Analysis of metabolomics, methylation and transcriptomic of Breast cancer

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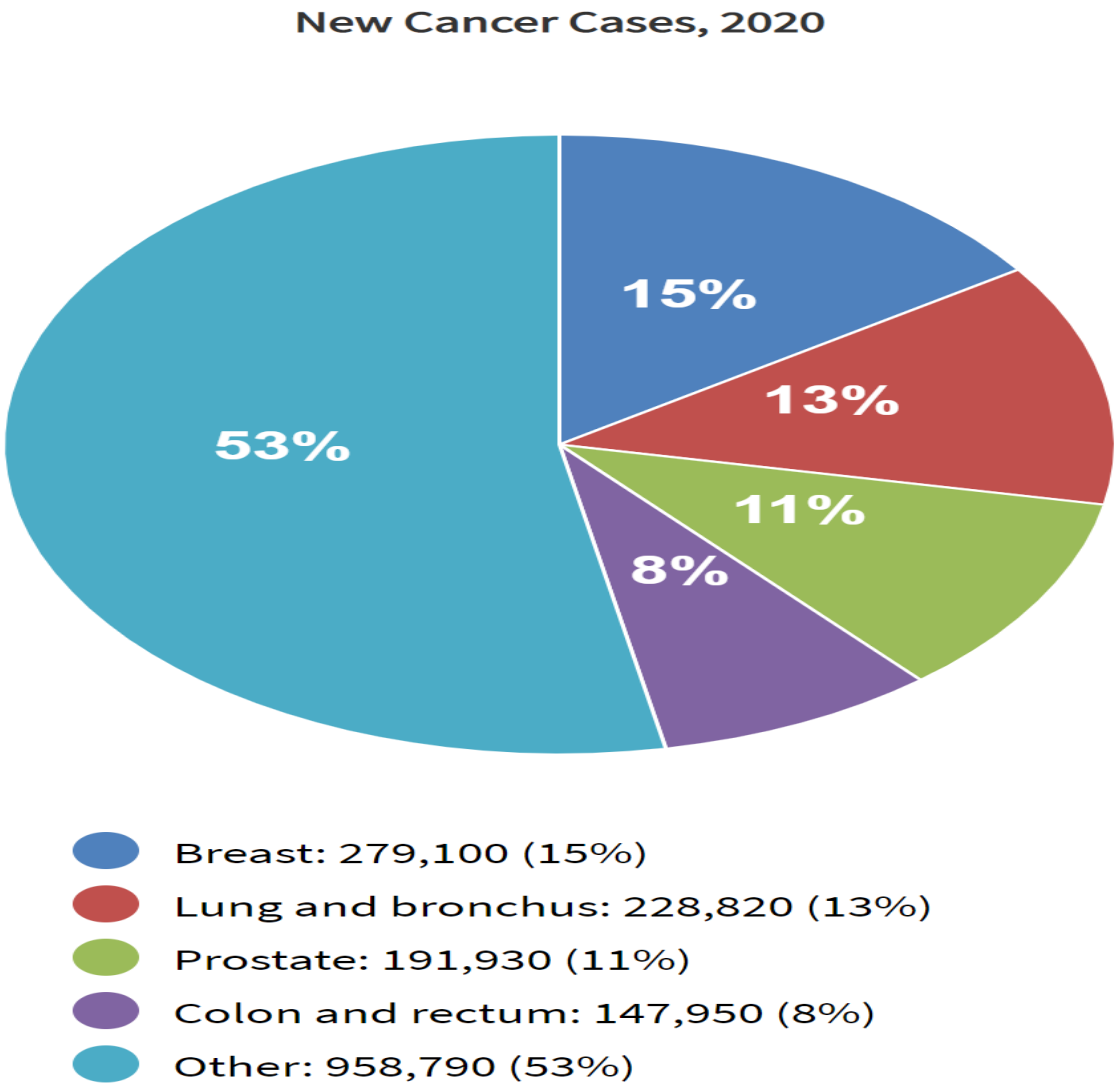
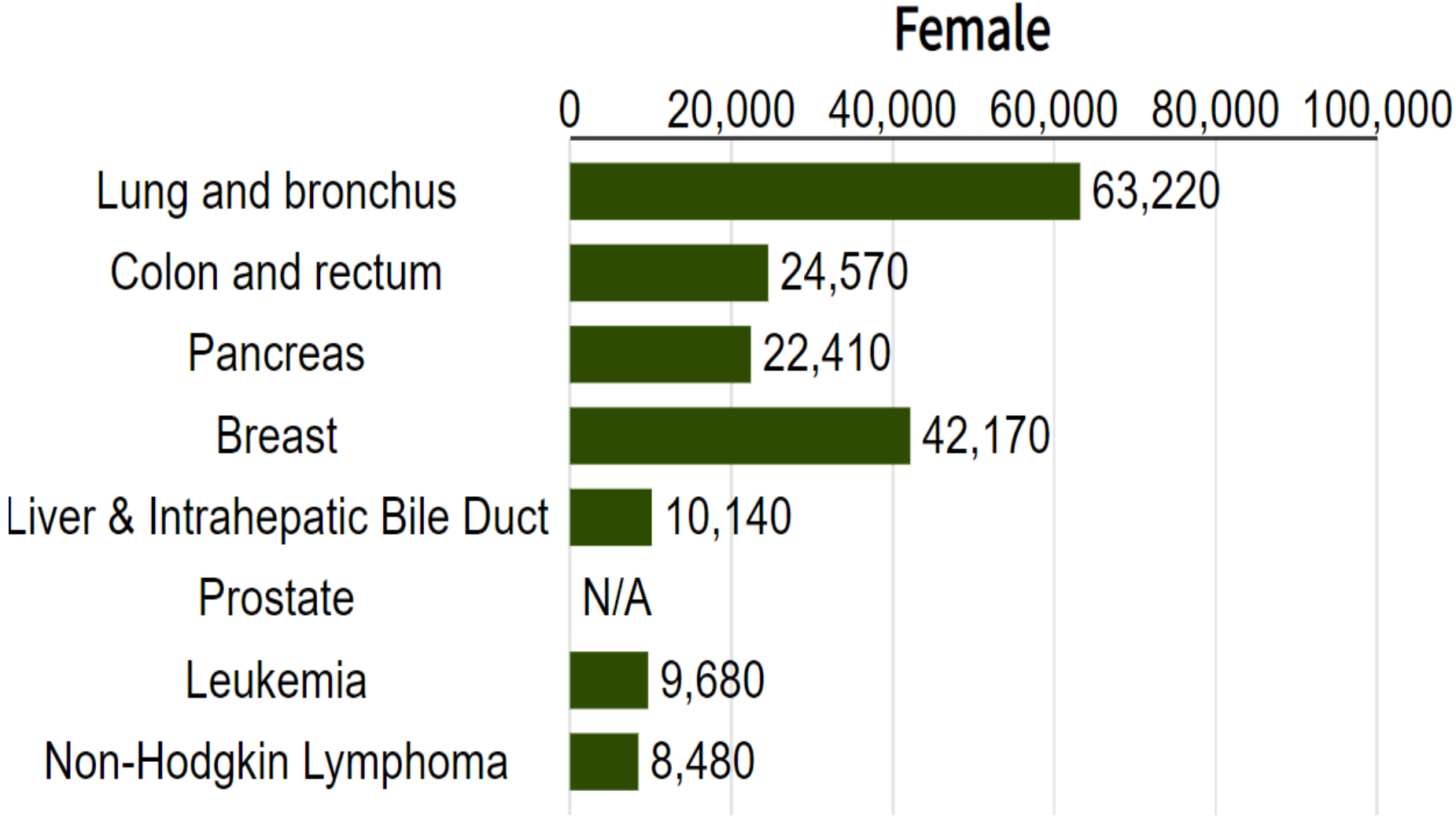
https://github.com/FADHLyemen/Metabolomics_signature

https://pubs.acs.org/doi/abs/10.1021/acs.jproteome.9b00755



- https://seer.cancer.gov/statfacts/html/common.html

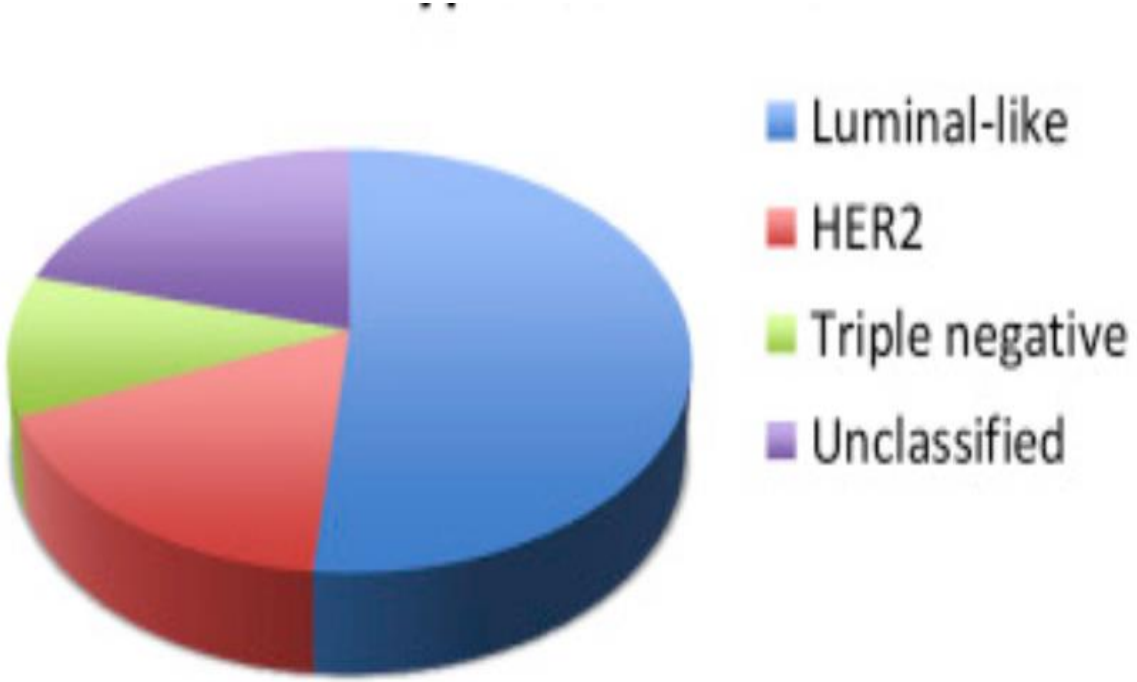
Breast cancer mortality rate (2020)



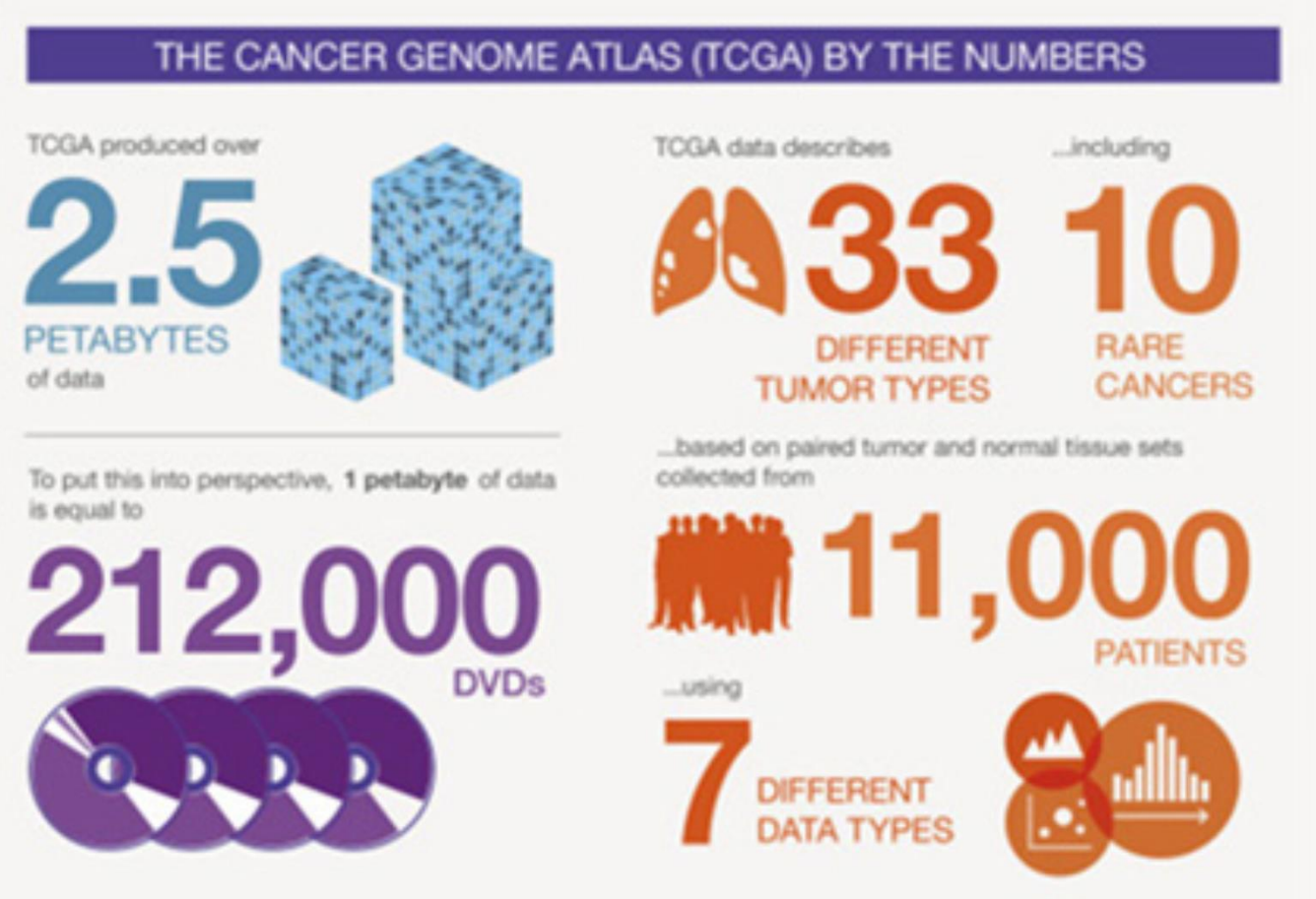
- https://seer.cancer.gov/statfacts/html/common.html

Breast cancer subtypes

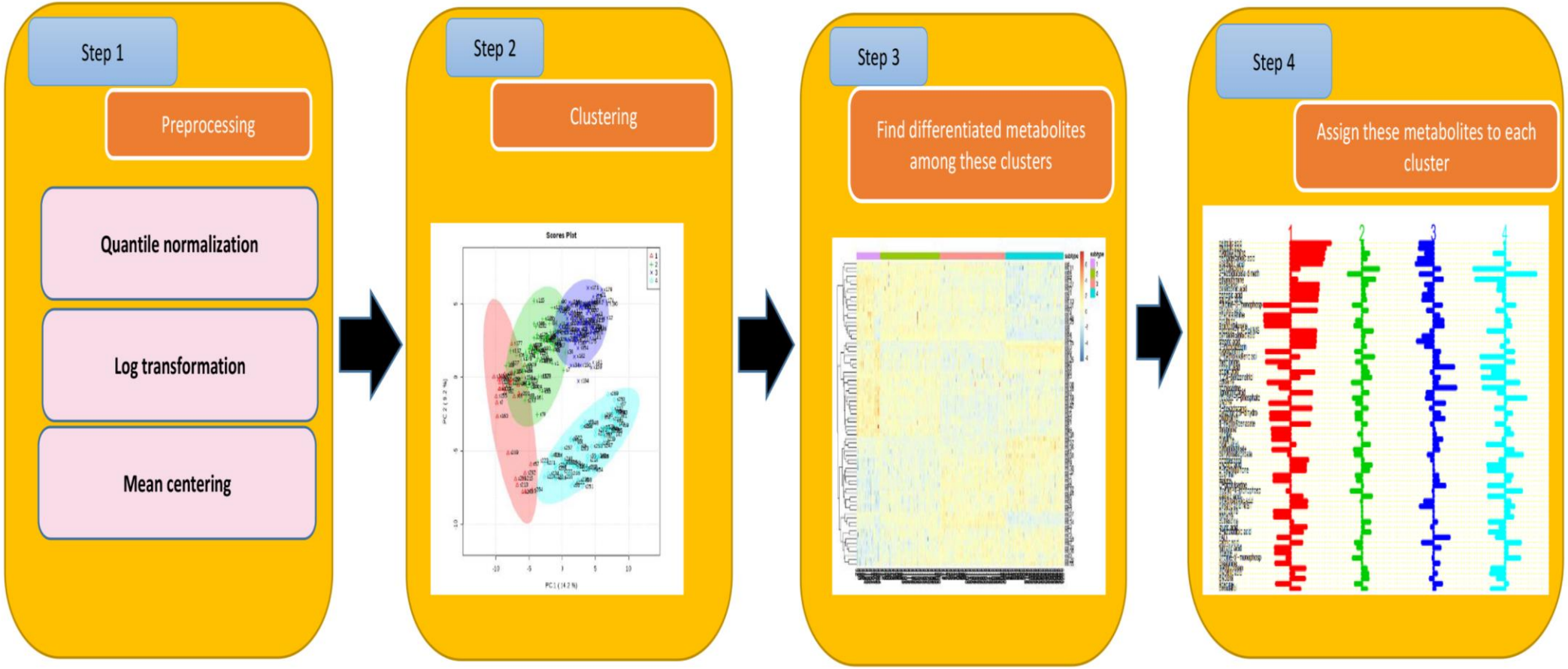
- Subtyping based on transcriptomic omics data.
- Treatment based on subtyping.
- Could we use other omics data for subtyping?
- Non-invasive and cheaper.



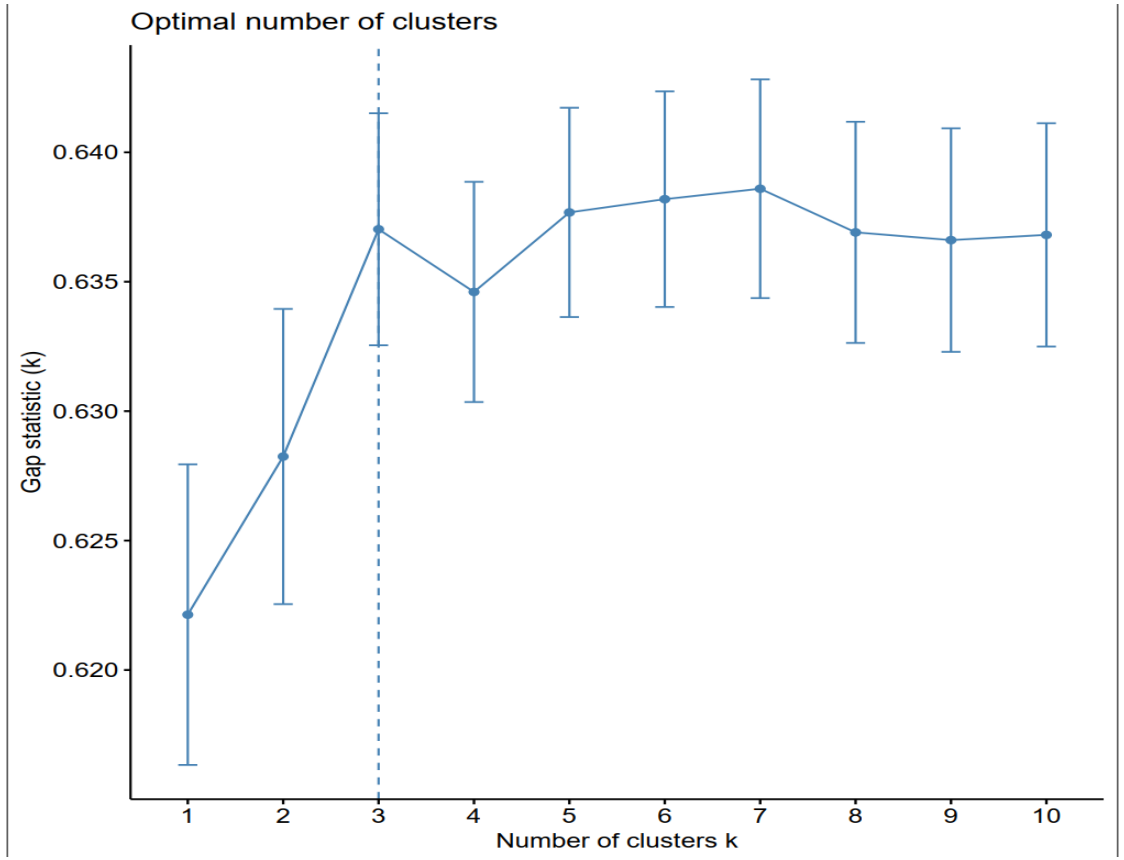
The Cancer Genome Atlas Program (TCGA)



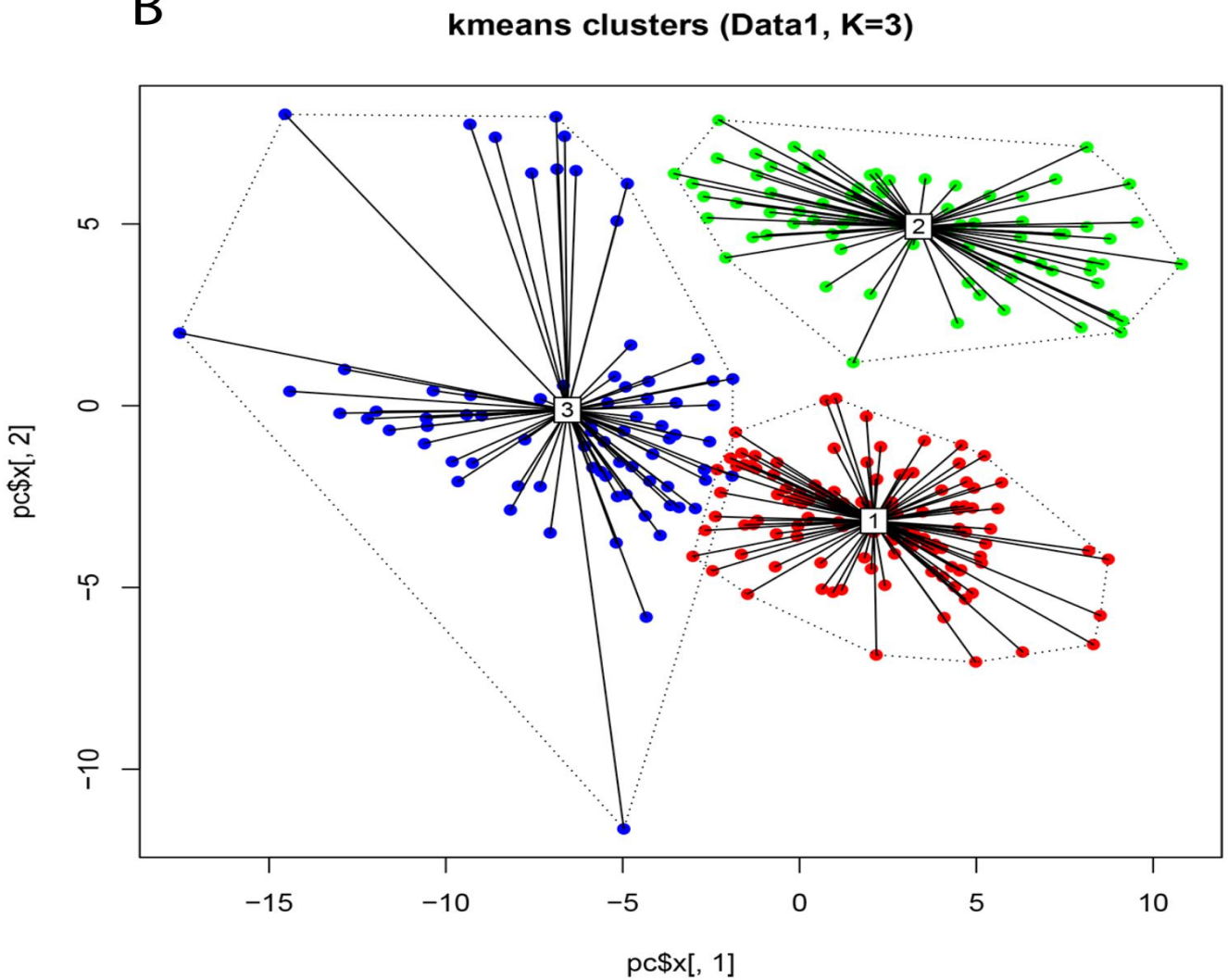
Pipeline



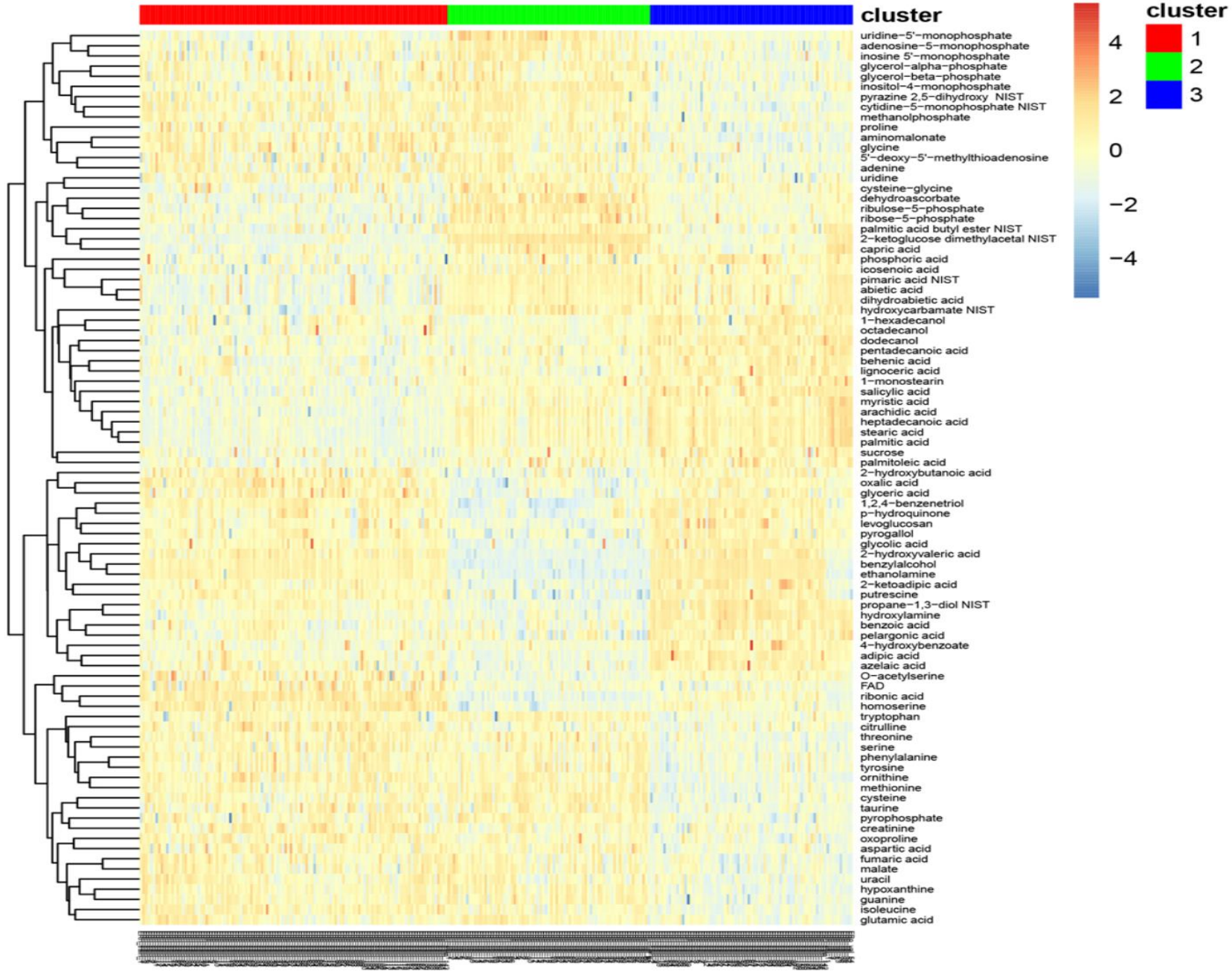
- Tools: K-means, SAM, PAM
- https://github.com/FADHLyemen/Metabolomics_signature

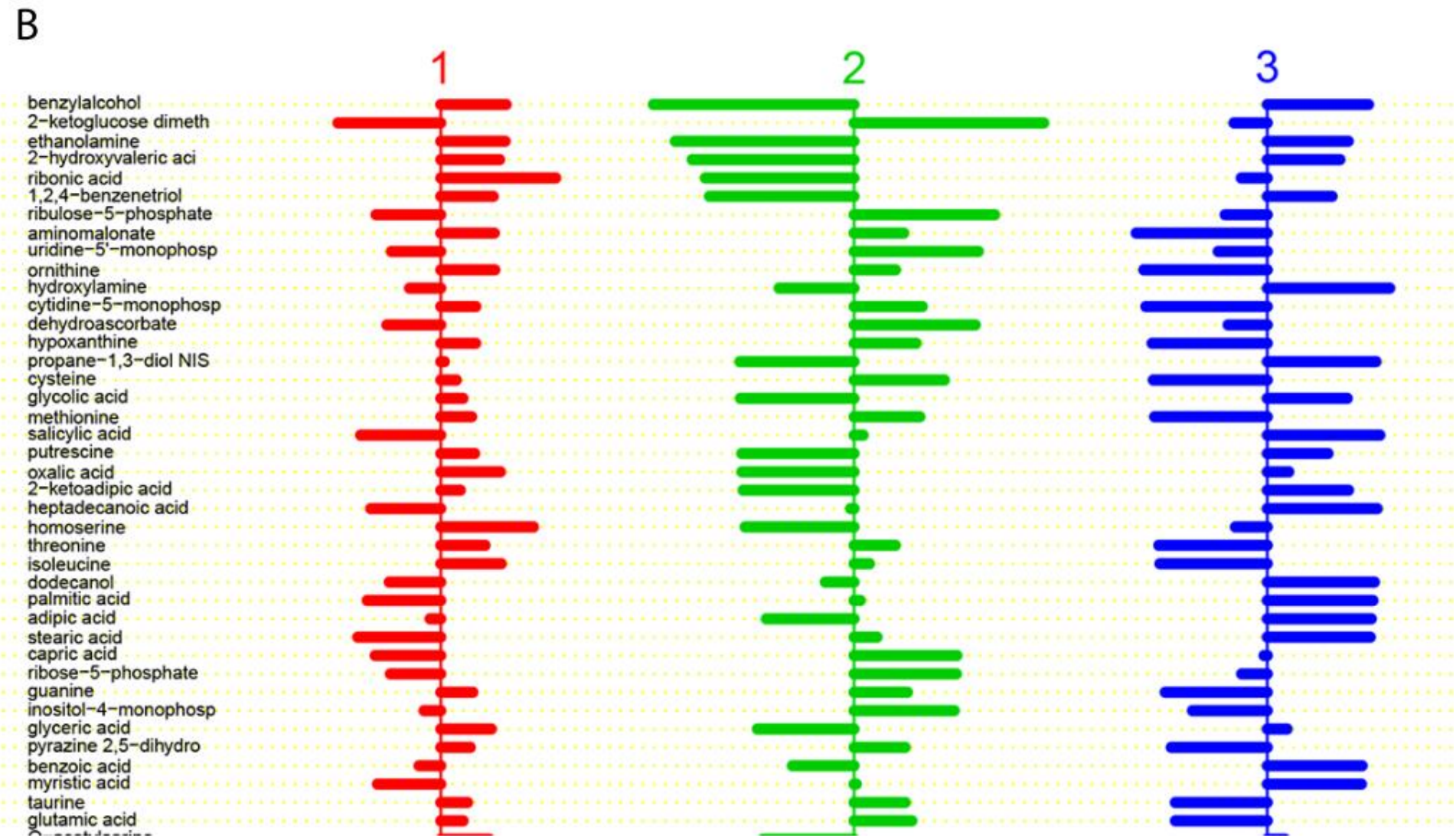

Optimal number of clusters
Gap statistic (k)
0.640
0.635
0.630
0.625
0.620
1
2
3
4
5
6
7
8
9
10
Number of clusters k

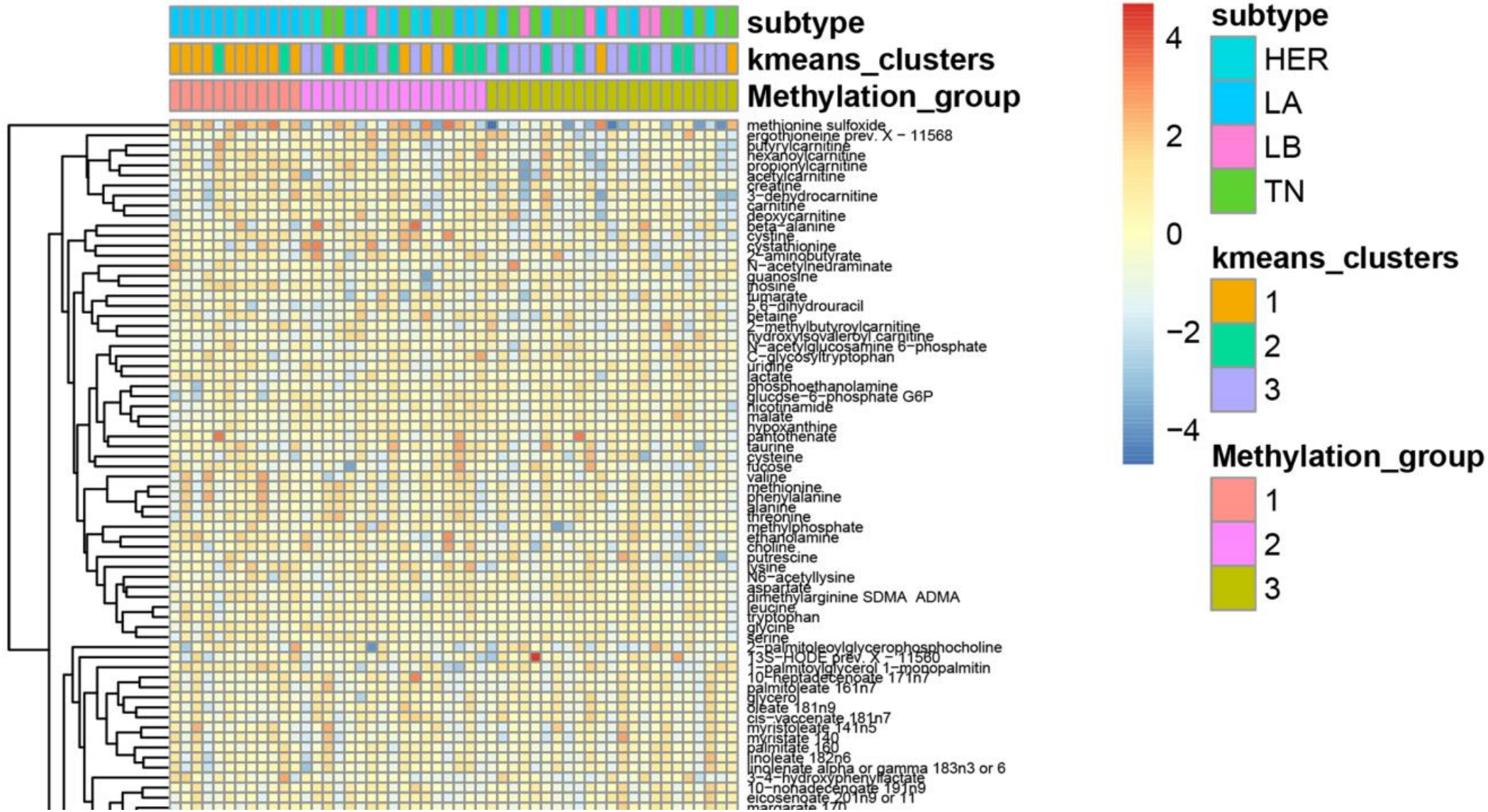
B


kmeans clusters (Data1, K=3)
pc$x[, 2]
5
0
−5
−10
−15
−10
−5
0
5
10
pc$x[, 1]
1
2
3

D

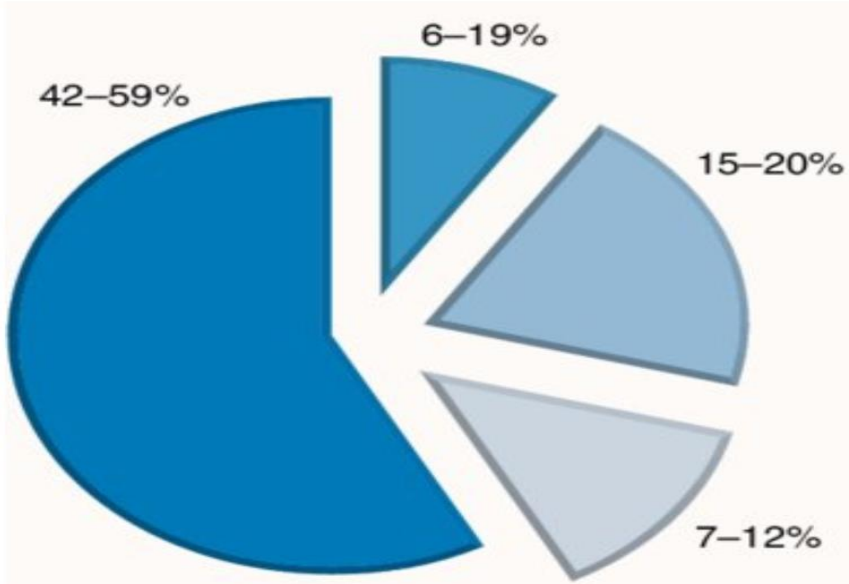

cluster
uridine−5'−monophosphate
adenosine−5−monophosphate
inosine 5'−monophosphate
glycerol−alpha−phosphate
glycerol−beta−phosphate
inositol−4−monophosphate
pyrazine 2,5−dihydroxy NIST
cytidine−5−monophosphate NIST
methanolphosphate
proline
aminomalonate
glycine
5'−deoxy−5'−methylthioadenosine
adenine
uridine
cysteine−glycine
dehydroascorbate
ribulose−5−phosphate
ribose−5−phosphate
palmitic acid butyl ester NIST
2−ketoglucose dimethylacetal NIST
capric acid
phosphoric acid
icosenoic acid
pimaric acid NIST
abietic acid
dihydroabietic acid
hydroxycarbamate NIST
1−hexadecanol
octadecanol
dodecanol
pentadecanoic acid
behenic acid
lignoceric acid
1−monostearin
salicylic acid
myristic acid
arachidic acid
heptadecanoic acid
stearic acid
palmitic acid
sucrose
palmitoleic acid
2−hydroxybutanoic acid
oxalic acid
glyceric acid
1,2,4−benzenetriol
p−hydroquinone
levoglucosan
pyrogallol
glycolic acid
2−hydroxyvaleric acid
benzylalcohol
ethanolamine
2−ketoadipic acid
putrescine
propane−1,3−diol NIST
hydroxylamine
benzoic acid
pelargonic acid
4−hydroxybenzoate
adipic acid
azelaic acid
O−acetylserine
FAD
ribonic acid
homoserine
tryptophan
citrulline
threonine
serine
phenylalanine
tyrosine
ornithine
methionine
cysteine
taurine
pyrophosphate
creatinine
oxoproline
aspartic acid
fumaric acid
malate
uracil
hypoxanthine
guanine
isoleucine
glutamic acid
4
2
0
−2
−4
cluster
1
2
3


B
1
2
3
benzylalcohol
2−ketoglucose dimeth
ethanolamine
2−hydroxyvaleric aci
ribonic acid
1,2,4−benzenetriol
ribulose−5−phosphate
aminomalonate
uridine−5'−monophosp
ornithine
hydroxylamine
cytidine−5−monophosp
dehydroascorbate
hypoxanthine
propane−1,3−diol NIS
cysteine
glycolic acid
methionine
salicylic acid
putrescine
oxalic acid
2−ketoadipic acid
heptadecanoic acid
homoserine
threonine
isoleucine
dodecanol
palmitic acid
adipic acid
stearic acid
capric acid
ribose−5−phosphate
guanine
inositol−4−monophosp
glyceric acid
pyrazine 2,5−dihydro
benzoic acid
myristic acid
taurine
glutamic acid


subtype
kmeans_clusters
Methylation_group
methionine sulfoxide
ergothioneine prev. X − 11568
butyrylcarnitine
hexanoylcarnitine
propionylcarnitine
acetylcarnitine
creatine
3−dehydrocarnitine
carnitine
deoxycarnitine
beta−alanine
cystine
cystathionine
2−aminobutyrate
N−acetylneuraminate
guanosine
inosine
fumarate
5,6−dihydrouracil
betaine
2−methylbutyroylcarnitine
hydroxyisovaleroyl carnitine
N−acetylglucosamine 6−phosphate
C−glycosyltryptophan
uridine
lactate
phosphoethanolamine
glucose−6−phosphate G6P
nicotinamide
malate
hypoxanthine
pantothenate
taurine
cysteine
fucose
valine
methionine
phenylalanine
alanine
threonine
methylphosphate
ethanolamine
choline
putrescine
lysine
N6−acetyllysine
aspartate
dimethylarginine SDMA ADMA
leucine
tryptophan
glycine
serine
2−palmitoleoylglycerophosphocholine
13S−HODE prev. X − 11580
1−palmitoylglycerol 1−monopalmitin
10−heptadecenoate 171n7
palmitoleate 161n7
glycerol
oleate 181n9
cis−vaccenate 181n7
myristoleate 141n5
myristate 140
palmitate 160
linoleate 182n6
linolenate alpha or gamma 183n3 or 6
3−4−hydroxyphenyllactate
10−nonadecenoate 191n9
eicosenoate 201n9 or 11
margarate 170
4
2
0
−2
−4
subtype
HER
LA
LB
TN
kmeans_clusters
1
2
3
Methylation_group
1
2
3

Conclusion

- Generally, metabolome-defined BC subtypes were different from the well-known receptor- or transcriptome-defined subtypes.
- We identified a strong association BC clusters identified from metabolomics and methylation data.
- Our proposed pipeline revealed clusters characterized by unique metabolic signatures that may potentially stratify BC patients and tailor precision treatment.



Targets and tasks

- Hampering of insulin resistance (metabolic syndrome)-related manifestations
- Inhibition of proliferation and stimulation of apoptosis
- Restoration of tumor tissue hormonal sensitivity
- Optimization of DNA repair process and cellular immunity

Luminal A | Luminal B | TNBC | HER2+

The tumor subtypes are classified as†:

Luminal A:	ER+ and/or PR+, HER2-, low Ki67
Luminal B:	ER+ and/or PR+, HER2+ (or HER2- with high Ki67)
TNBC:	ER-, PR-, HER2- cytokeratin 5/6+ and/or HER1(EGFR)+
HER2+:	ER-, PR-, HER2+

†These are the most common profiles for each subtype. However, not all tumors within each subtype will have all these features.
TNBC: Triple-negative breast cancer.
Adapted from [102].