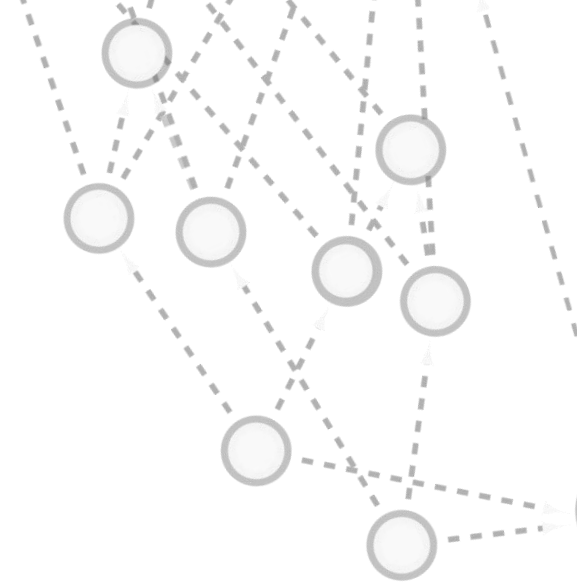




Utrecht University

*dept. Biochemistry & Cell Biology
faculty of Veterinary Medicine*



LION/web:

a web-based ontology enrichment
tool for lipidomic data analysis

Martijn Molenaar

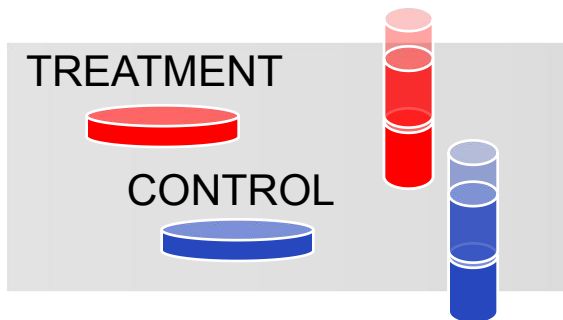
Typical lipidomics workflow

samples

extraction

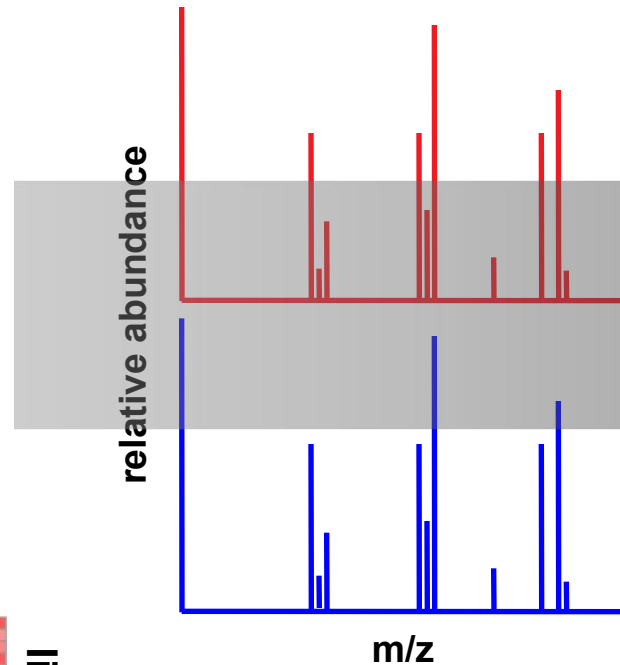
LC-MS

time-series of MS-spectra



treatment

control

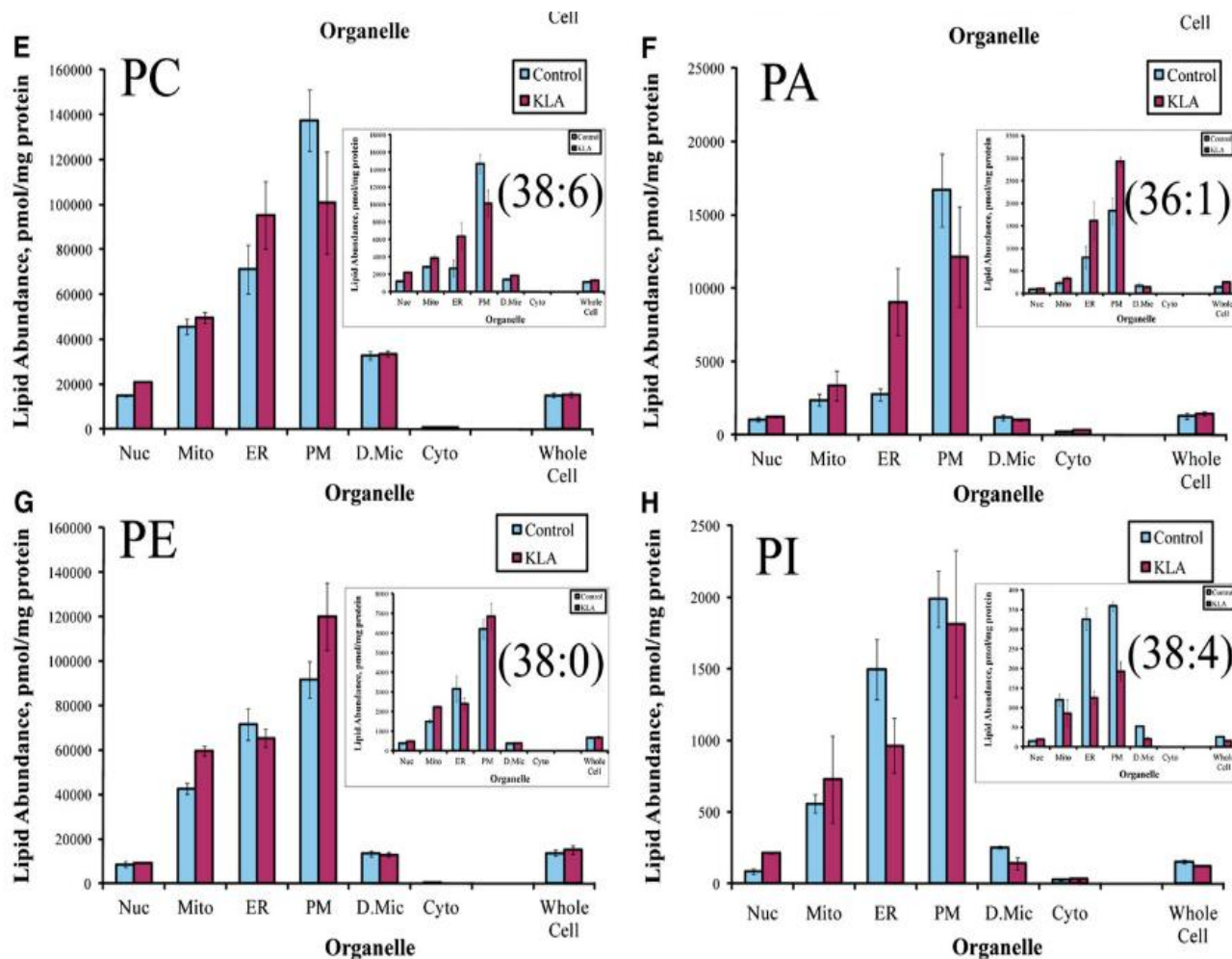


lipids

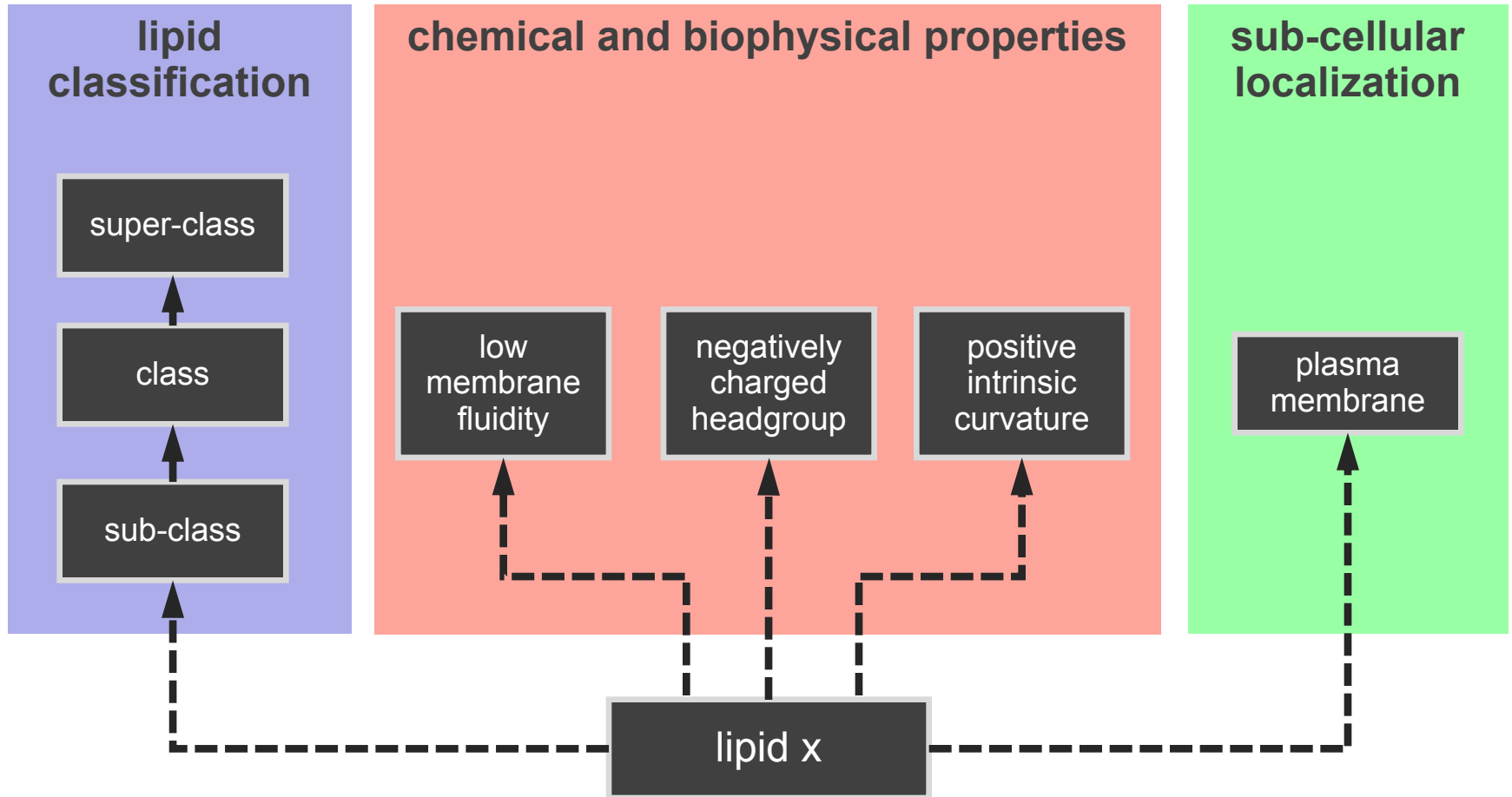


- deisotoping
- peak detection
- peak annotation

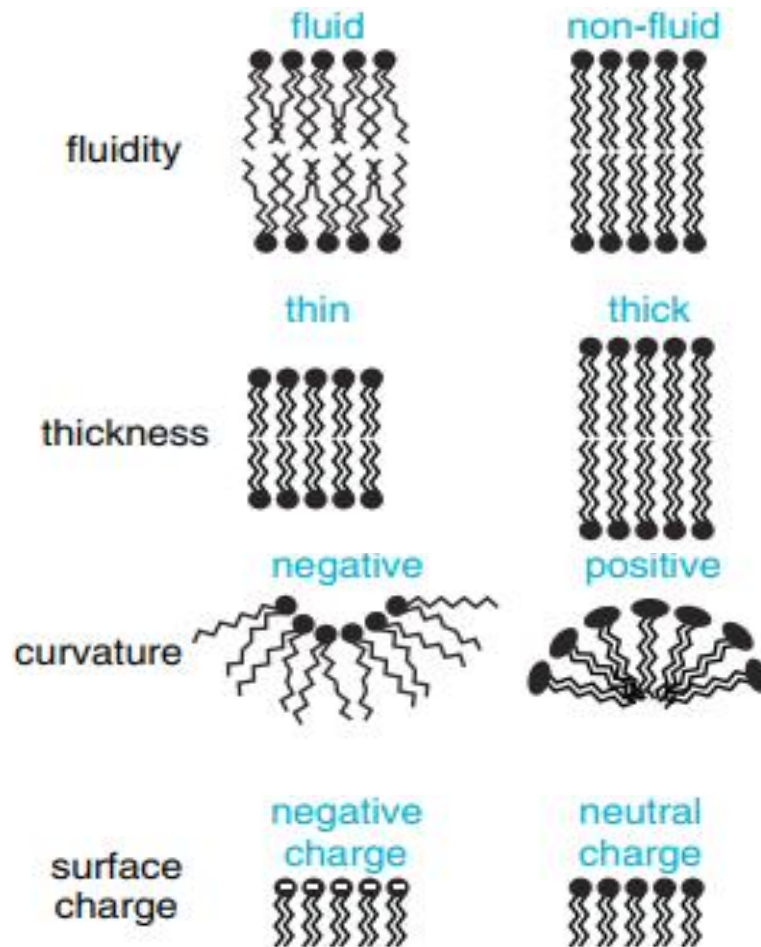
Reporting lipidomics data



Functional lipidomics



Functional lipidomics

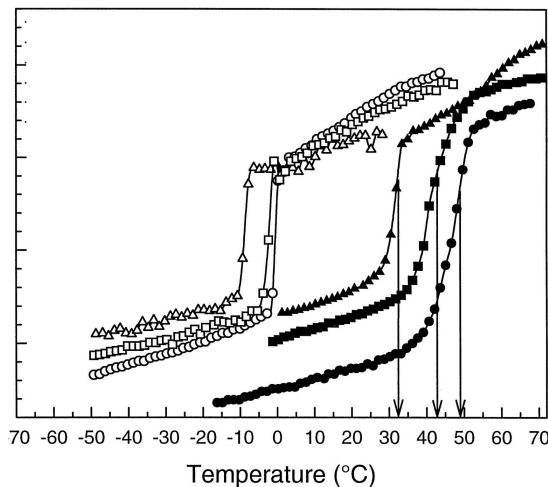


Adapted from:

Klose C, Surma MA, Simons K. **Organellar lipidomics--background and perspectives.** *Curr Opin Cell Biol.* 2013.

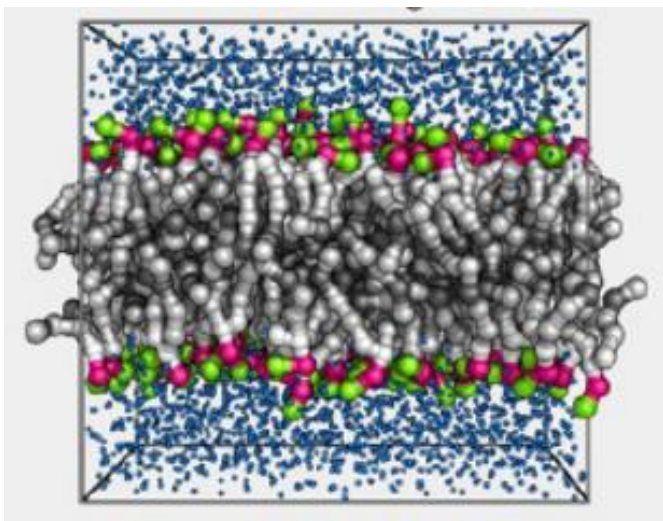
Functional lipidomics: sources

1 Experimental transition temperatures (T_m)



→ transition temperature

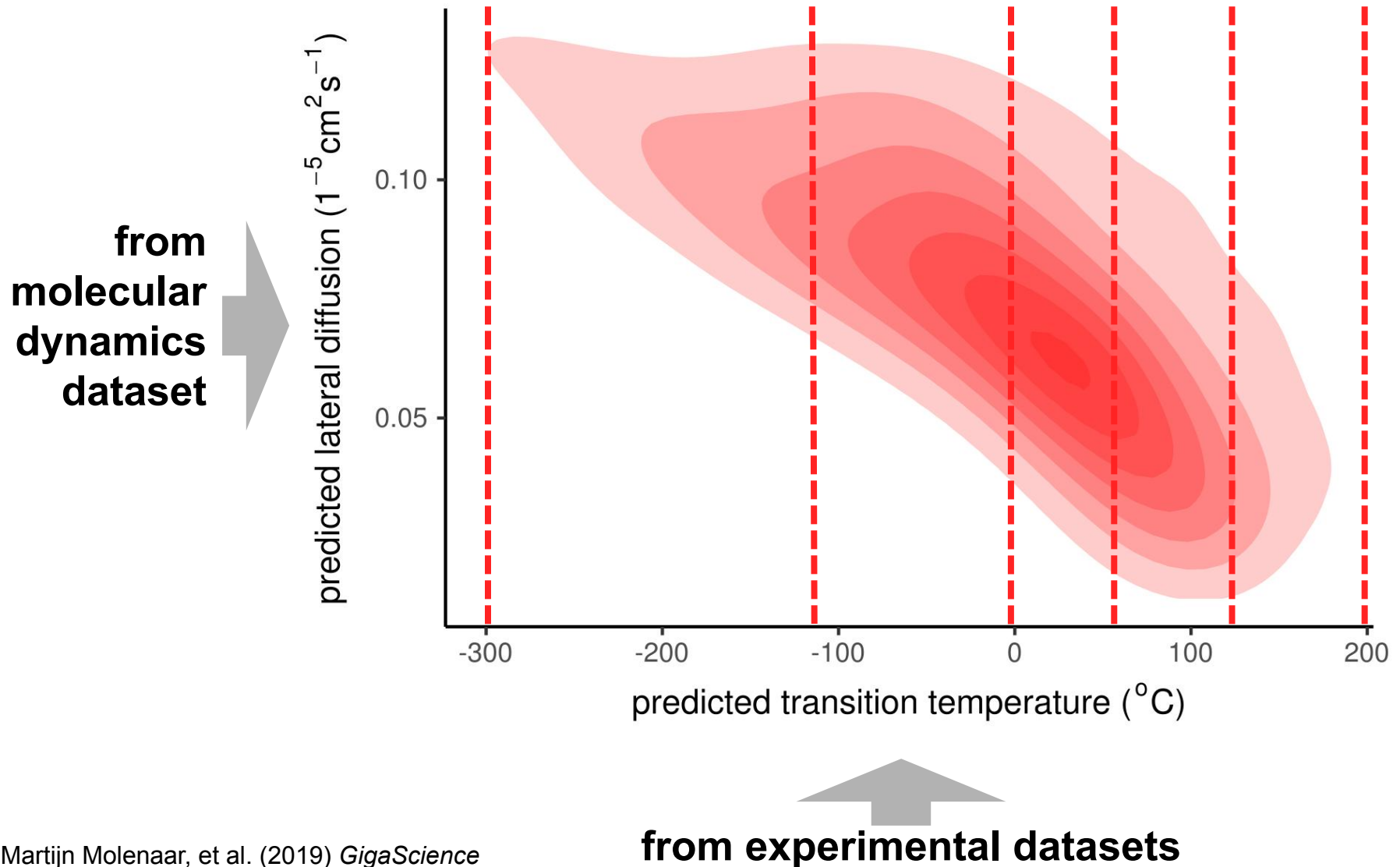
2 Coarse-grained Molecular Dynamics (MARTINI)



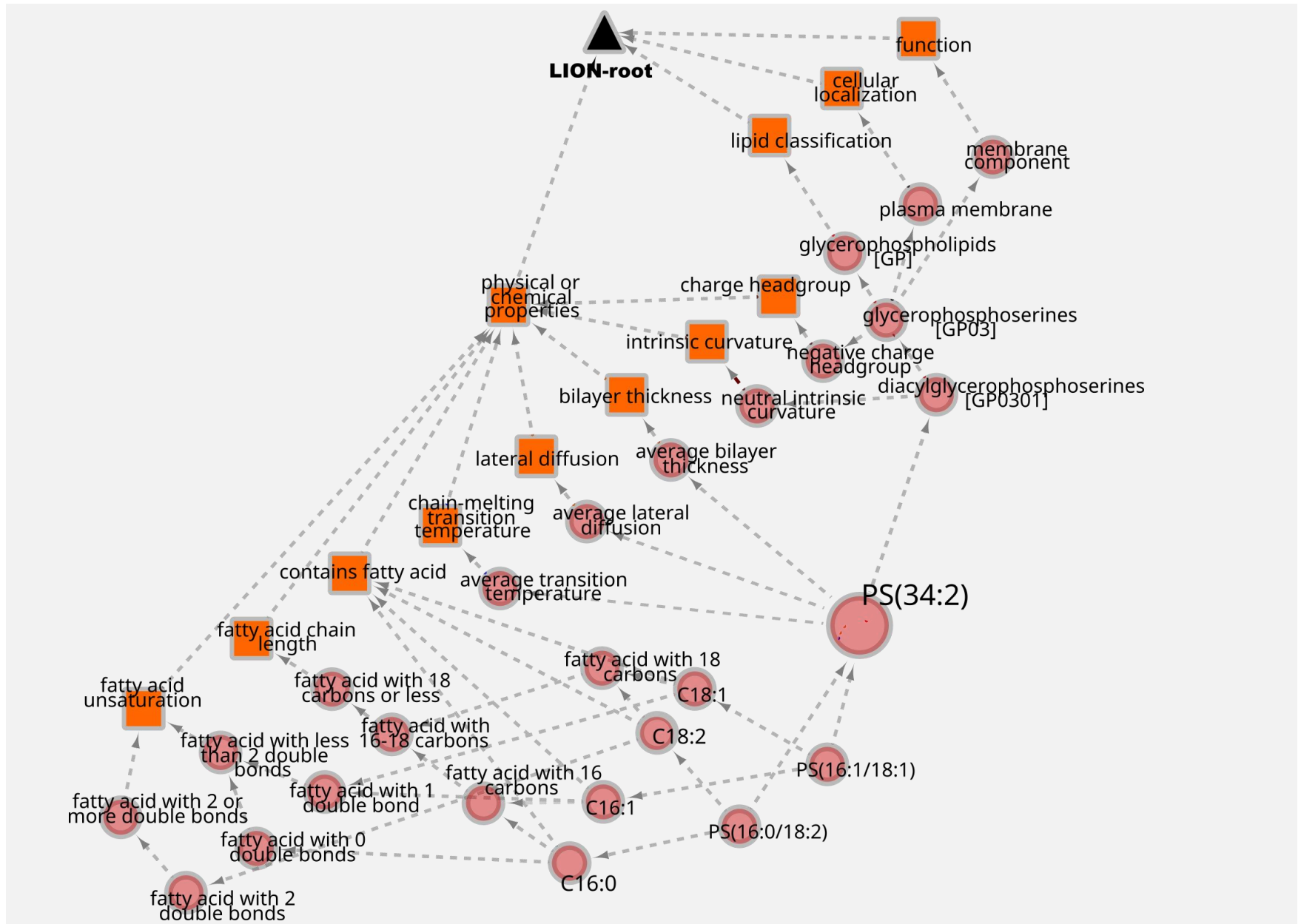
→ bilayer thickness

→ lateral diffusion

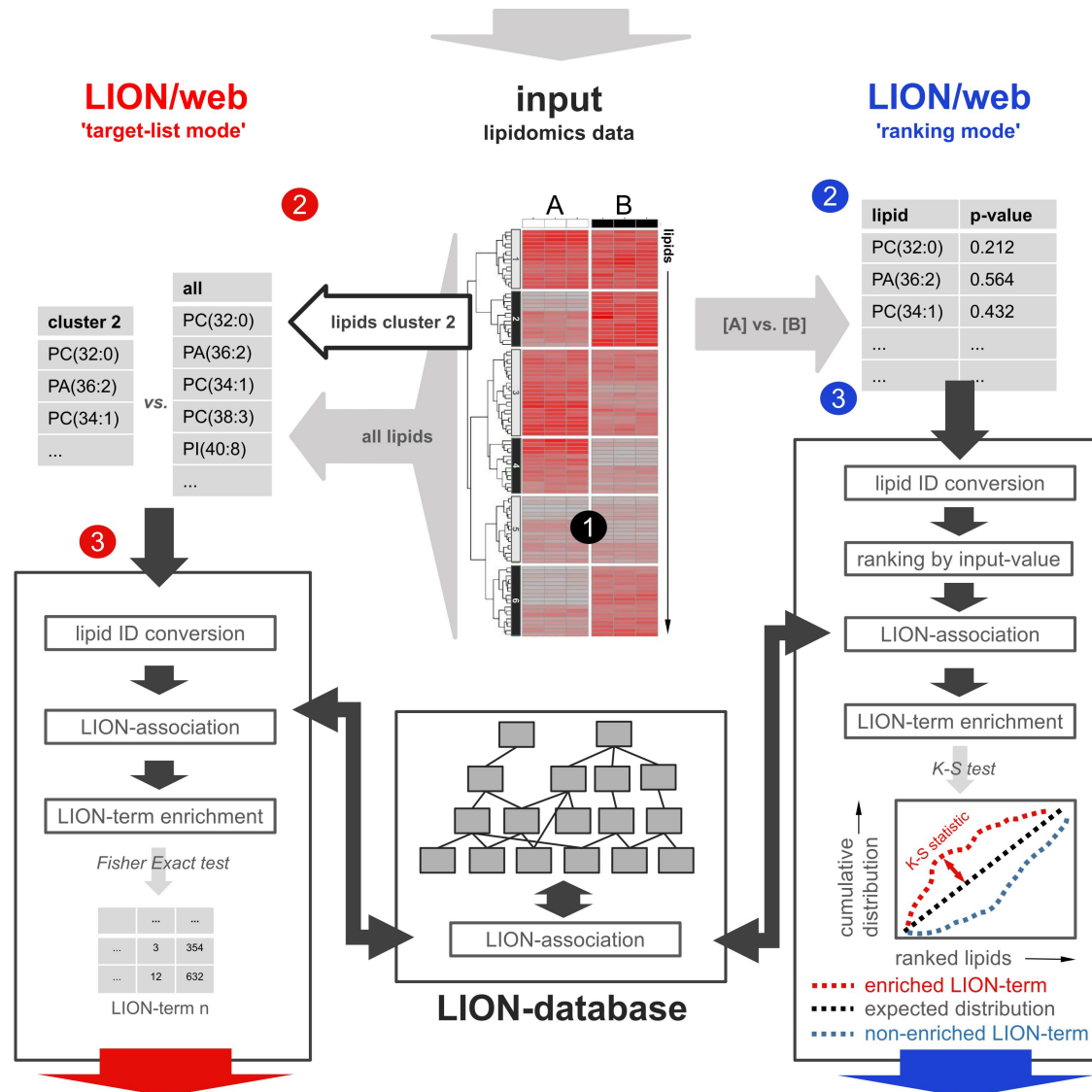
Functional lipidomics: membrane fluidity



Lipid Ontology: LION -- example of PS(34:2)



LION/web: a web-tool for LION enrichment



LION/web: a web-tool for LION enrichment

LION/web | Lipid Ontology enrichment analysis

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Ranking mode

Target-list mode

[Contact](#)

lipid target list:

GPA(30:1)
GPA(34:2)
GPA(36:2)
GPA(38:2)

lipid background list:

GPA(30:1)
GPA(30:0)
GPA(32:4)
GPA(32:1)
GPA(32:0)
GPA(34:2)
GPA(34:1)
GPA(34:0)
GPA(36:3)
GPA(36:2)
GPA(36:1)

Submit

example 1 (plasma membrane vs ER fraction)*
example 2 (mitochondrial fraction vs homogenate)*
example 3 (stimulated vs non-stimulated ER fractions)*

[General information](#)

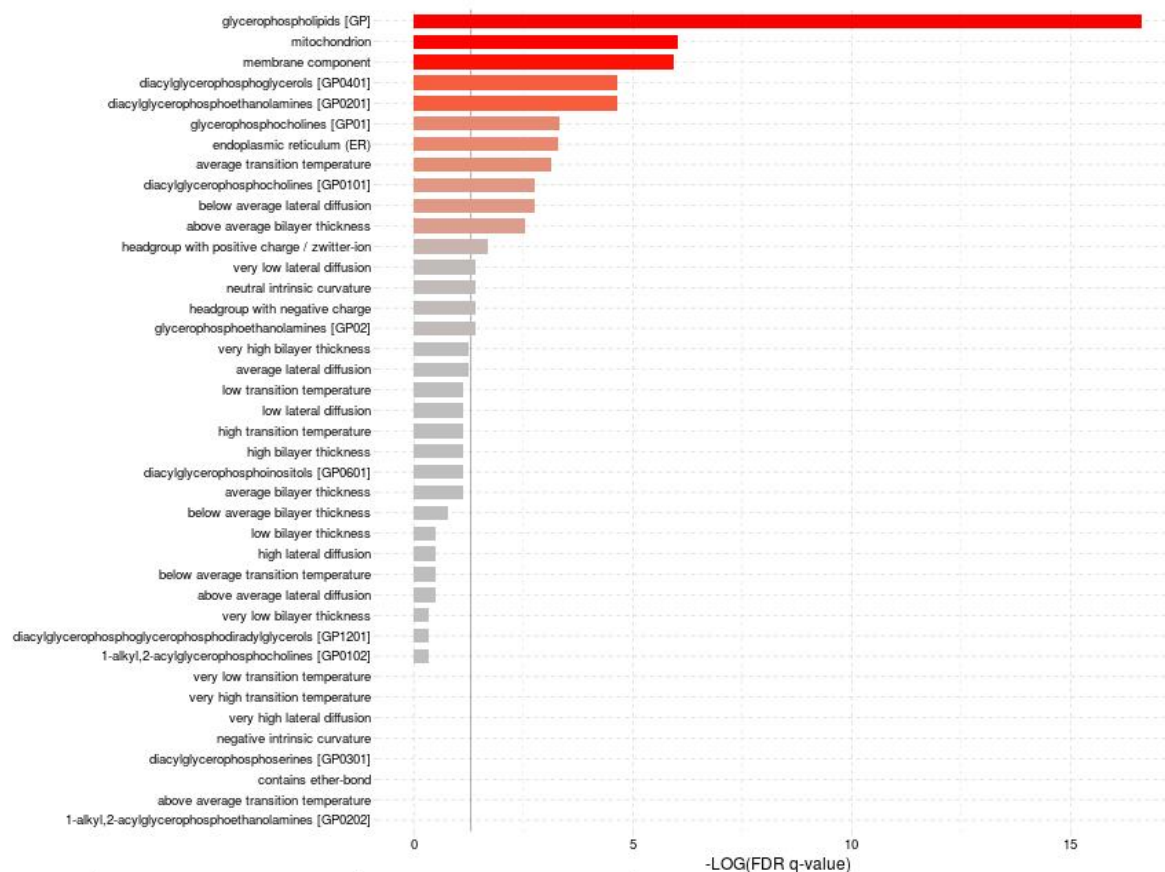
[LION input](#)

[LION enrichment table](#)

[LION enrichment graph](#)

[LION network view](#)

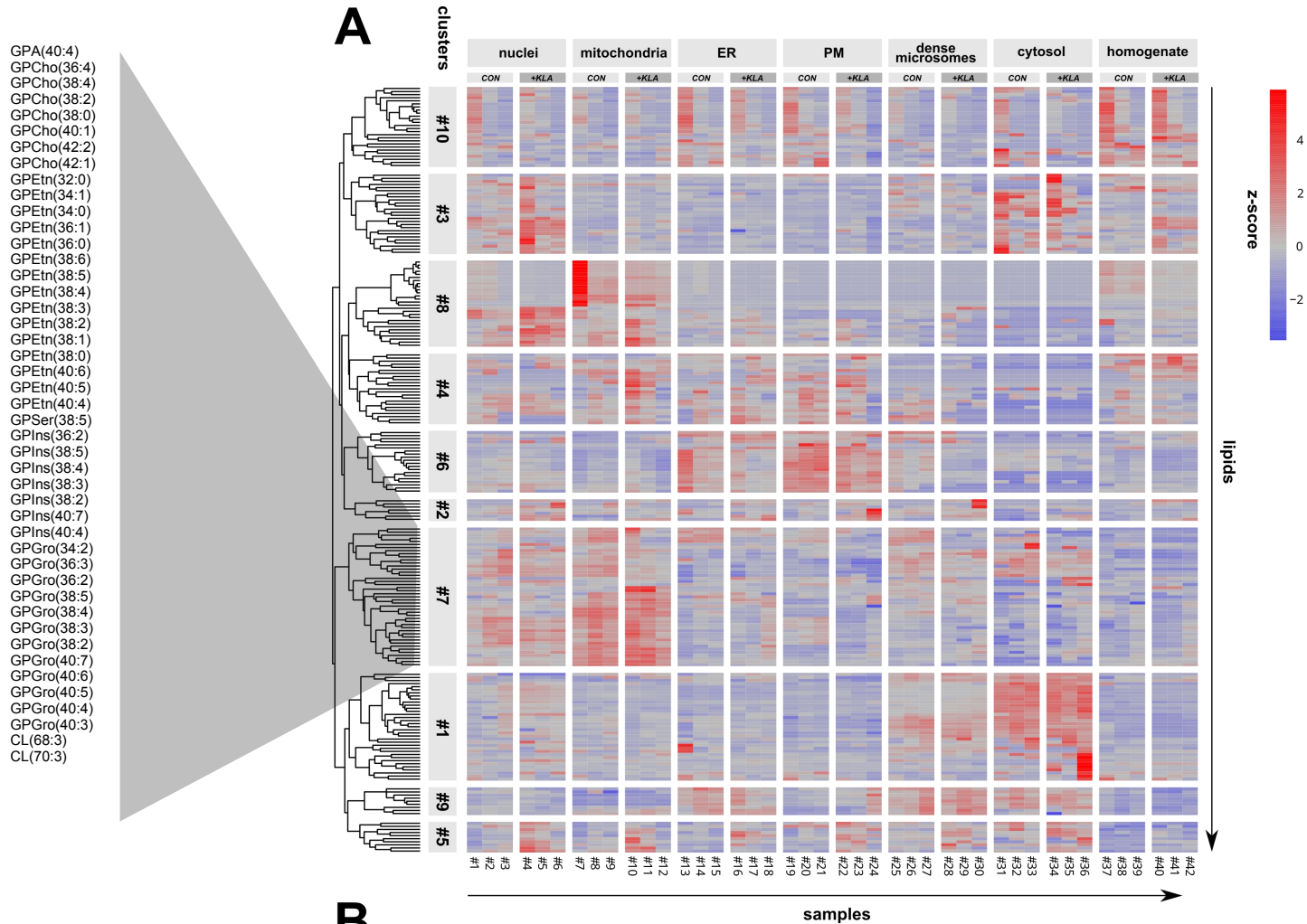
LION-term enrichment



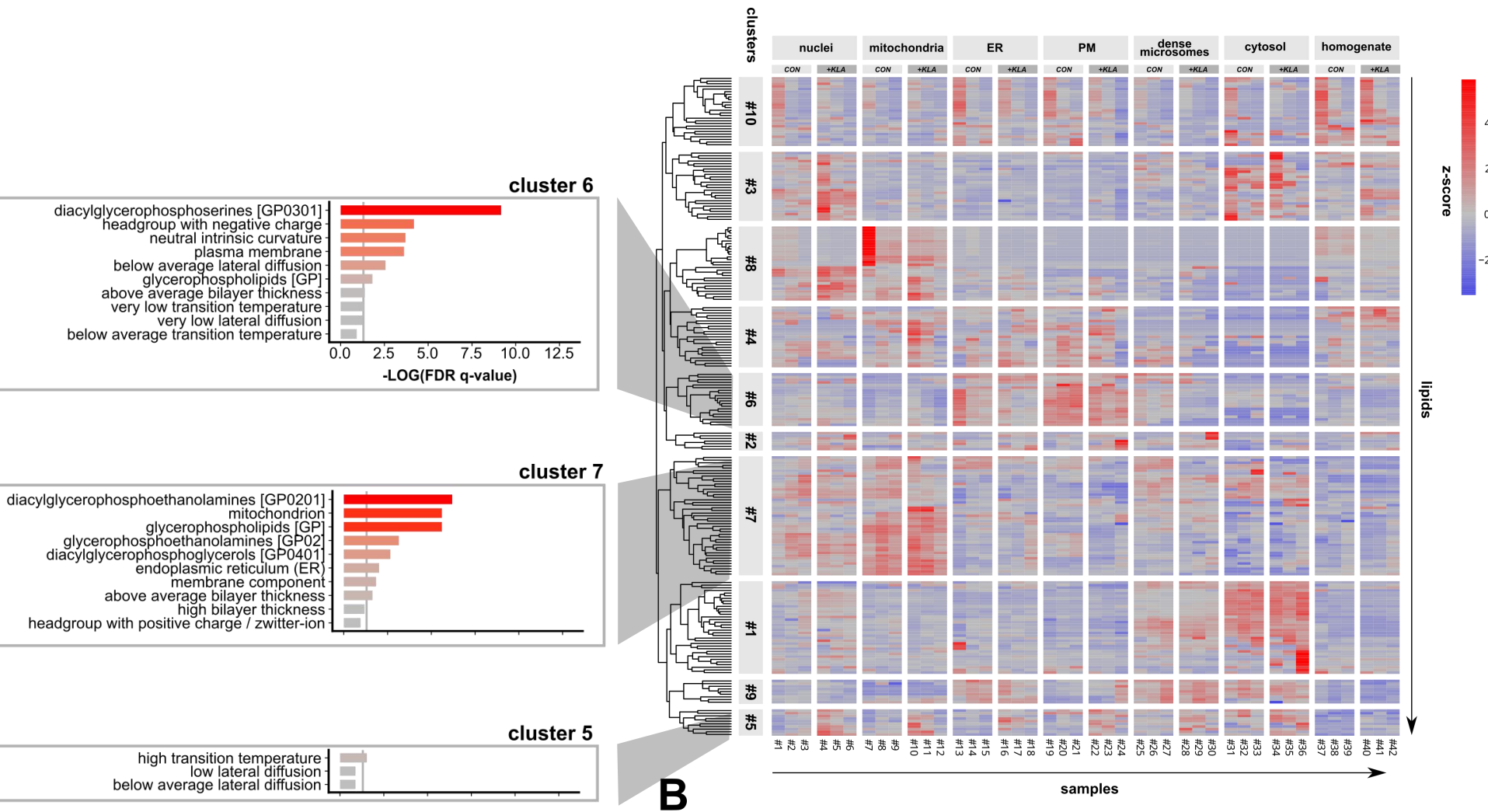
Download plot as SVG

Download plot as PNG

LION/web: a web-tool for LION enrichment



LION/web: a web-tool for LION enrichment



**>> there is a demand for user-friendly
lipidomics data analysis tools!**

summer 2018

**LION
enrichment
analysis**

spring 2019

**LION
heatmap**

sept 2019

**LION
pathway
analysis**

LION/web 2.0: pathway analysis

LION/web | Lipid Ontology path x +

← → ↻ ⚠ Not secure pathway.lipidontology.com

🇩🇪 psipred : sec struct... ☁ Clouds in Peel the... 🌐 Regular Expression... 📊 R ggplot2 cheatsh... 📄 apply indeces 📝 Scientific Writing 📁 Browse Sketches ... 📡 KaijinQ - OpenProc... 🏠 EMBO Funding & a... 🏠 Home — Publons 🌱 Metabolomics Bioi...

LION/web | Lipid Ontology

FAQ 📄 Report issues 🐦 @LipidOntology About

⚙ Pathway analysis Contact

Data upload Construct pathway

Select two conditions for pair-wise comparison

condition of interest control condition

24h AA 24h CON

Build network by adding links with LIONIDs

	from	found to	found
1	LION:0000030	59 LION:0000034	6
2	LION:0000034	6 LION:0000030	59
3	LION:0000030	59 LION:0000013	56
4	LION:0000030	59 LION:0000059	2
5	LION:0000030	59 LION:0000069	4
6	LION:0000030	59 LION:0000038	32
7	LION:0000069	4 LION:0000013	56
8	LION:0000013	56 LION:0000038	32
9	LION:0000059	2 LION:0000067	31
10	LION:0000069	4 LION:0000047	24
11	LION:0000047	24 LION:0000069	4
12	LION:0000030	59 LION:0000084	16
13	LION:0000084	16 LION:0000030	59
14	LION:0000084	16 LION:0000077	0
15	LION:0000077	0 LION:0000084	16
16	LION:0000077	0 LION:0012017	6
17	LION:0012017	6 LION:0012018	5
18	LION:0012018	5 LION:0012017	6
19	LION:0012017	6 LION:0000088	0

General information LION input LION pathway nodes LION pathway table LION pathway view

24h AA vs. 24h CON

activity score

■ -2
■ -1
■ 0
■ 1
■ 2
■ 3
■ 4
■ N/A

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16:12

Outlook

- Construction of lipid ontology (LION):
 - LIPIDMAPS classification
 - biophysical and chemical associations
 - predominant sub-cellular localizations
- LION enrichment analysis (LION/web):
 - <http://www.lipidontology.com/>
 - from lipid species to generalized LION-terms
 - publication-ready figures after analysis
 - increasing user-base
 - recently added new statistical modules

Acknowledgements



Utrecht University

*dept. Biochemistry & Cell Biology
faculty of Veterinary Medicine*

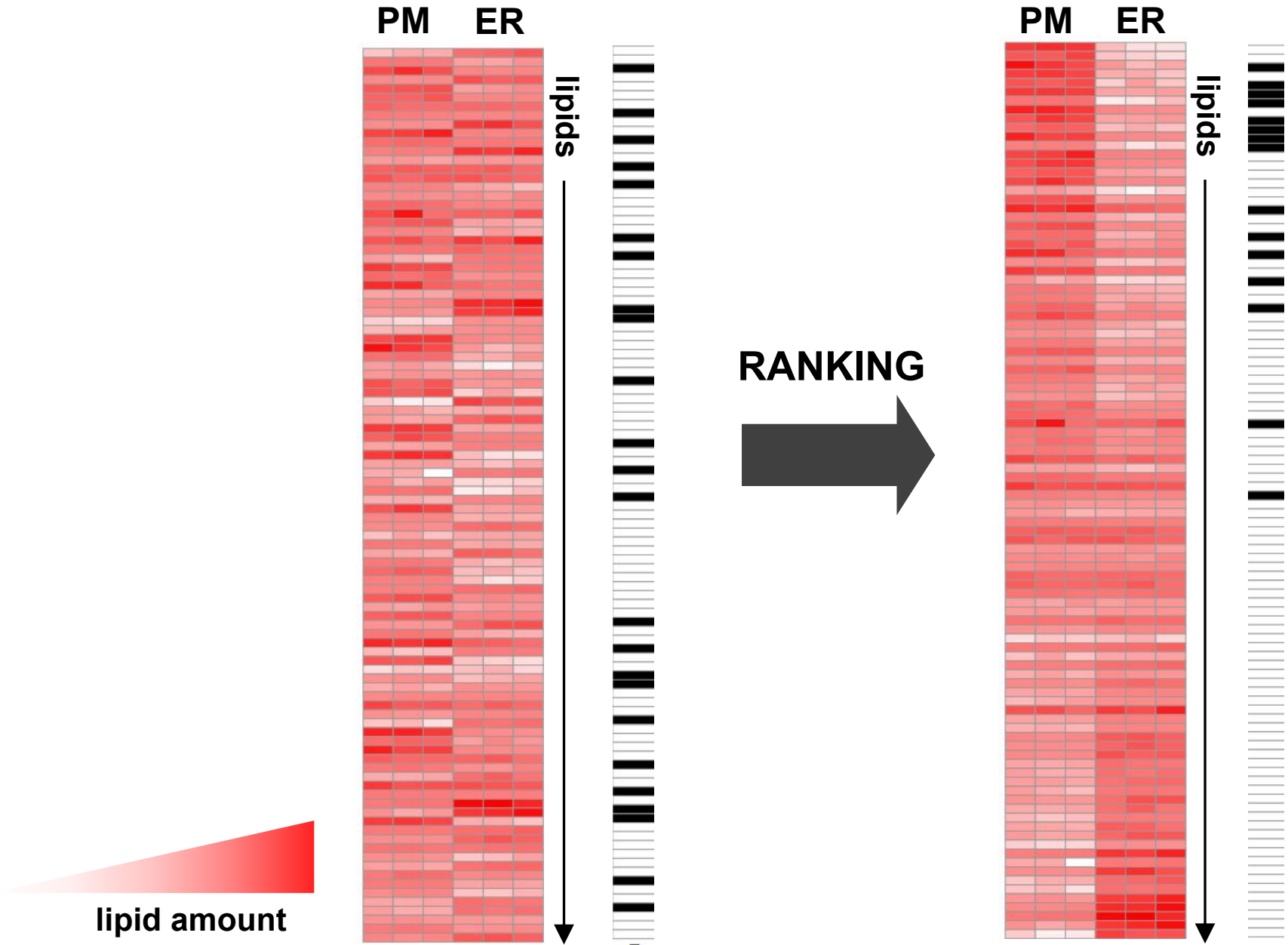
Aike Jeucken, MSc
ing. Jeroen Jansen
Chris van de Lest, PhD
Jos Brouwers, PhD
prof. dr. Bernd Helms



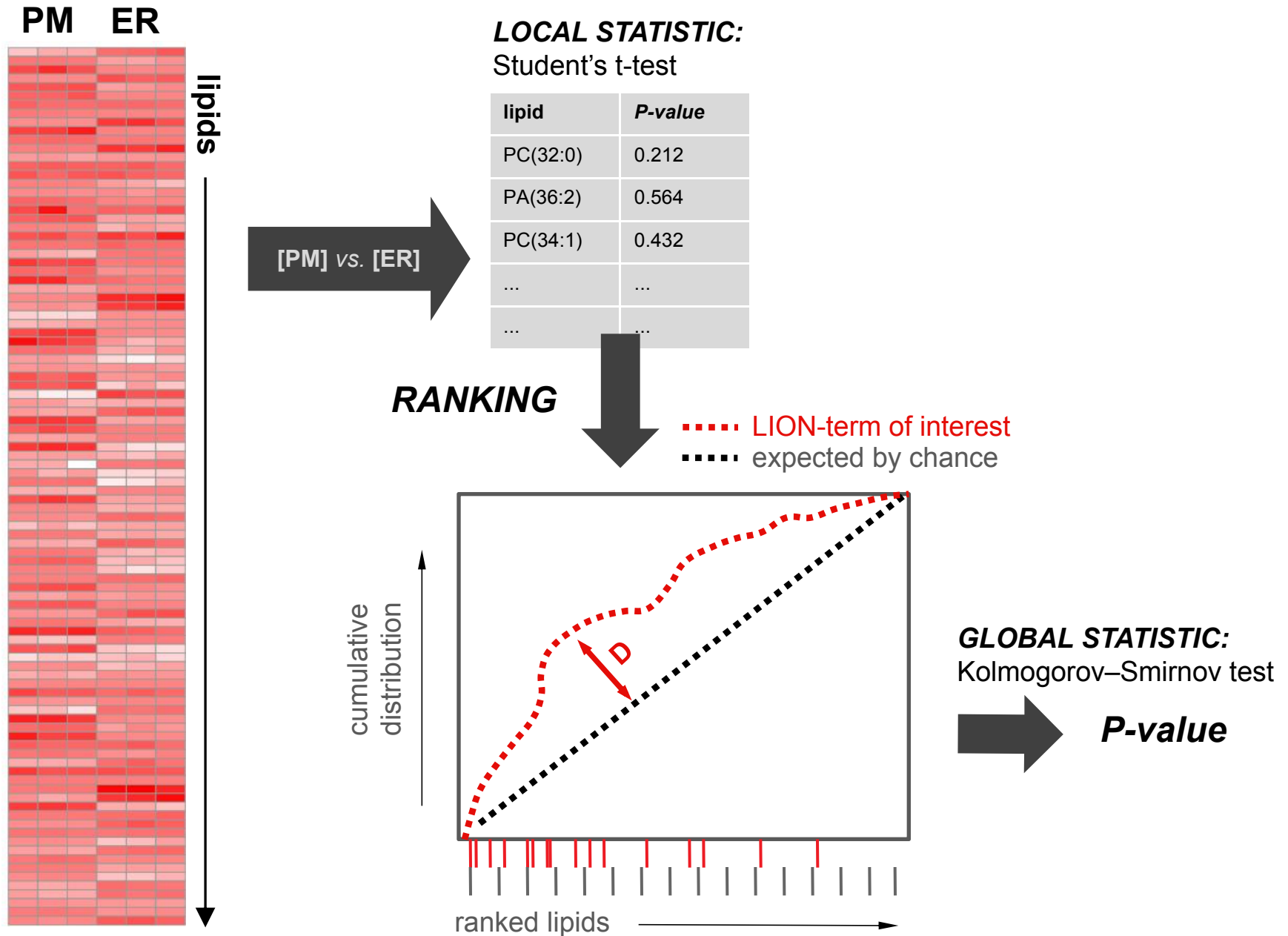
**rijksuniversiteit
 groningen**

Tsjerk Wassenaar, PhD

LION-enrichment by distribution



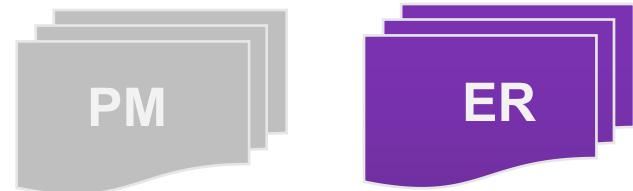
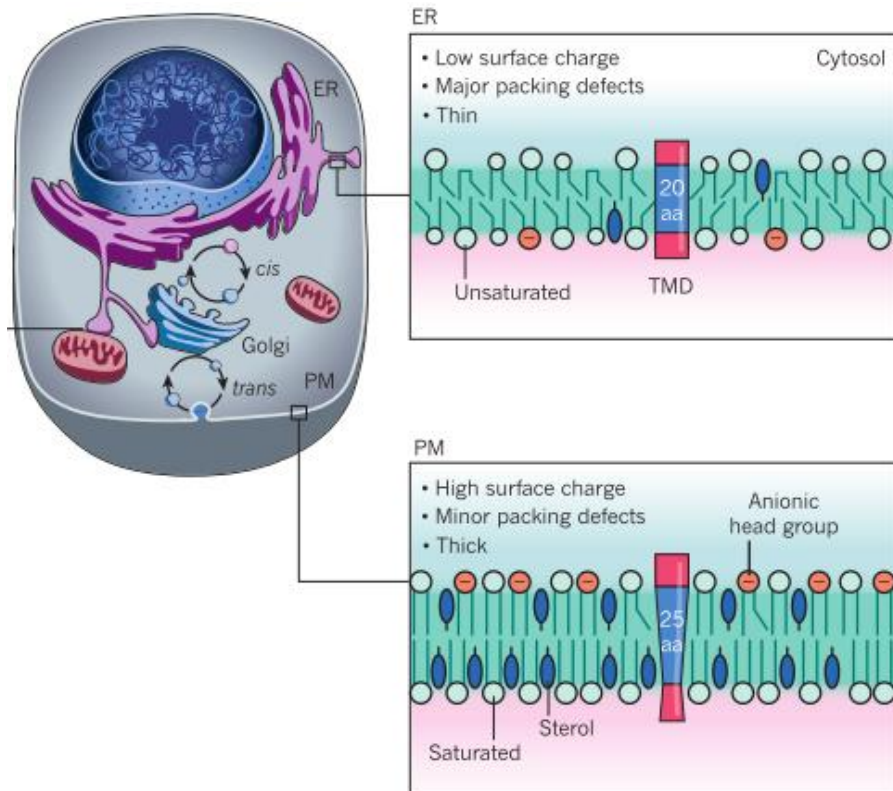
LION-enrichment by distribution



lipidomes PM vs. ER

Test case: *comparison lipidomic datasets of PM and ER*

Does LION/web report enrichment of terms associated with the mammalian plasma membrane?



dataset from:

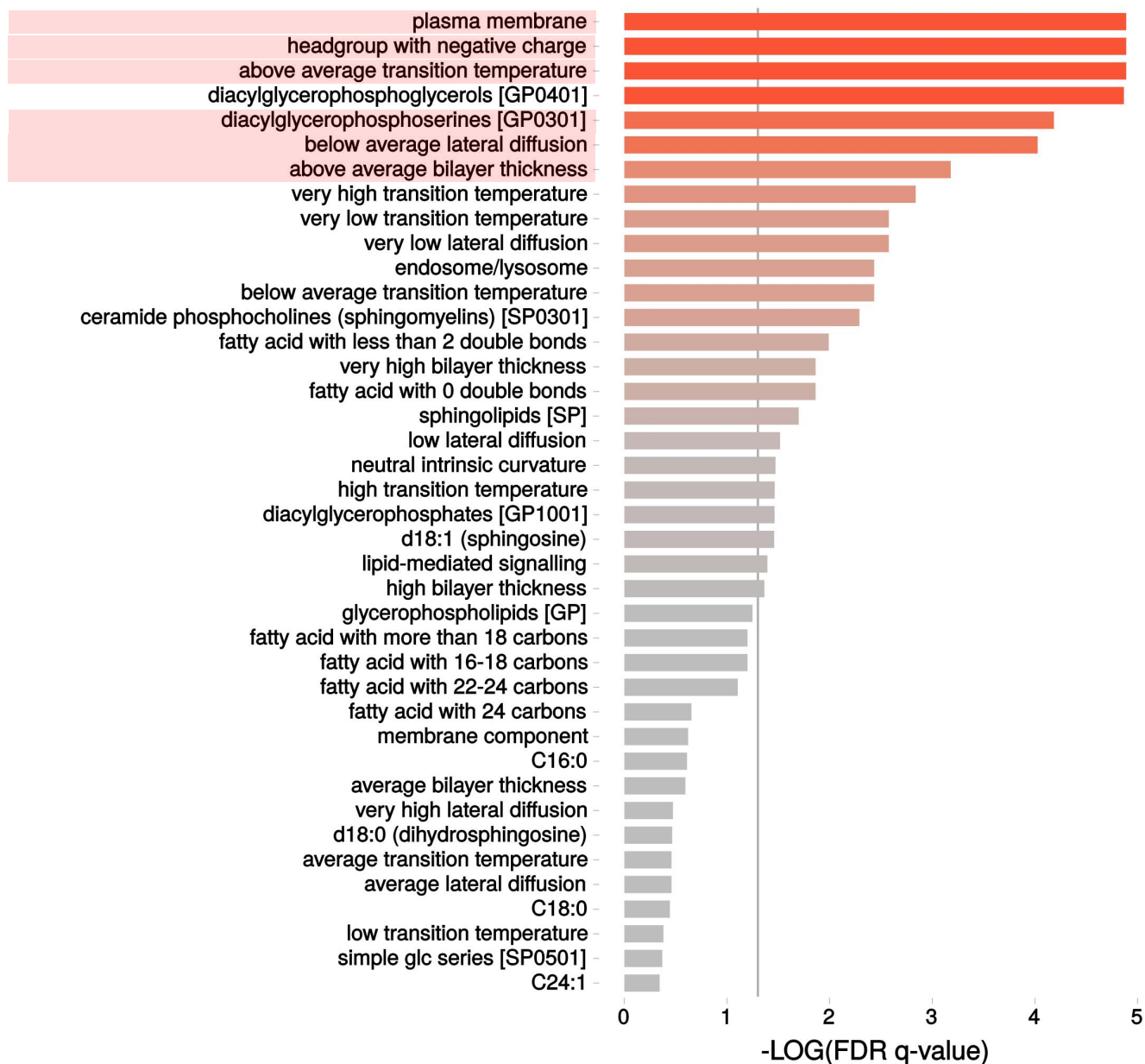
Andreyev AY *et al.* Subcellular organelle lipidomics in TLR-4-activated macrophages. *J Lipid Res.* 2010 Sep;51(9):2785-97.



LION/web

<http://www.lipidontology.com/>

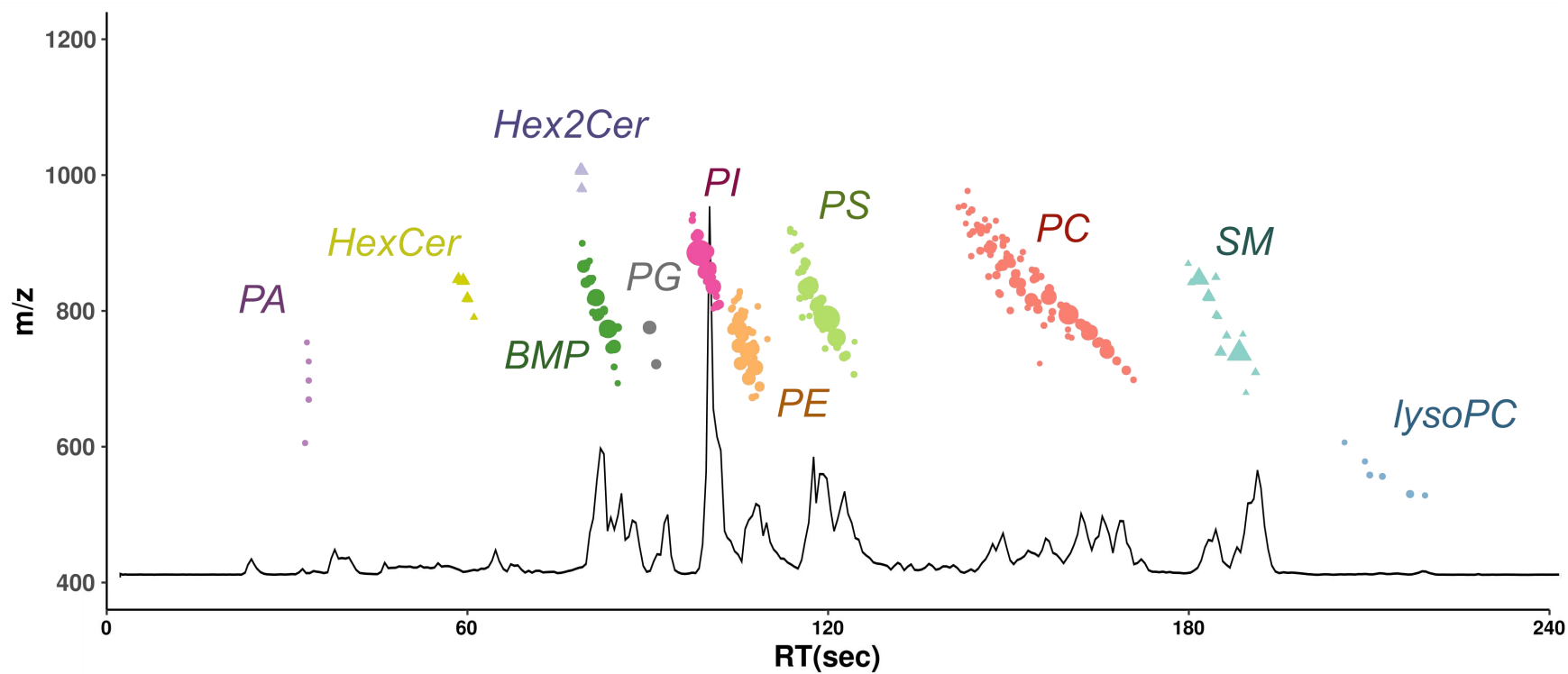
lipidomes PM vs. ER



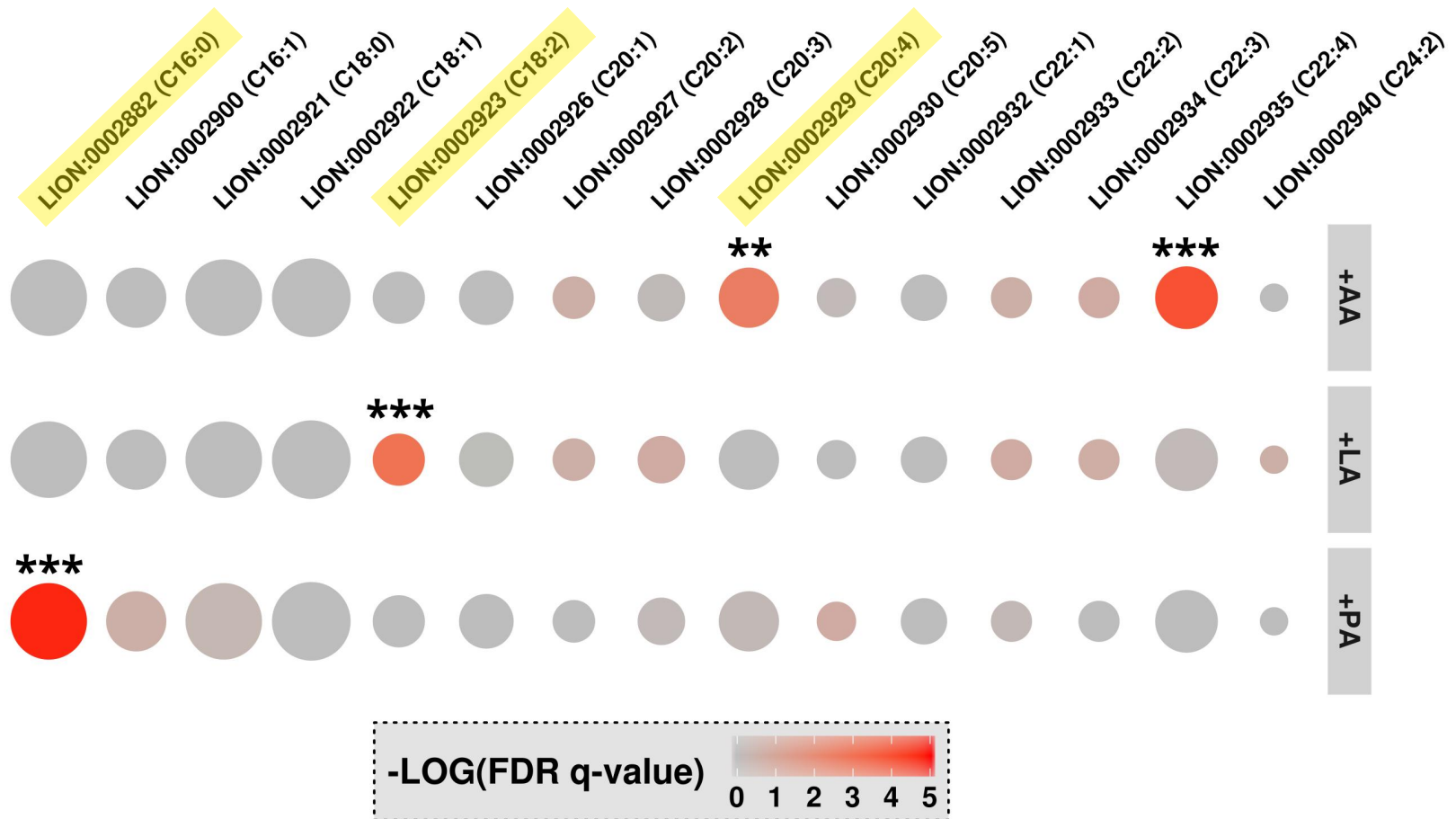
LION/web validation: +FFA

Experiment 1: *addition of free fatty acids 16:0, 18:2, 20:4 to CHO-k1 cells*

Does LION/web report enrichment of these FFAs?



LION/web validation: +FFA

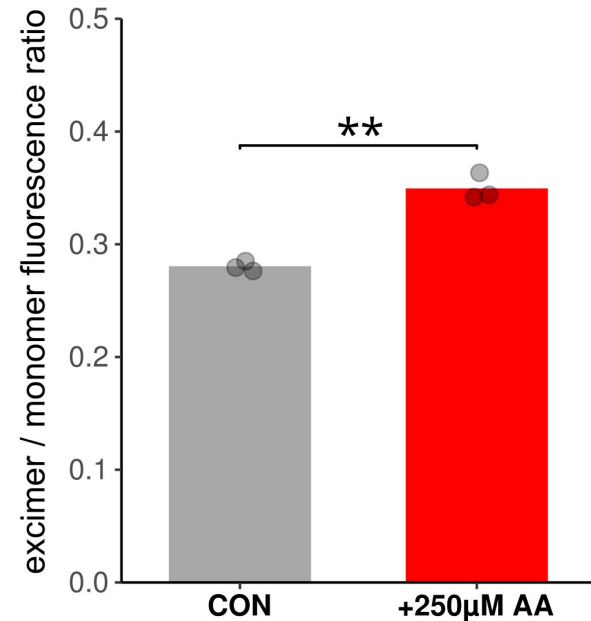
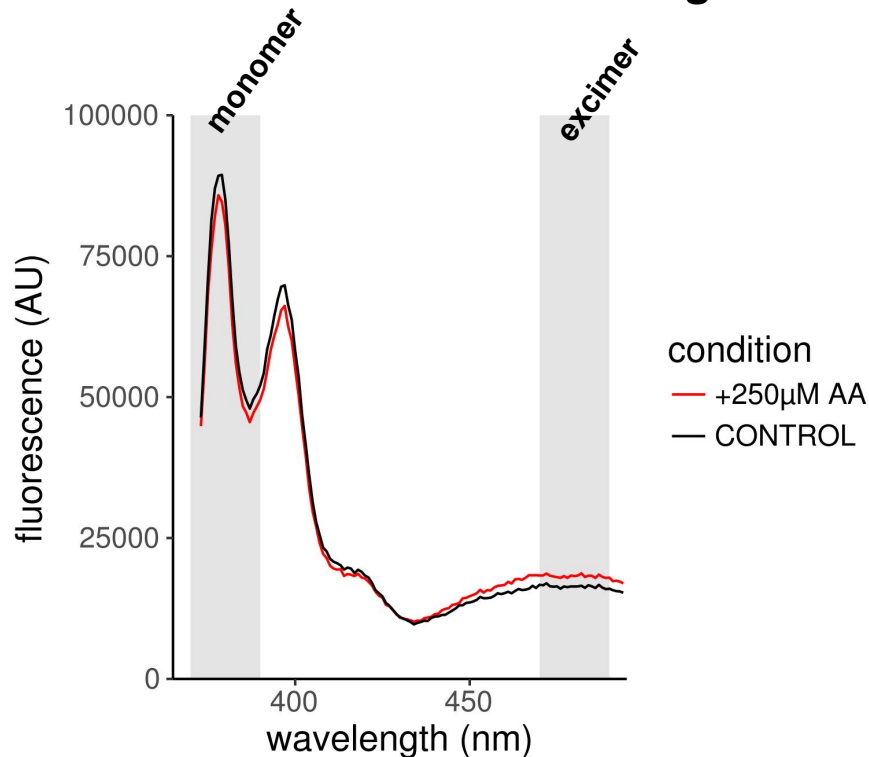


LION/web validation: membrane fluidity

Experiment 2: *addition of free fatty acid 20:4 to CHO-k1 cells to increase membrane fluidity*

Does LION/web report enrichment of terms associated with increased membrane fluidity?

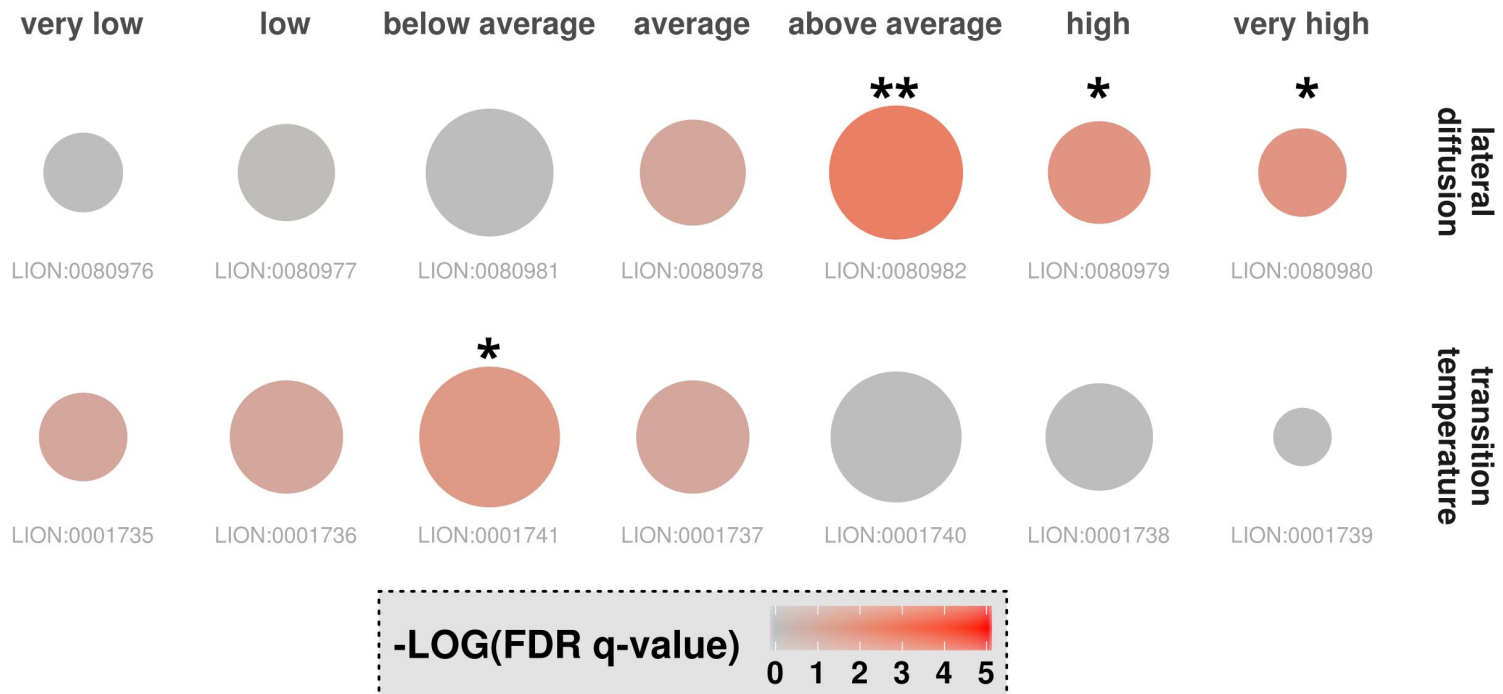
homogenates + pyrenedecanoic acid



LION/web validation: membrane fluidity

Experiment 2: *addition of free fatty acid 20:4 to CHO-k1 cells to increase membrane fluidity*

Does LION/web report enrichment of terms associated with increased membrane fluidity?



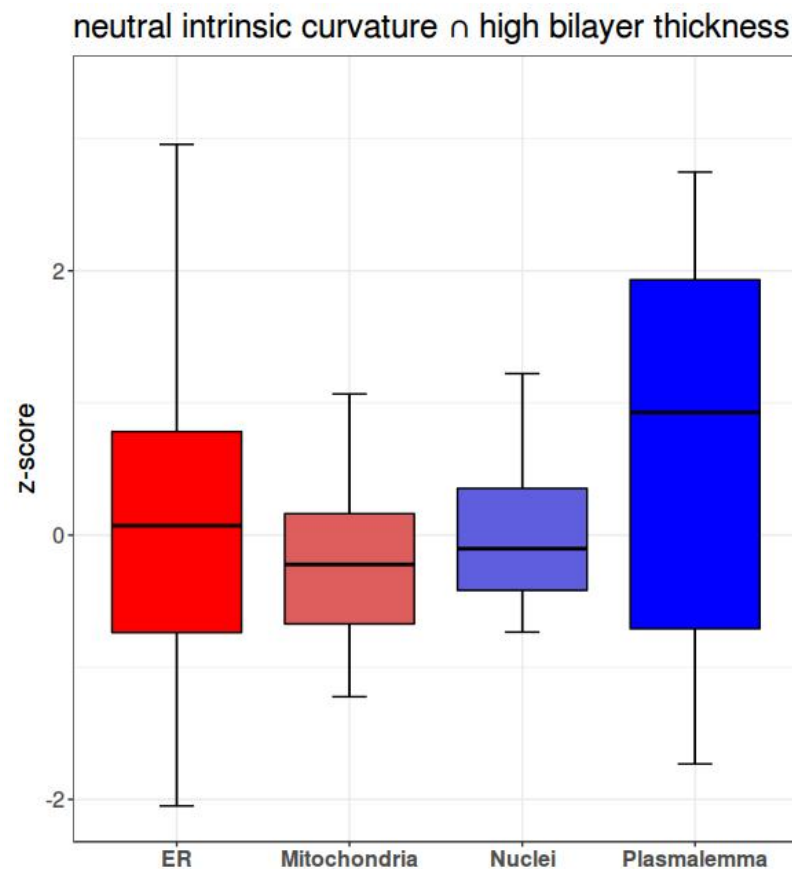
Lipid Ontology: LION -- in-depth lipid annotation

```
> lipidsInTerm(ORGANELLES) [[names(LIONTerms) [LIONTerms=="low bilayer thickness"]]]
[1] "PA(30:1)" "PA(38:5)" "PC(32:1)" "PC(32:2)" "PC(34:2)" "PC(34:3)" "PC(36:4)"
[8] "PC(38:5)" "PC(40:6)" "PC(40:7)" "PE(36:4)" "PE(38:6)" "PG(34:3)" "PG(36:4)"
[15] "PG(38:5)" "PG(40:7)" "PS(36:4)" "PS(38:5)"
```

```
> intersect(
+ lipidsInTerm(ORGANELLES) [[
+ names(LIONTerms) [LIONTerms==
+ "neutral intrinsic curvature"]]],
+ lipidsInTerm(ORGANELLES) [[
+ names(LIONTerms) [LIONTerms==
+ "high bilayer thickness"]]])
[1] "PC(34:0)" "PC(36:0)" "PC(36:1)"
[4] "PC(38:2)" "PC(40:4)" "PS(34:0)"
[7] "PS(36:1)" "PS(38:2)" "PS(38:3)"
[10] "PS(40:3)" "PS(40:4)" "PS(42:4)"
```

organelle

- ER
- Mitochondria
- Nuclei
- Plasmalemma



Functional lipidomics: transition temperature

lipid	class	FA-unsat	FA-length	T_m (°C)
PS(28:0)	PS	0	28	35
PG(34:1)	PG	1	34	-2
PE(40:0)	PE	0	40	83
...
...

