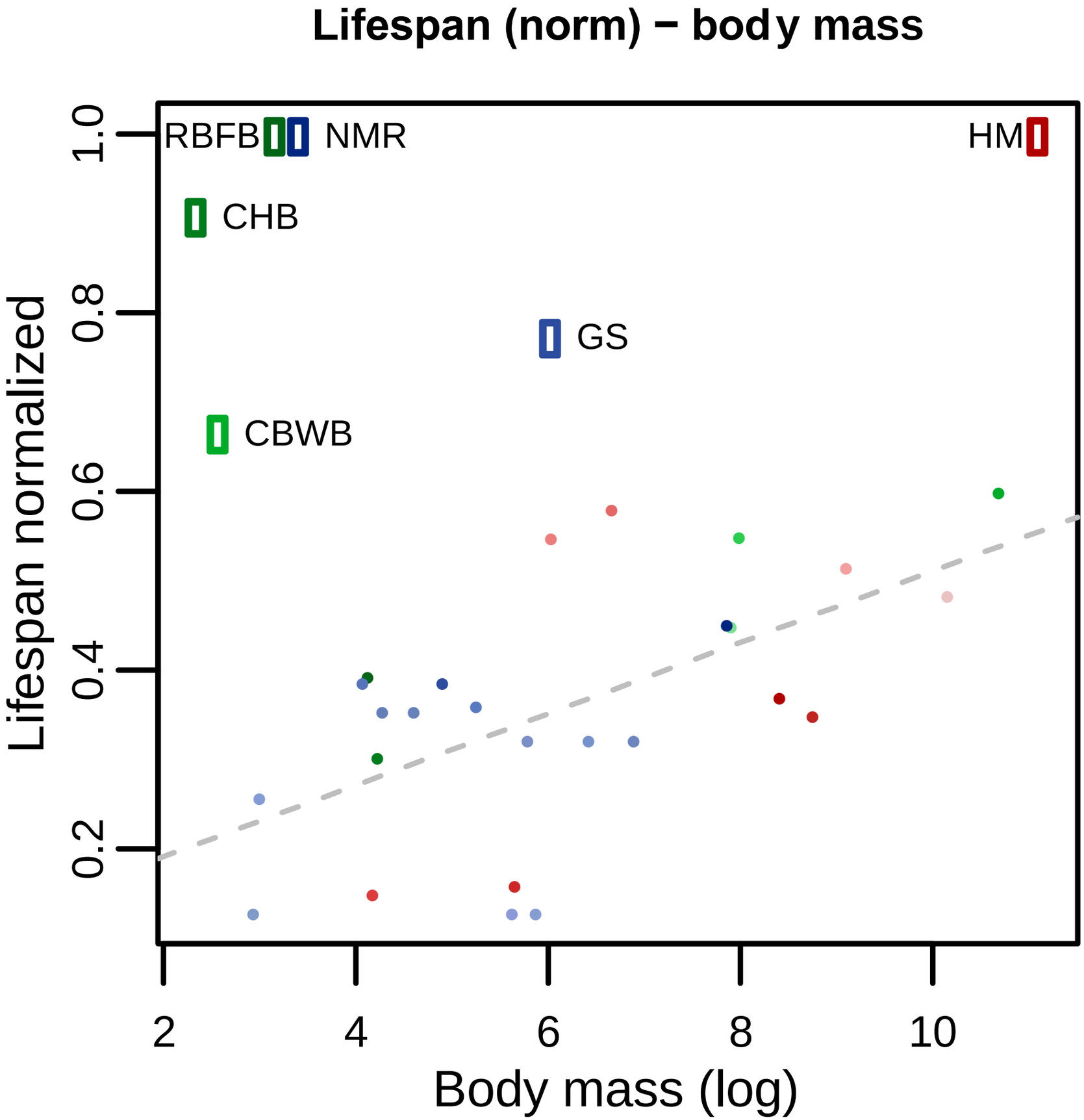
Liver

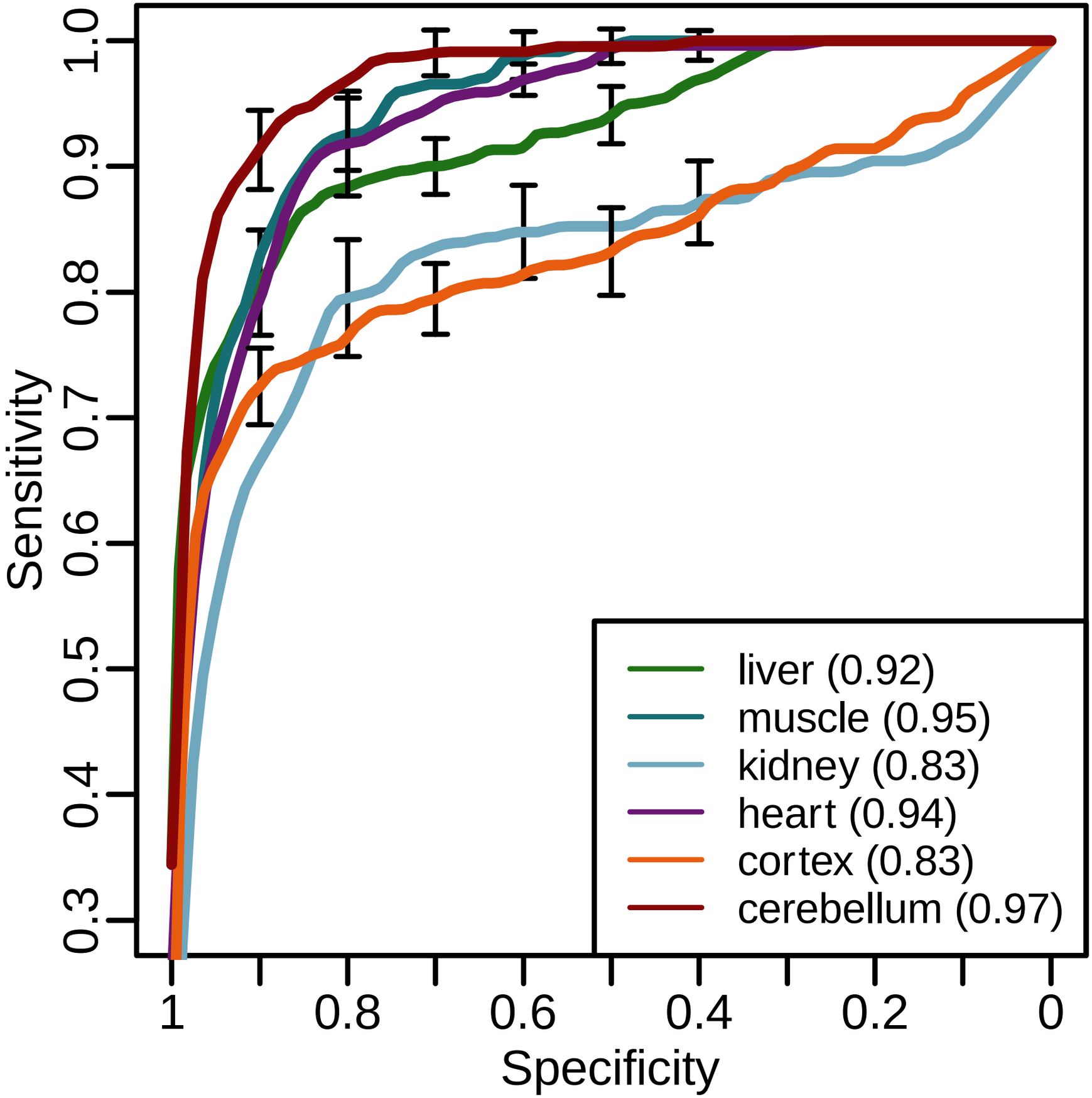
Heart

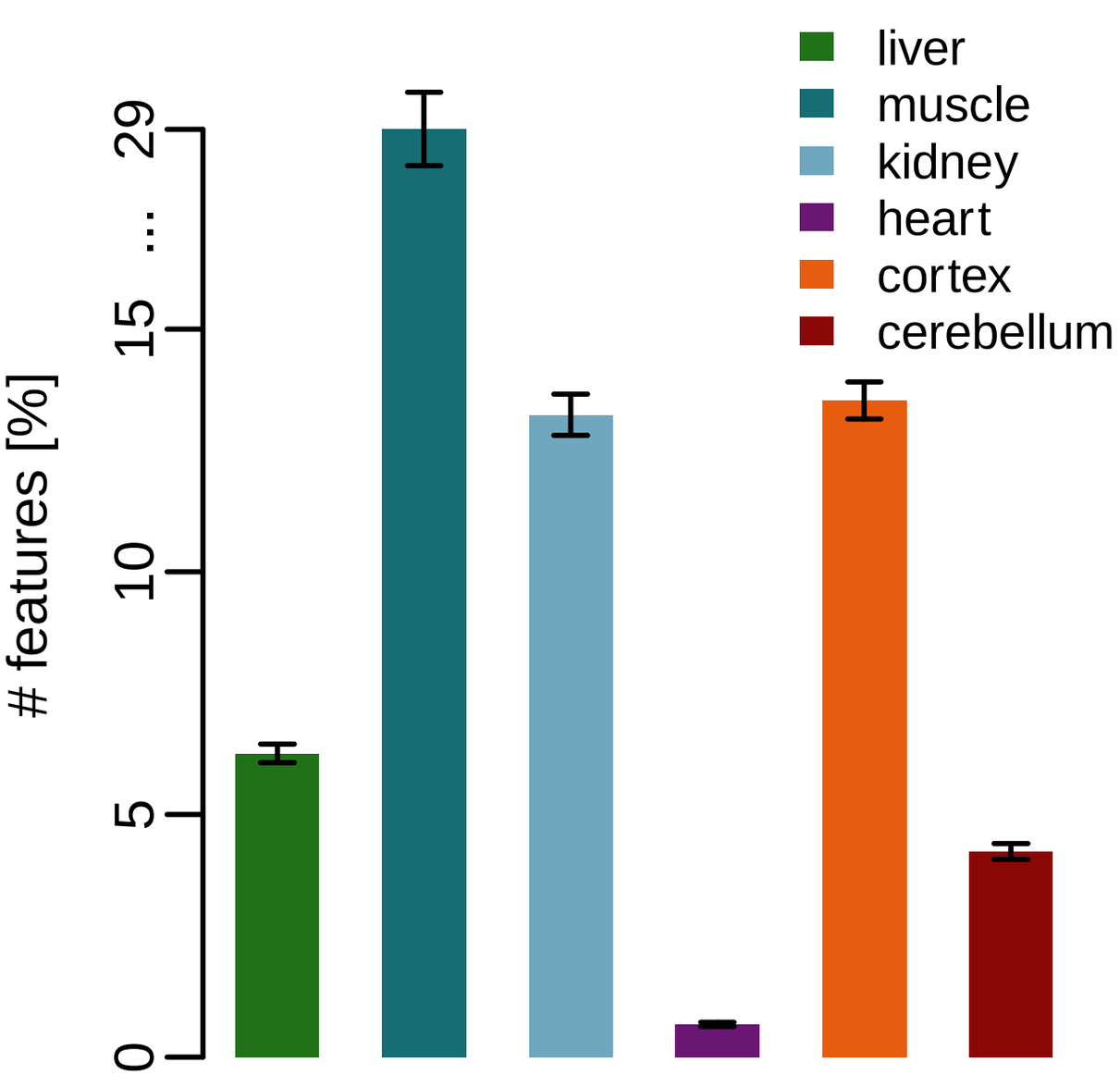


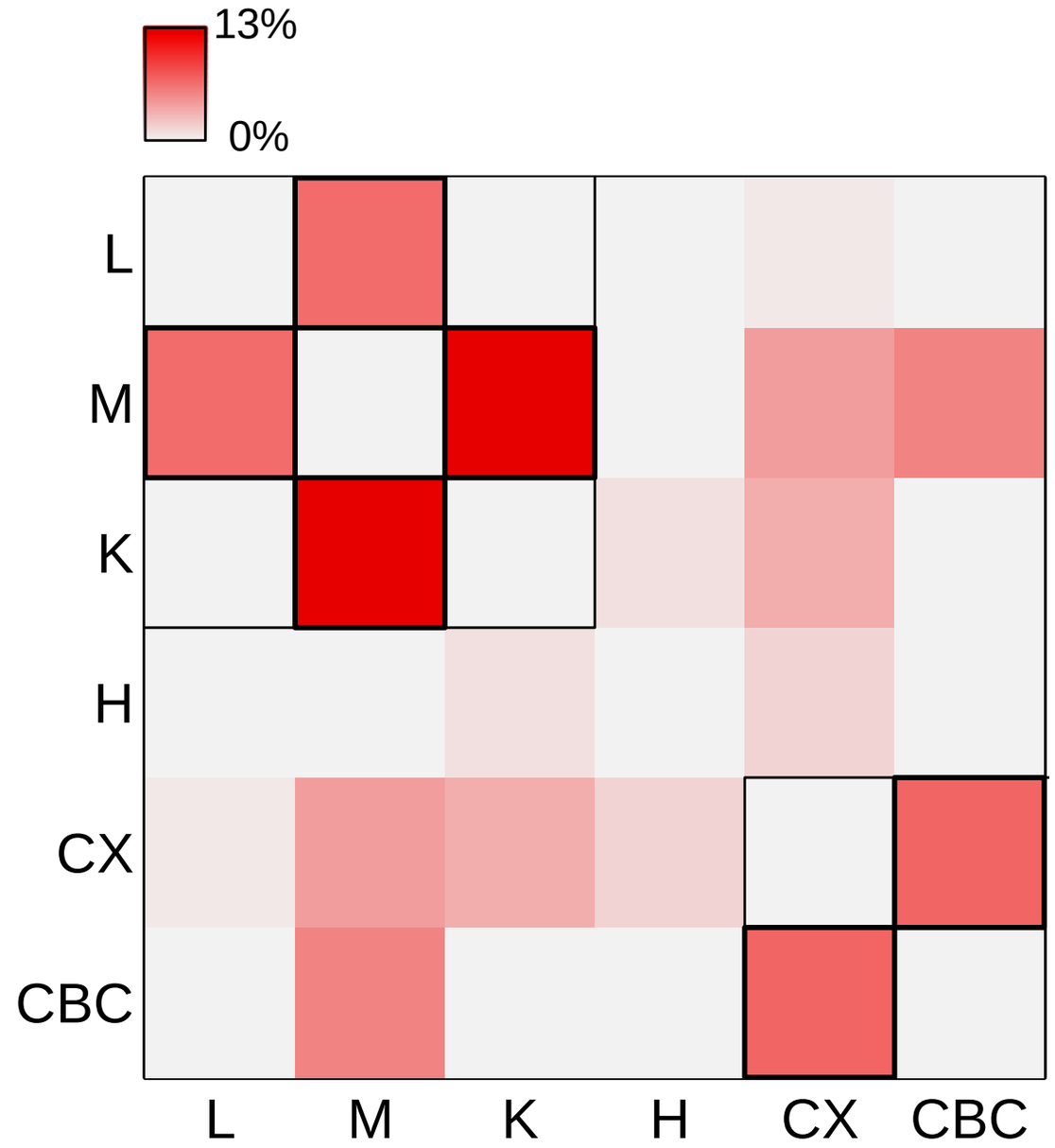

BATS
10
13
22
30
33
RODENTS
4
8
12
14
18
24
31
PRIMATES
15
35
45
60
100
Maximal lifespan

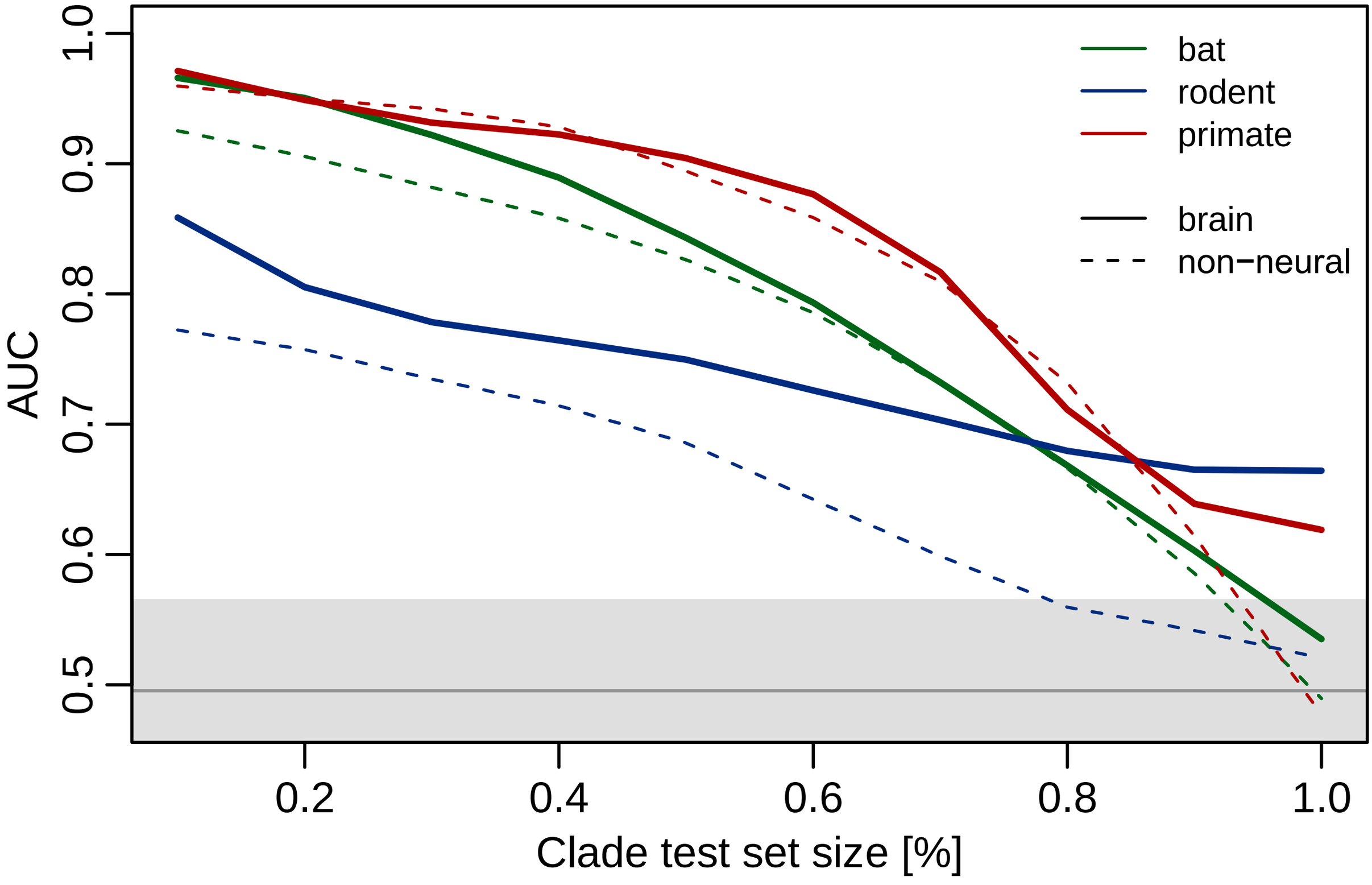

lipid compounds
0
5,000
10,000
15,000
20,000
liver
muscle
kidney
heart
cortex
cerebellum
annotated
all lipids
confounder−corrected


Lifespan (norm) – body mass
RBFB
NMR
HM
CHB
GS
CBWB
Lifespan normalized
1.0
0.8
0.6
0.4
0.2
2
4
6
8
10
Body mass (log)

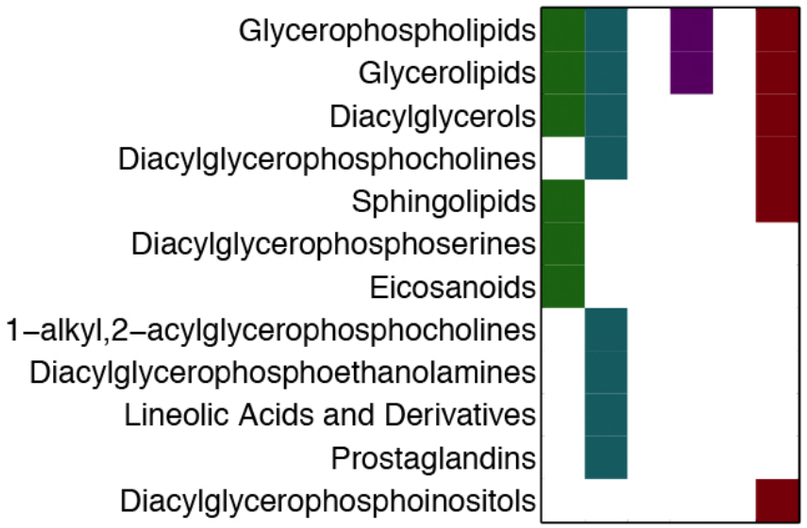

Sensitivity
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
1
0.8
0.6
0.4
0.2
0
Specificity
liver (0.92)
muscle (0.95)
kidney (0.83)
heart (0.94)
cortex (0.83)
cerebellum (0.97)

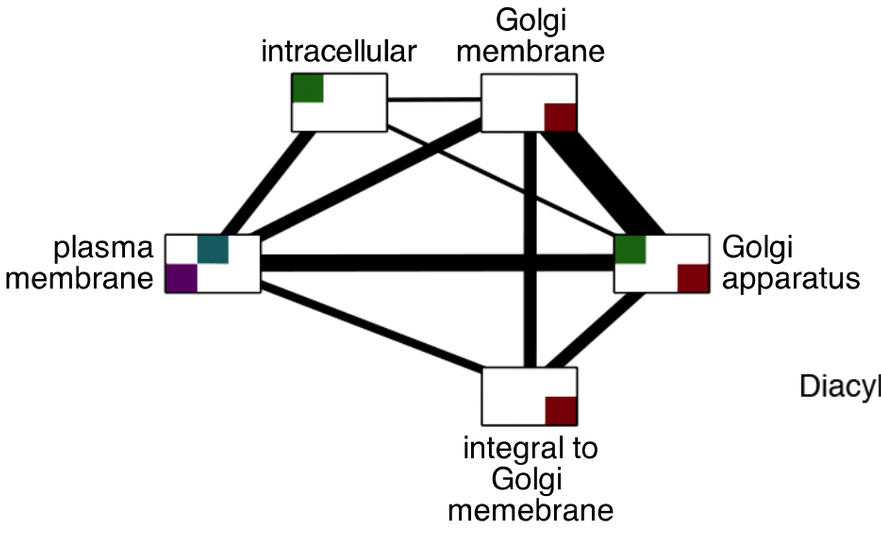

features [%]
0
5
10
15
...
29
liver
muscle
kidney
heart
cortex
cerebellum


13%
0%
L
M
K
H
CX
CBC
L
M
K
H
CX
CBC

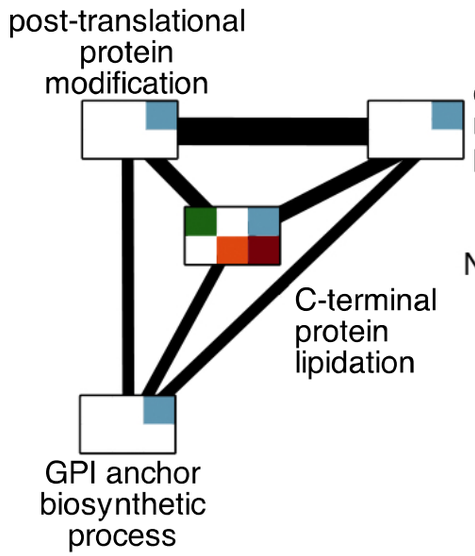

AUC
1.0
0.9
0.8
0.7
0.6
0.5
0.2
0.4
0.6
0.8
1.0
Clade test set size [%]
bat
rodent
primate
brain
non−neural

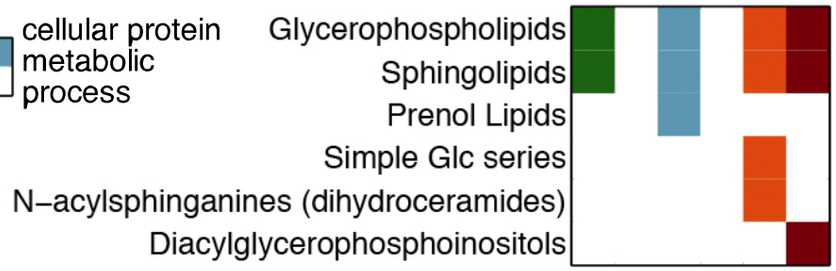
cellular compartment

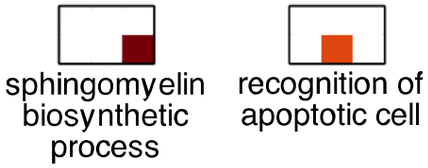




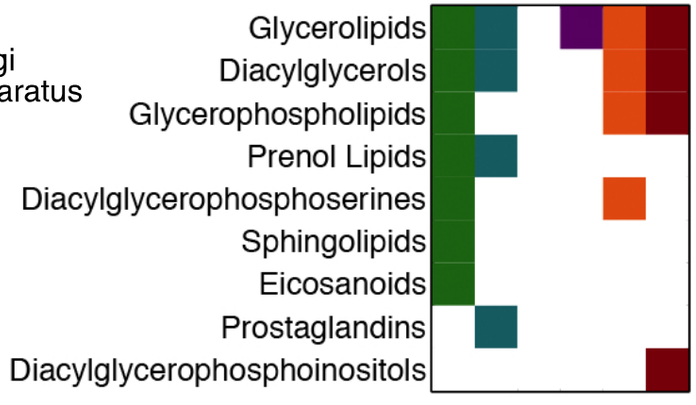
protein modification







signaling



Анализ липидомы мозга – новый и перспективный инструмент изучения мозга человека.

Спасибо!