DATA PRESENTATION

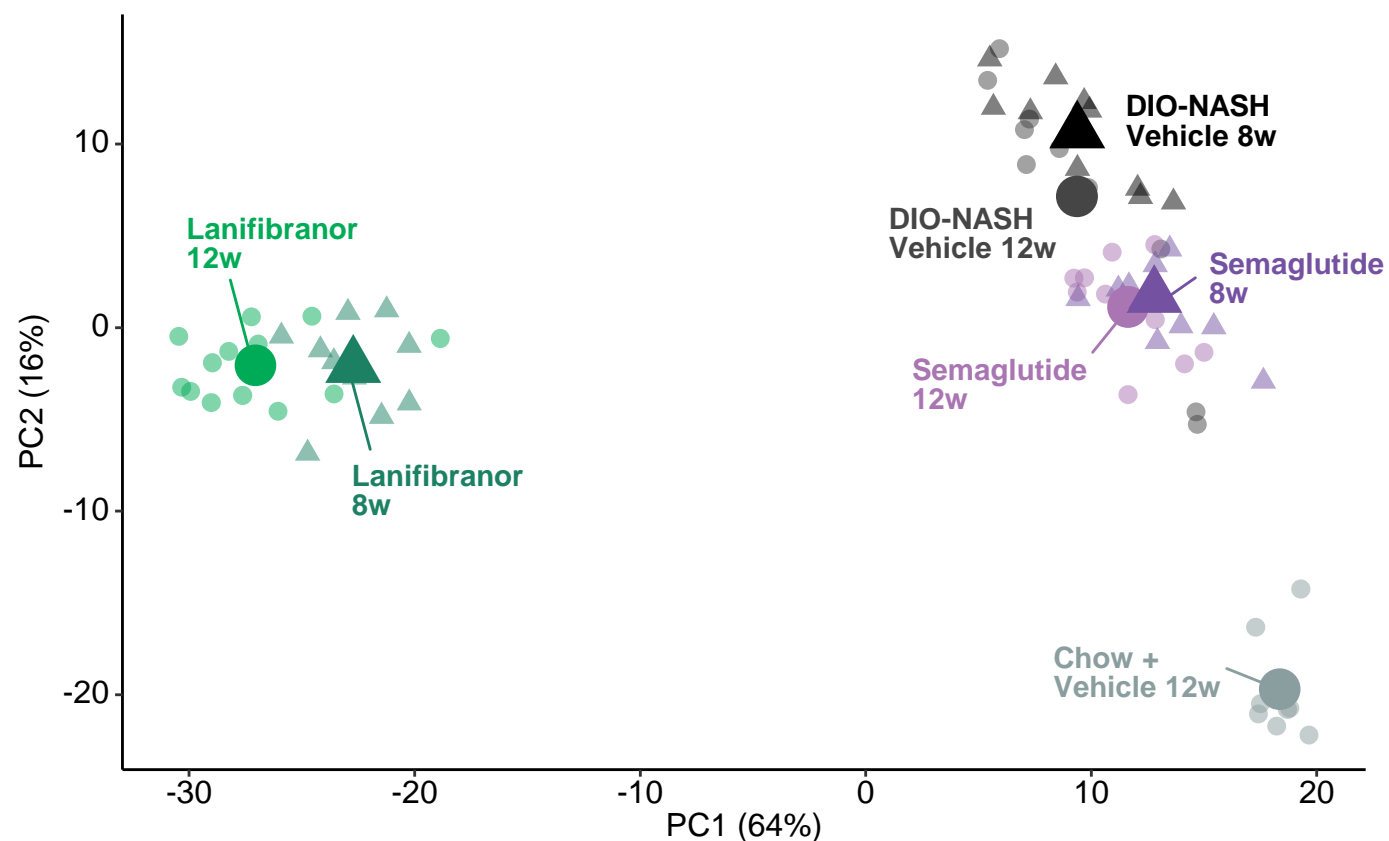# RNA-seq data package

2023

gubra

SCIENCE OF CERTAINTY

# Sample clustering analyses

Principal component analysis

Principal component analysis of the 500 most variable genes. The points indicate the relationship between samples (animals) across their gene expression profile. If there is pronounced gene expression differences between groups, points should cluster together with members of same group and away from samples from other groups. Value in brackets indicate amount of variability in percent explained by axis.
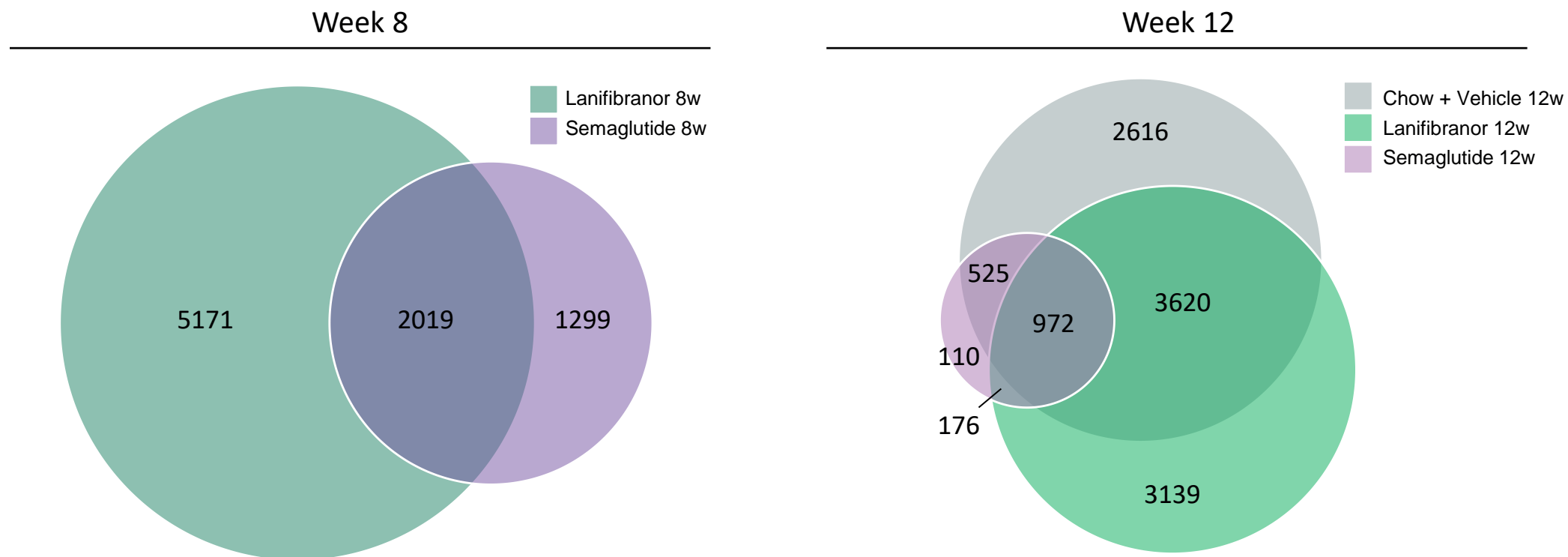
Differential expression analysis

Overview of regulated genes
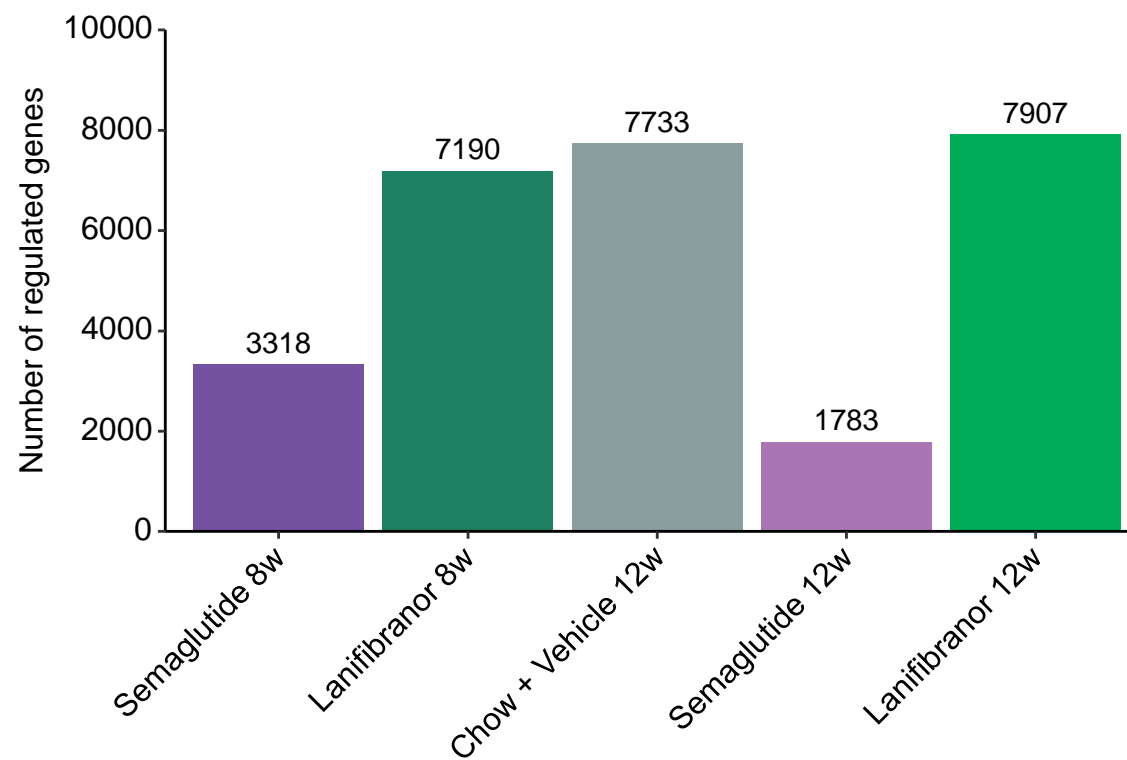
Total number of genes differentially expressed versus the corresponding DIO-NASH Vehicle at significance level $p < 0.05$ after correction for multiple testing. n = 8 - 13.
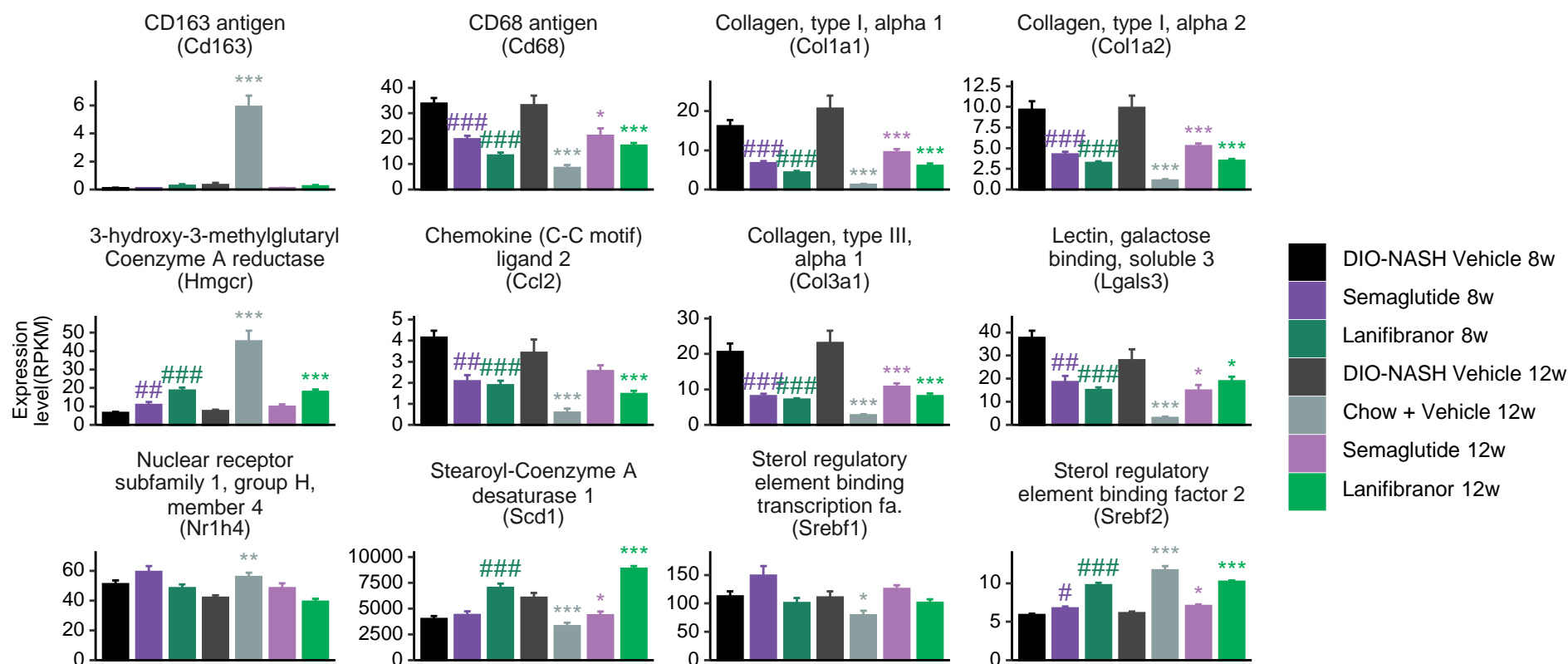
Gene regulation overlaps

Overview of compound effect overlap

Week 8

Week 12

Visualization of the number of genes regulated by combinations of compounds compared to the corresponding DIO-NASH Vehicle. n = 8 - 13.
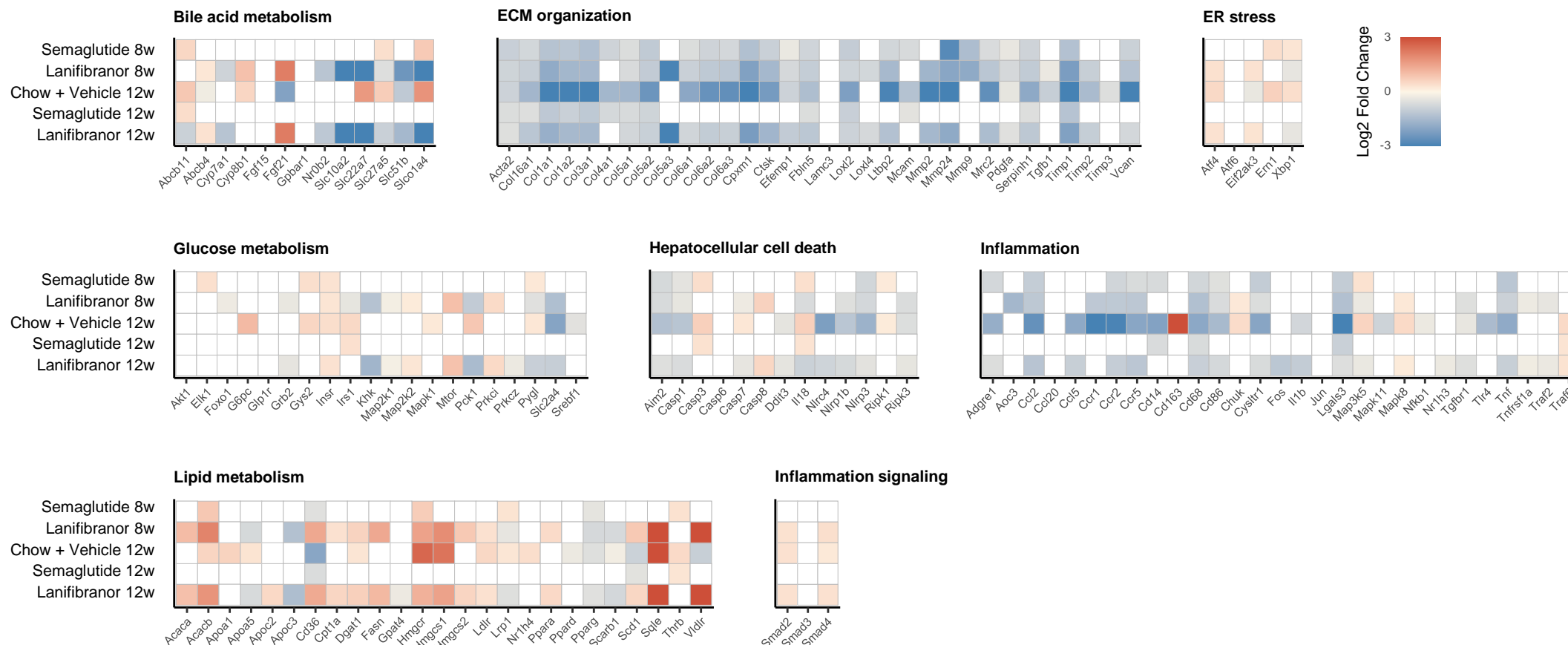
NASH gene of interest shortlist

Values expressed as mean of n = 8 - 13 + SEM of expression levels of genes. */#:$p < 0.05$, **/##:$p < 0.01$, ***/###:$p < 0.001$ compared to the corresponding DIO-NASH Vehicle after correction for gene-wise multiple testing.

Pathway summary

Overview of regulations in pathways

Heatmap summarizing gene regulation within pathways. Red and blue colours represent genes significantly (p < 0.05 after correction for multiple testing) up and down regulated, respectively, compared to the corresponding DIO-NASH Vehicle. A white box means that the gene was not significantly regulated. n = 8 - 13.
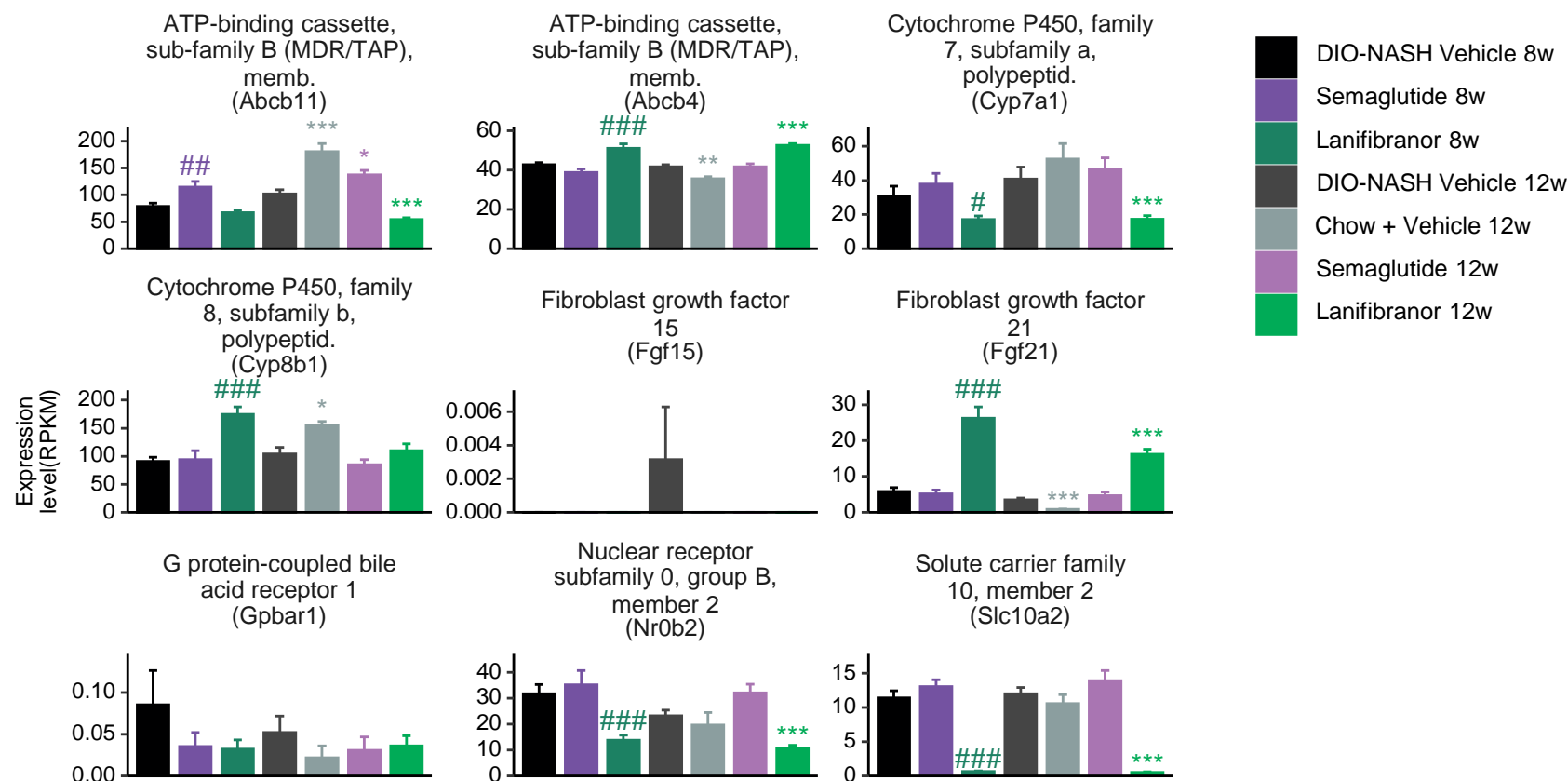
Gene expression data in GubraView

(Movie, click top-left corner to start). Demonstration of the RNAseq database, developed to allow on-the-fly browsing and visualization of RNAseq data through GubraView.

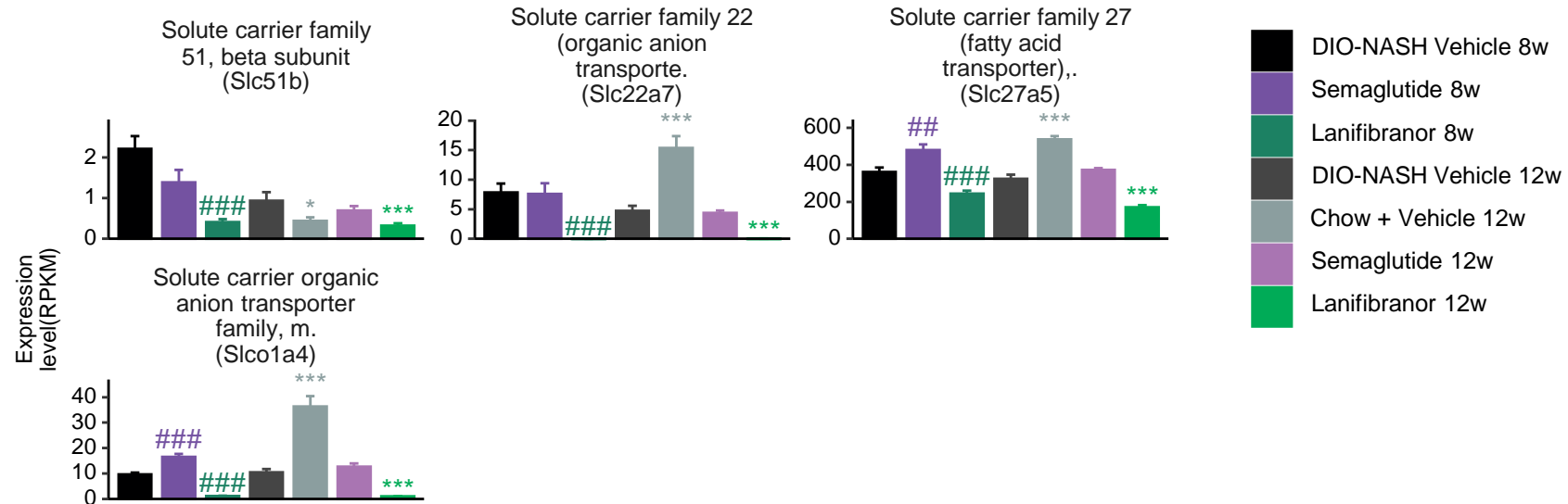# Appendix

Bile acid metabolism

Bile acid metabolism - 1/2

Values expressed as mean of n = 8 - 13 of expression levels of pathway subset genes. */#:$p <$ 0.05, **/##:$p < 0.01$, ***/###:$p < 0.001$ compared to the corresponding DIO-NASH Vehicle after correction for gene-wise multiple testing.

Bile acid metabolism
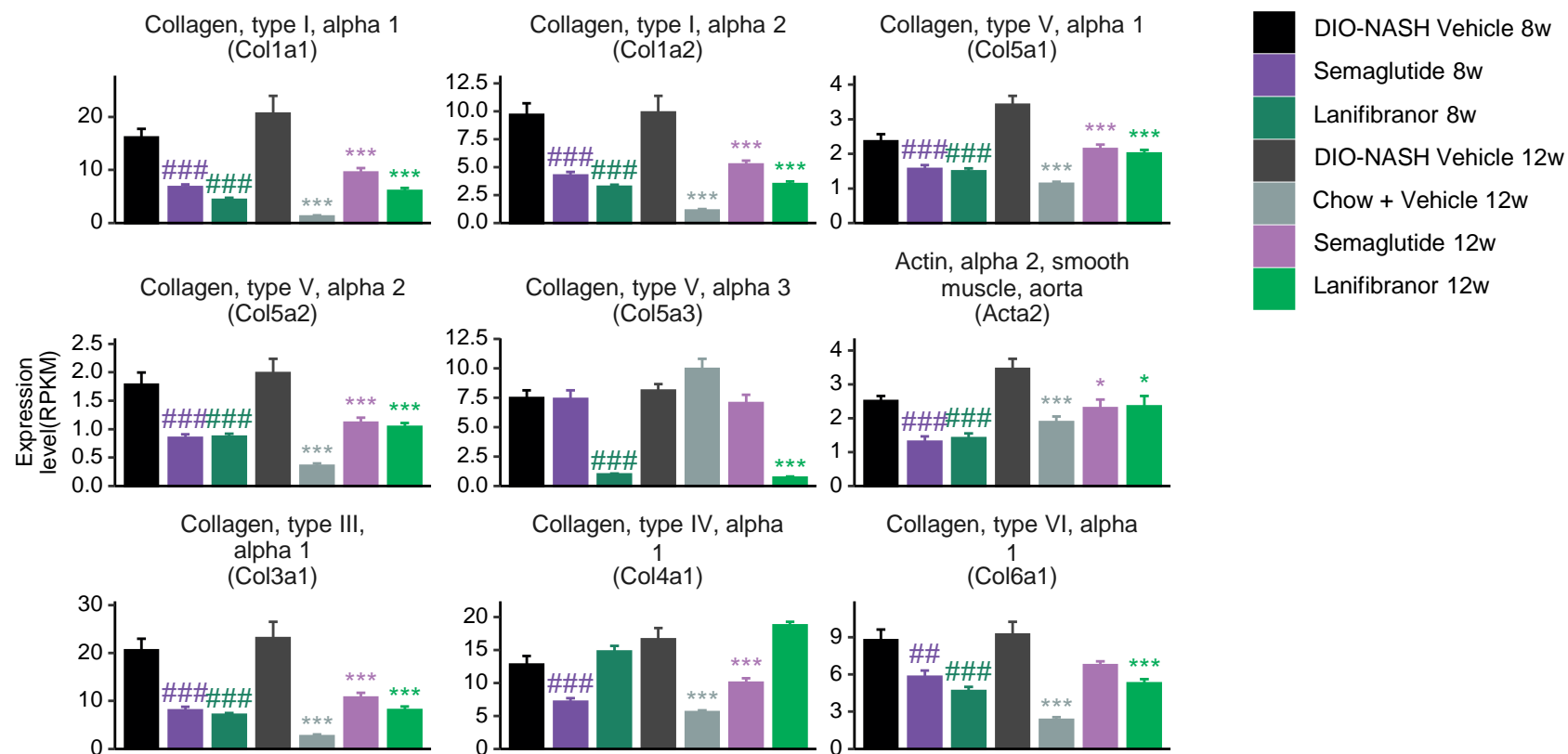
Bile acid metabolism - 2/2

Values expressed as mean of n = 8 - 13 of expression levels of pathway subset genes. *:p < 0.05, ##:p < 0.01, ***/###:p < 0.001 compared to the corresponding DIO-NASH Vehicle after correction for gene-wise multiple testing.

ECM organization

ECM organization - 1/4

Values expressed as mean of n = 8 - 13 of expression levels of pathway subset genes. *:p < 0.05, ##:p < 0.01, ***/###:p < 0.001 compared to the corresponding DIO-NASH Vehicle after correction for gene-wise multiple testing.
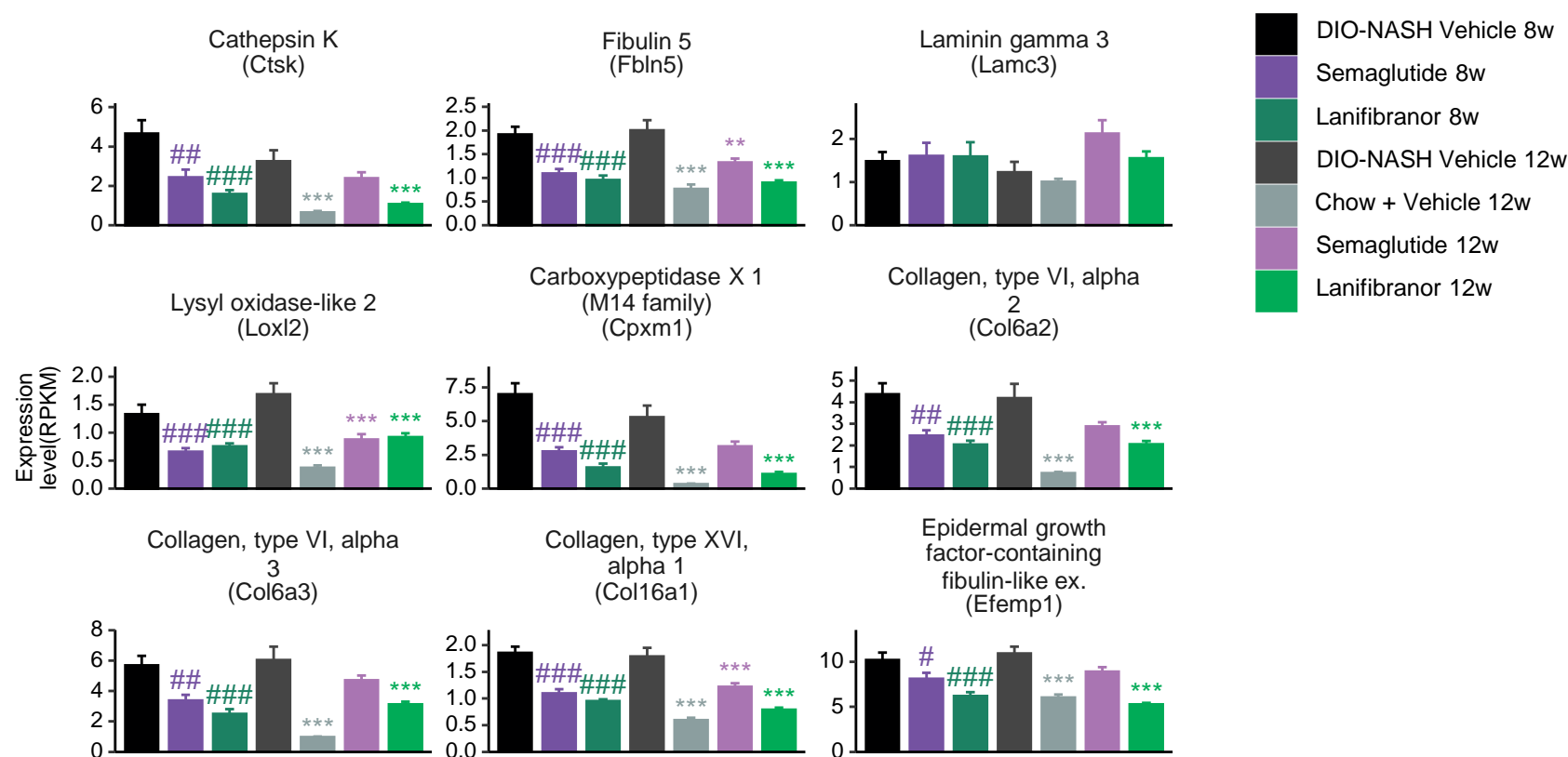
ECM organization

ECM organization - 2/4

Legend:
- DIO-NASH Vehicle 8w
- Semaglutide 8w
- Lanifibranor 8w
- DIO-NASH Vehicle 12w
- Chow + Vehicle 12w
- Semaglutide 12w
- Lanifibranor 12w

Values expressed as mean of n = 8 - 13 of expression levels of pathway subset genes. #:p < 0.05, **/##:p < 0.01, ***/###:p < 0.001 compared to the corresponding DIO-NASH Vehicle after correction for gene-wise multiple testing.
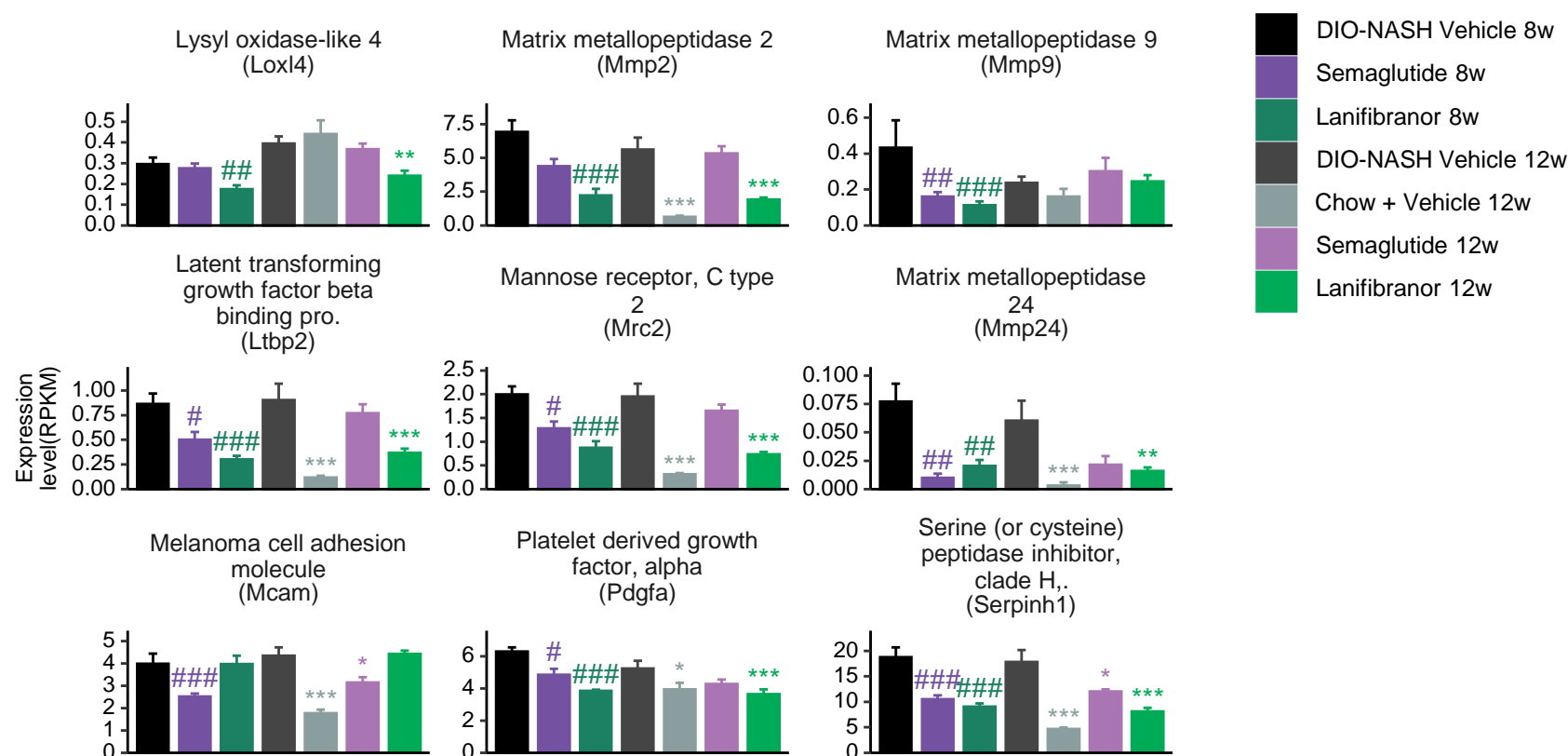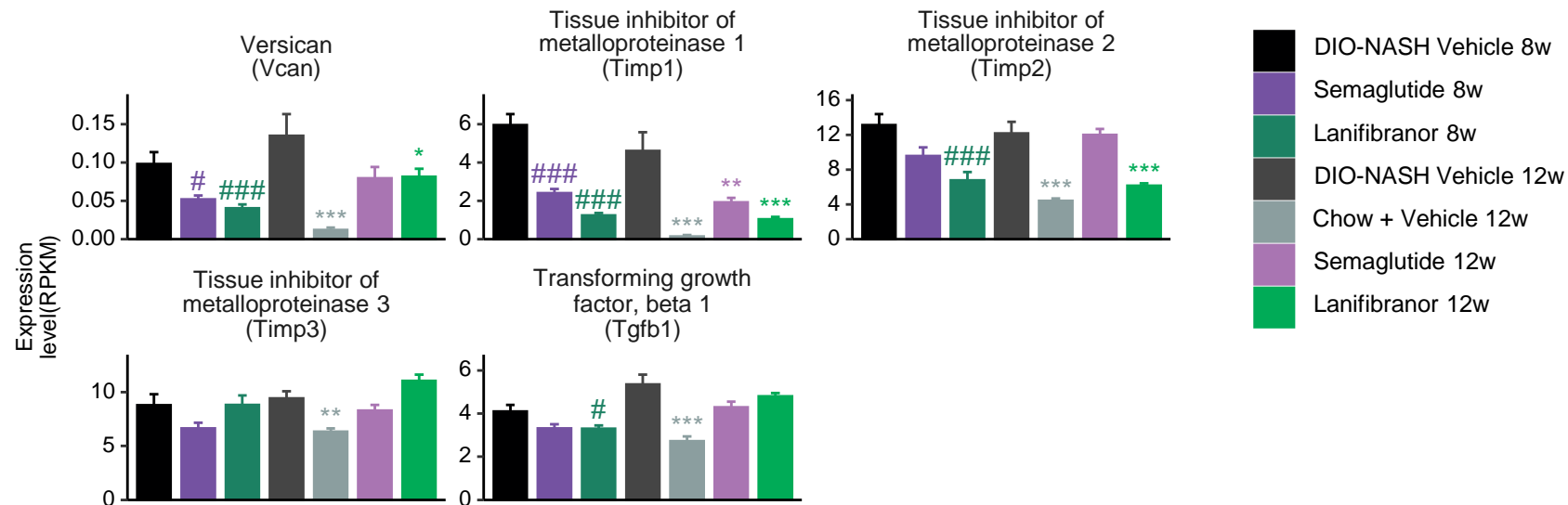
ECM organization

ECM organization - 3/4

Values expressed as mean of n = 8 - 13 of expression levels of pathway subset genes. */#:p < 0.05, **/##:p < 0.01, ***/###:p < 0.001 compared to the corresponding DIO-NASH Vehicle after correction for gene-wise multiple testing.
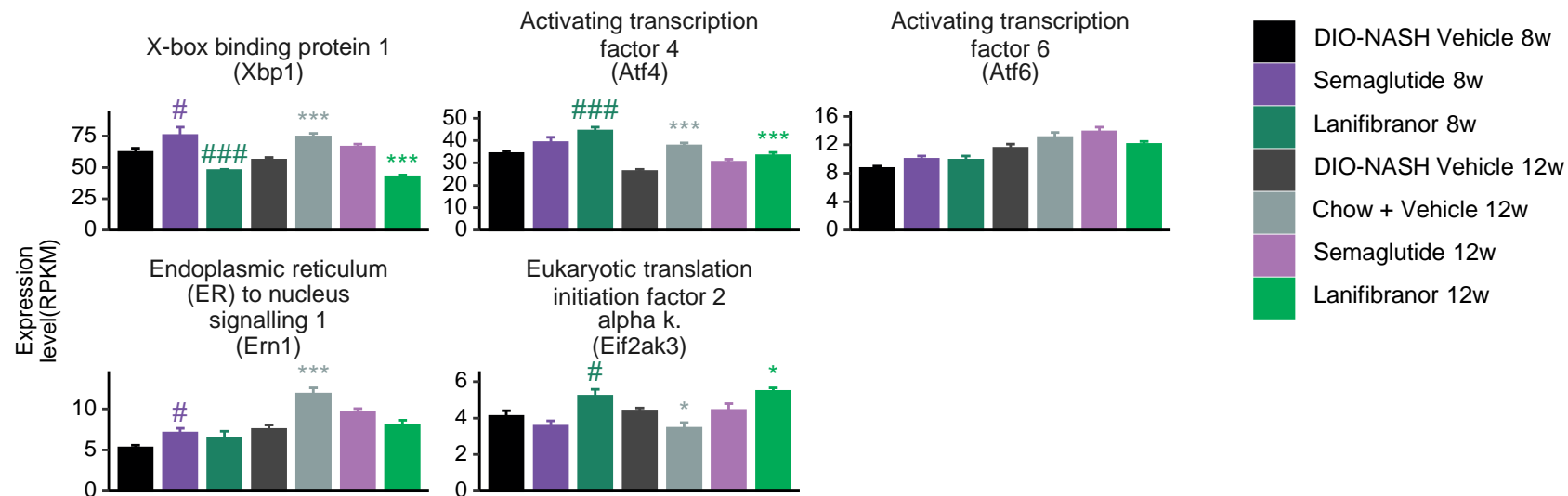
ECM organization

ECM organization - 4/4

Values expressed as mean of n = 8 - 13 of expression levels of pathway subset genes. */#:p < 0.05, **:p < 0.01, ***/###:p < 0.001 compared to the corresponding DIO-NASH Vehicle after correction for gene-wise multiple testing.
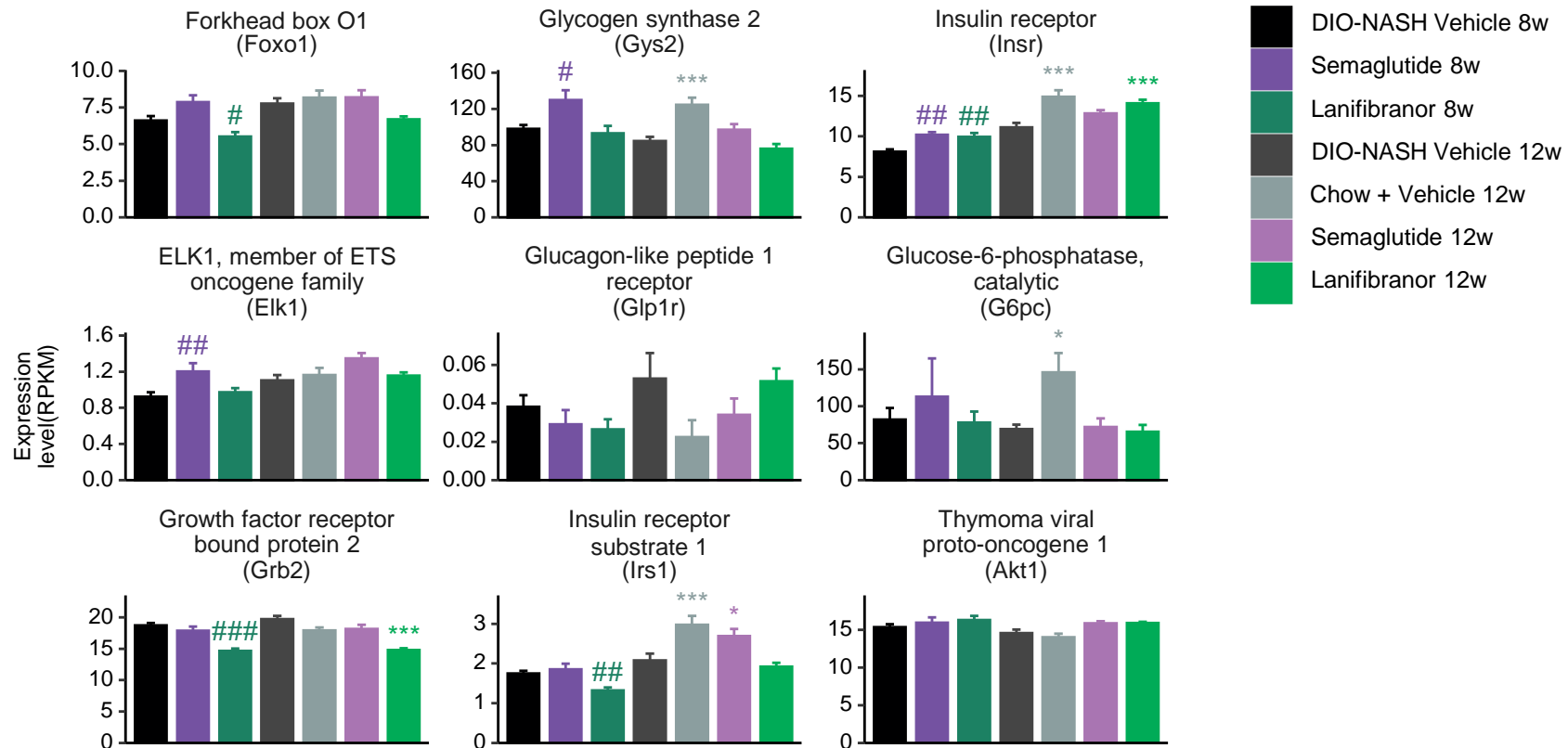
ER stress

ER stress

Values expressed as mean of n = 8 - 13 of expression levels of pathway subset genes. */#:$p <$ 0.05, ***/###:$p < 0.001$ compared to the corresponding DIO-NASH Vehicle after correction for gene-wise multiple testing.
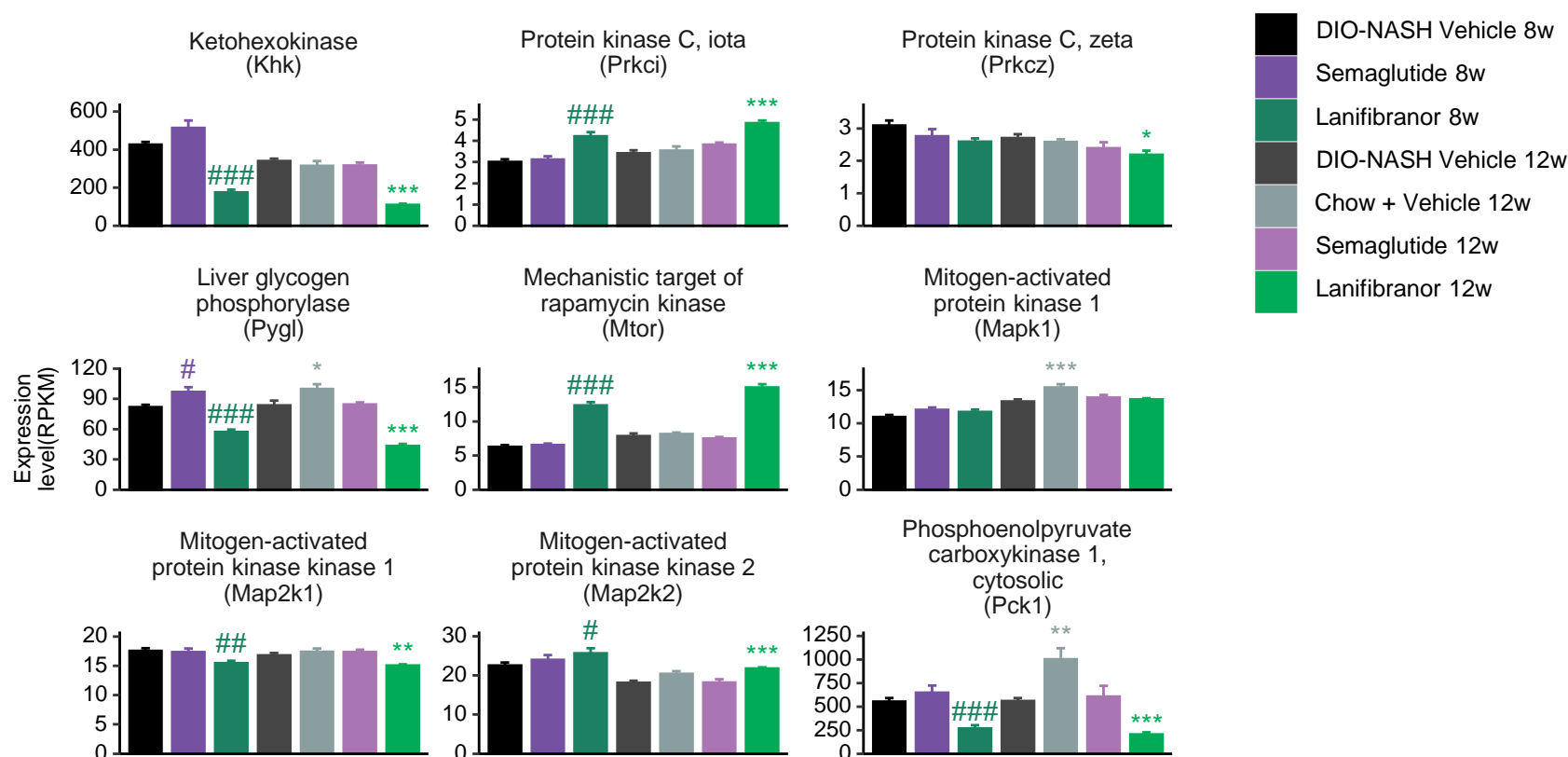
Glucose metabolism

Glucose metabolism - 1/3

Values expressed as mean of n = 8 - 13 of expression levels of pathway subset genes. */#:p < 0.05, ##:p < 0.01, ***/###:p < 0.001 compared to the corresponding DIO-NASH Vehicle after correction for gene-wise multiple testing.
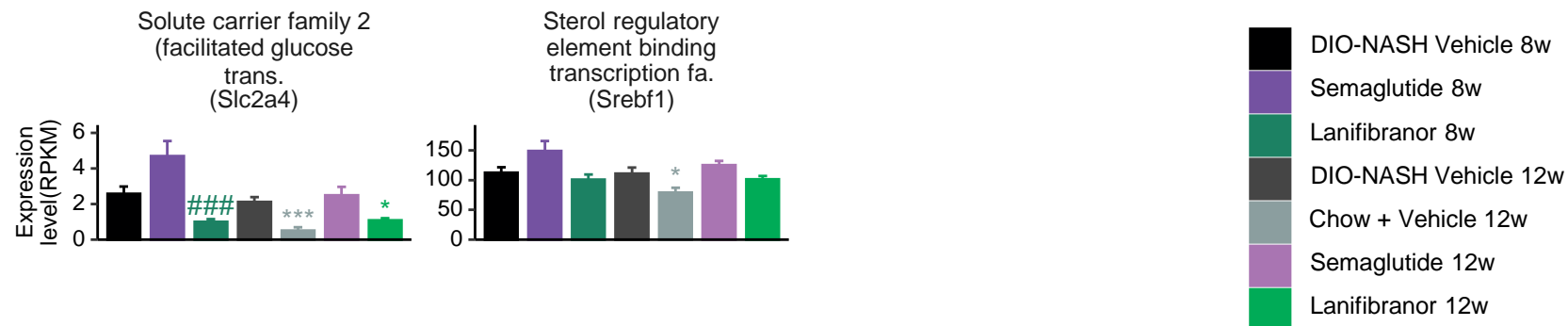
Glucose metabolism

Glucose metabolism - 2/3

Values expressed as mean of n = 8 - 13 of expression levels of pathway subset genes. */#:p < 0.05, **/##:p < 0.01, ***/###:p < 0.001 compared to the corresponding DIO-NASH Vehicle after correction for gene-wise multiple testing.
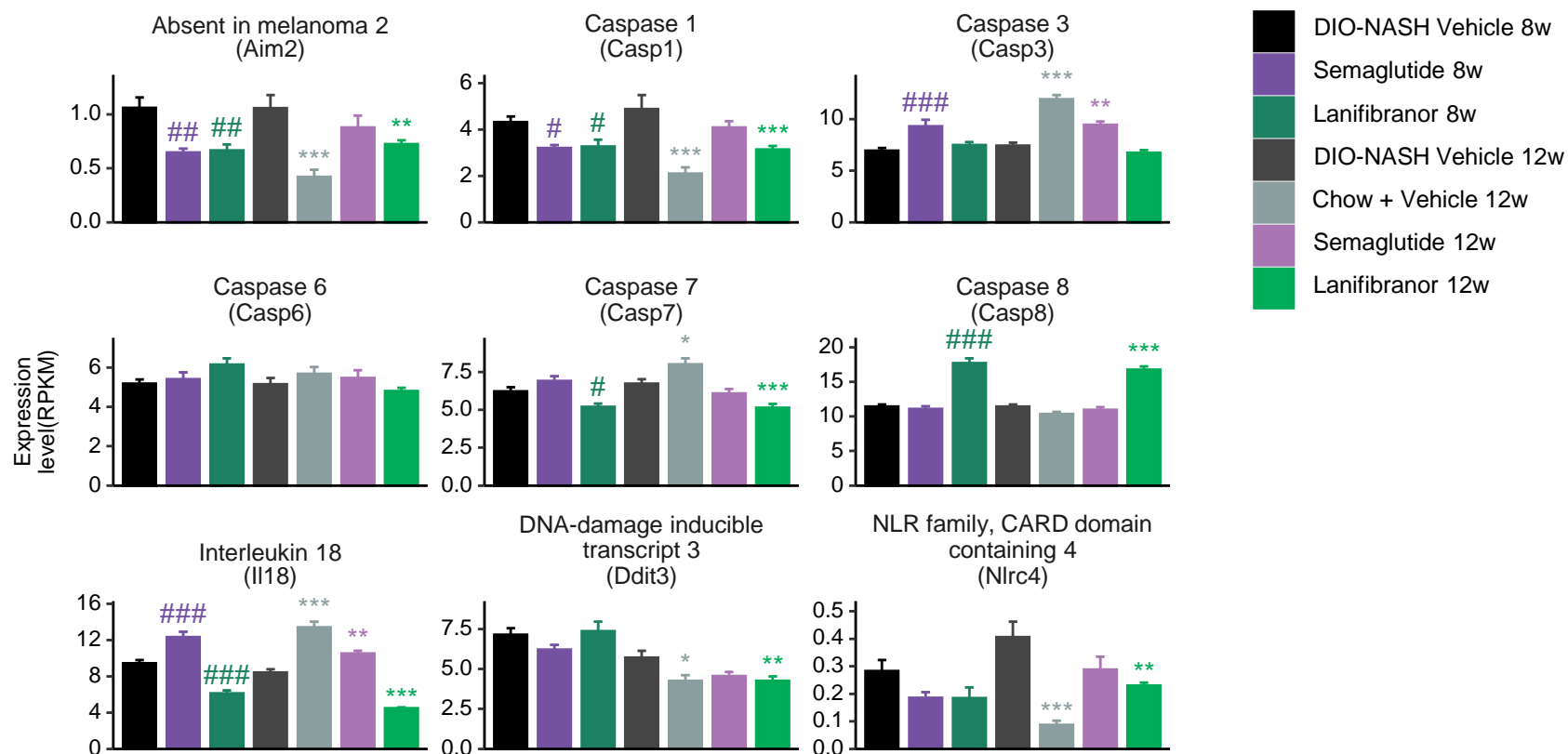
Glucose metabolism

Glucose metabolism - 3/3

Solute carrier family 2
(facilitated glucose
trans.
(Slc2a4)

Sterol regulatory
element binding
transcription fa.
(Srebf1)

- DIO-NASH Vehicle 8w
- Semaglutide 8w
- Lanifibranor 8w
- DIO-NASH Vehicle 12w
- Chow + Vehicle 12w
- Semaglutide 12w
- Lanifibranor 12w

Values expressed as mean of n = 8 - 13 of expression levels of pathway subset genes. *:p < 0.05, ***/###:p < 0.001 compared to the corresponding DIO-NASH Vehicle after correction for gene-wise multiple testing.
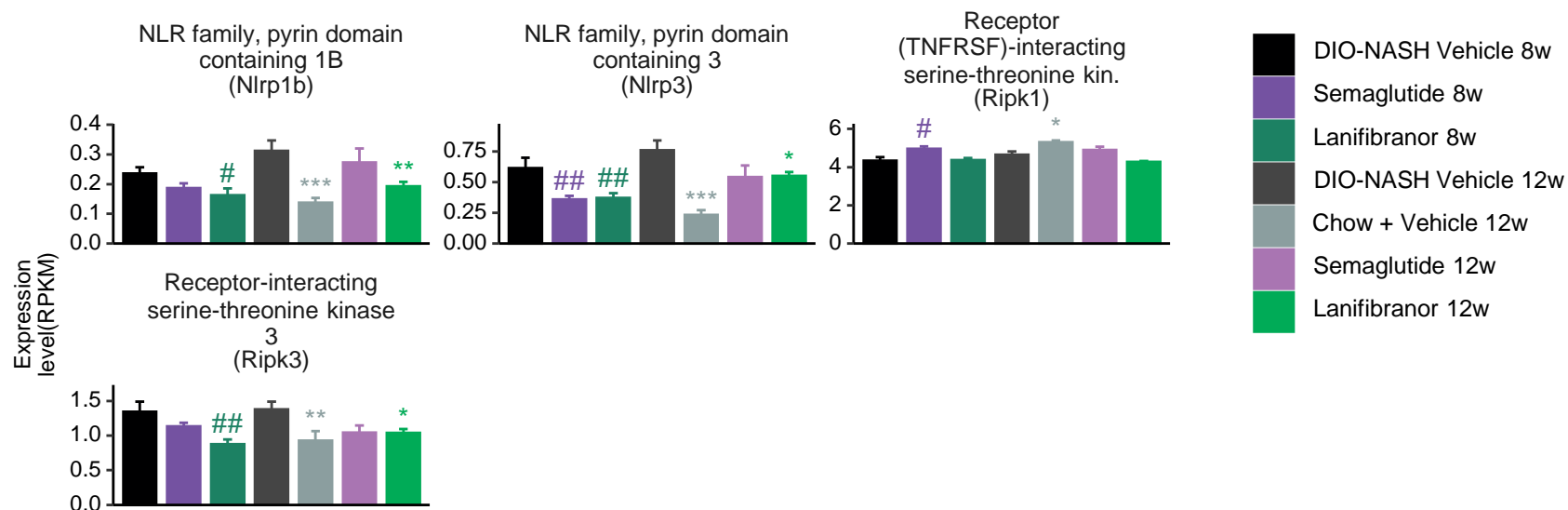
Hepatocellular cell death

Hepatocellular cell death - 1/2

Values expressed as mean of n = 8 - 13 of expression levels of pathway subset genes. */#:$p < 0.05$, **/##:$p < 0.01$, ***/###:$p < 0.001$ compared to the corresponding DIO-NASH Vehicle after correction for gene-wise multiple testing.
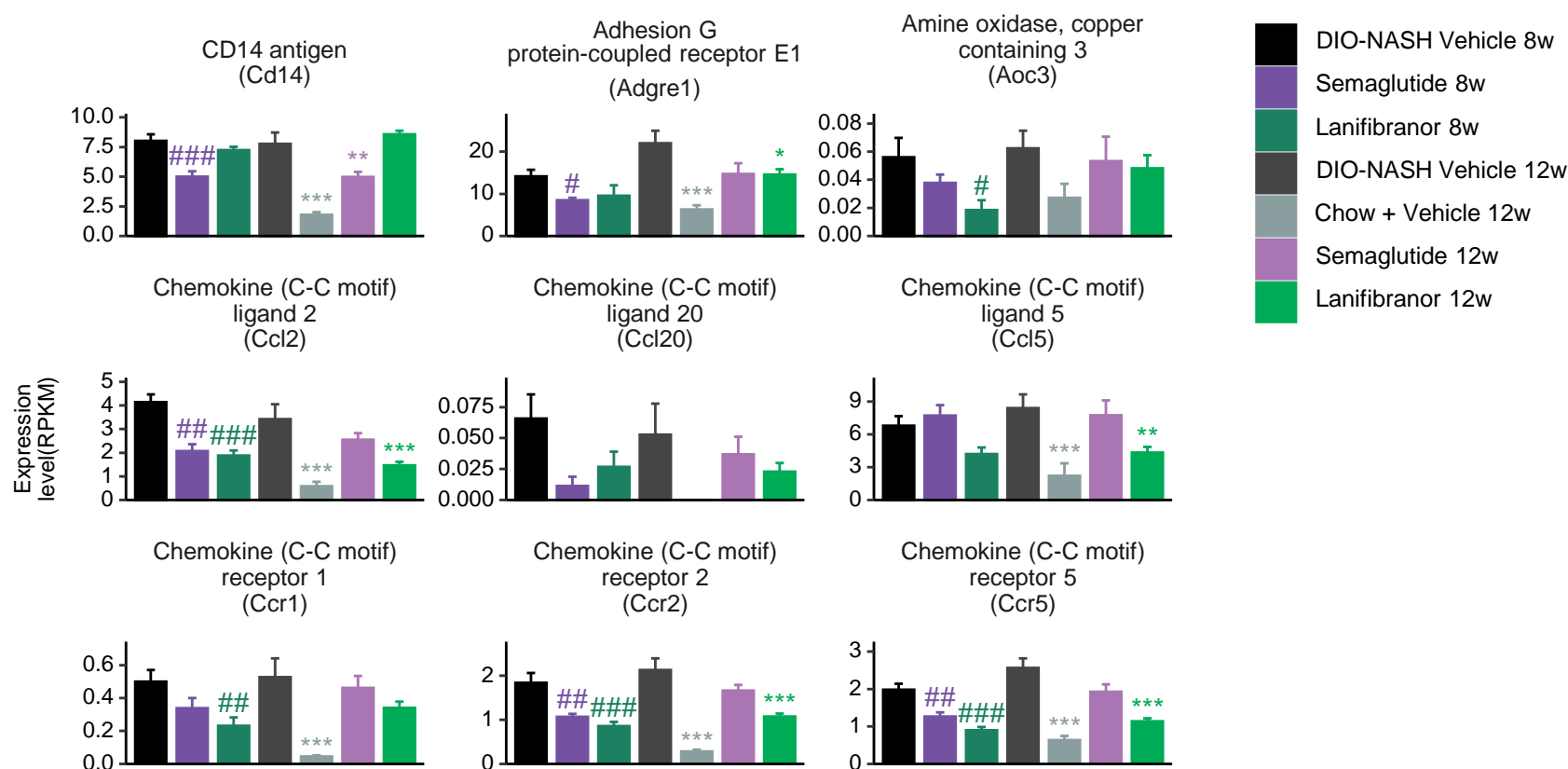
Hepatocellular cell death

Hepatocellular cell death - 2/2

Values expressed as mean of n = 8 - 13 of expression levels of pathway subset genes. */#:$p < 0.05$, **/##:$p < 0.01$, ***:$p < 0.001$ compared to the corresponding DIO-NASH Vehicle after correction for gene-wise multiple testing.
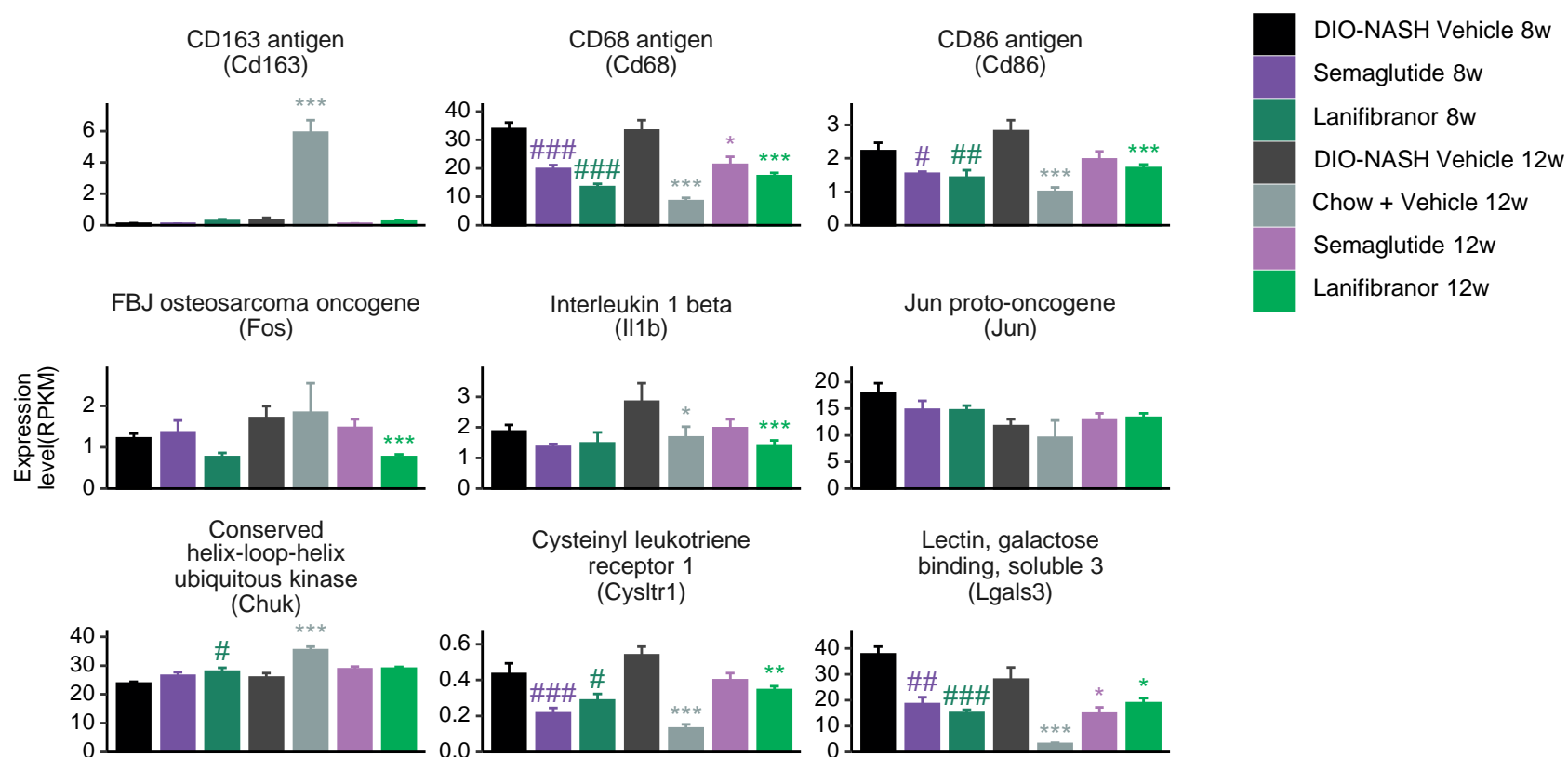
Inflammation

Inflammation - 1/4

Values expressed as mean of n = 8 - 13 of expression levels of pathway subset genes. */#:p < 0.05, **/##:p < 0.01, ***/###:p < 0.001 compared to the corresponding DIO-NASH Vehicle after correction for gene-wise multiple testing.
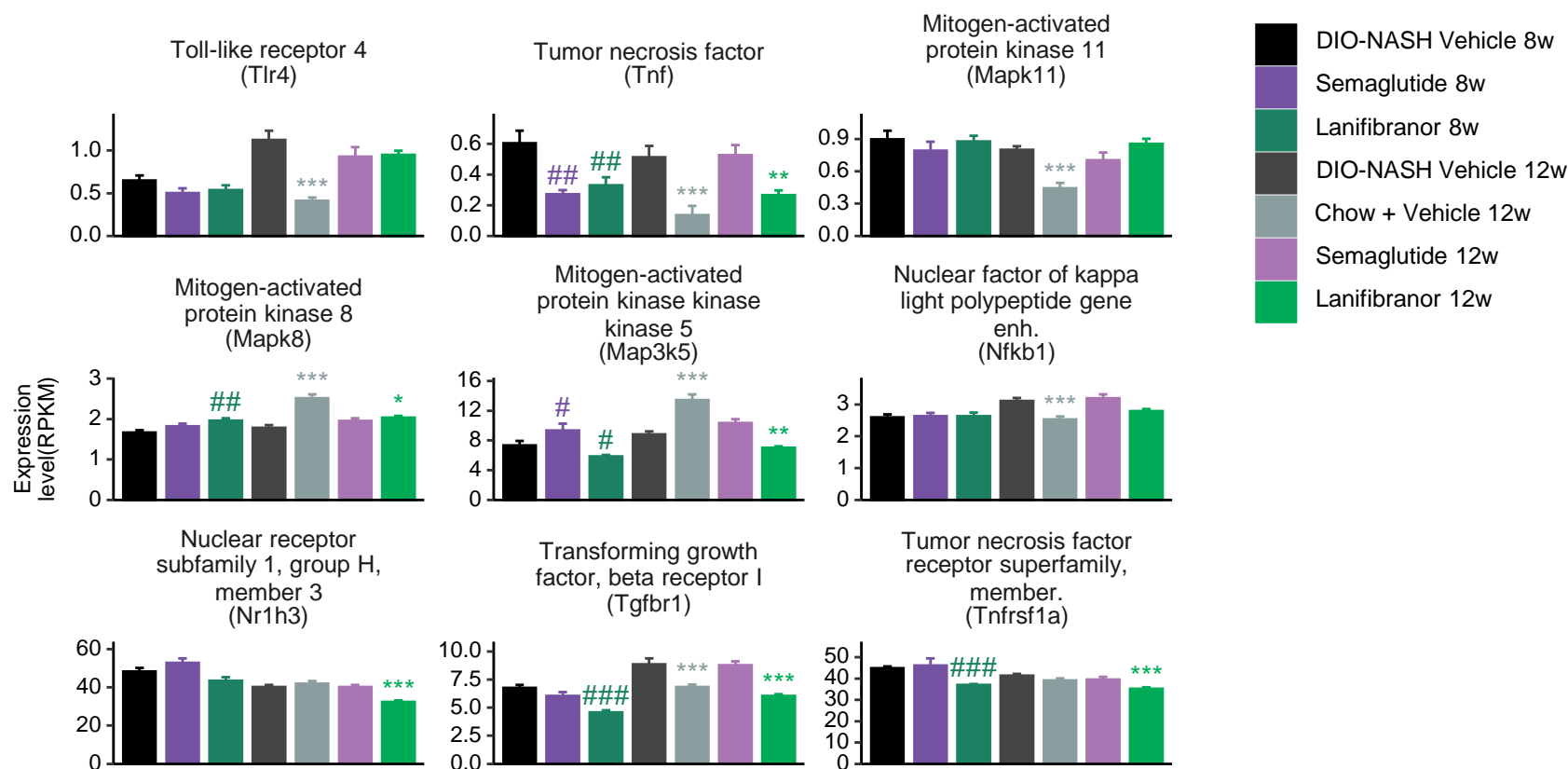
Inflammation

Inflammation - 2/4

Values expressed as mean of n = 8 - 13 of expression levels of pathway subset genes. */#:p < 0.05, **/##:p < 0.01, ***/###:p < 0.001 compared to the corresponding DIO-NASH Vehicle after correction for gene-wise multiple testing.
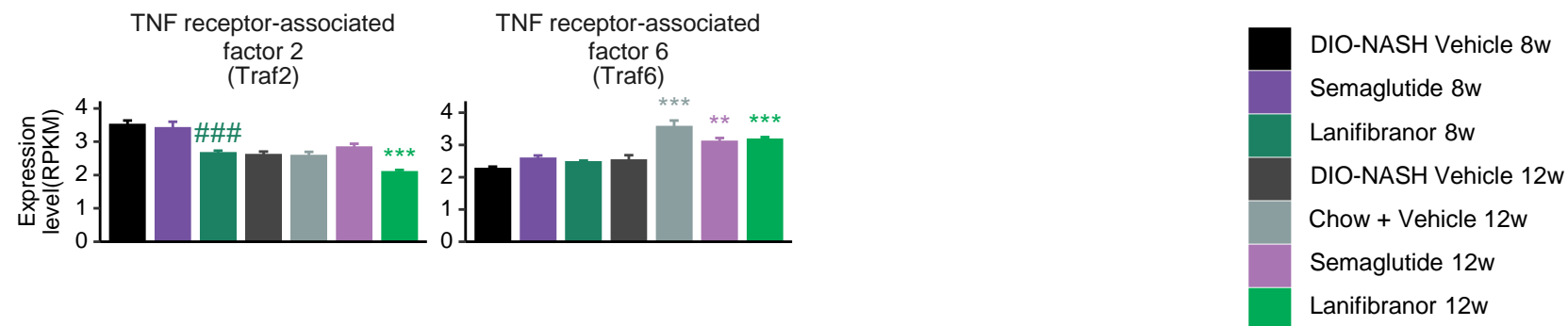
Inflammation

Inflammation - 3/4

Values expressed as mean of n = 8 - 13 of expression levels of pathway subset genes. */#:p < 0.05, **/##:p < 0.01, ***/###:p < 0.001 compared to the corresponding DIO-NASH Vehicle after correction for gene-wise multiple testing.
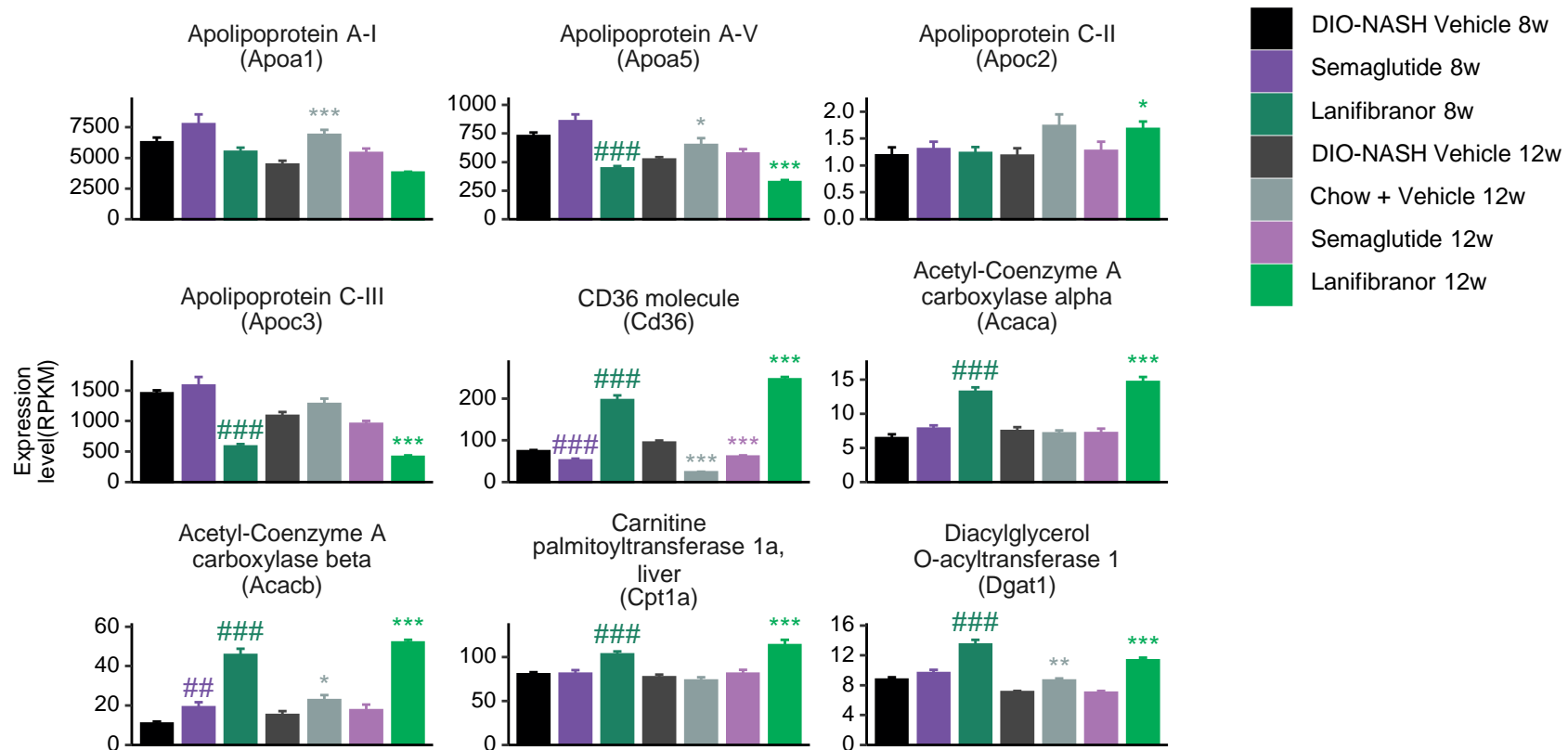
Inflammation

Inflammation - 4/4

Values expressed as mean of n = 8 - 13 of expression levels of pathway subset genes. **:p < 0.01, ***/###:p < 0.001 compared to the corresponding DIO-NASH Vehicle after correction for gene-wise multiple testing.
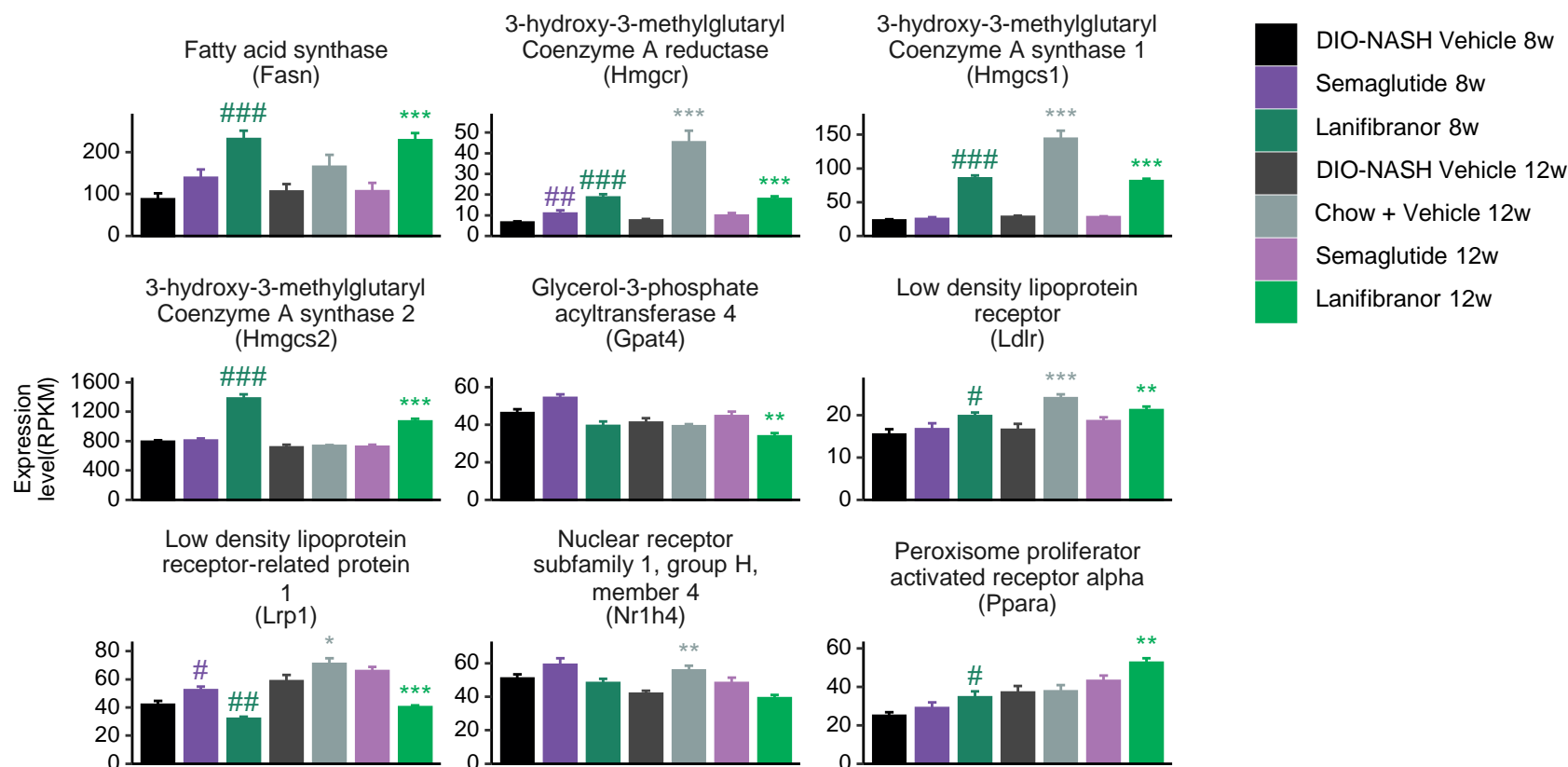
Lipid metabolism

Lipid metabolism - 1/3

Values expressed as mean of n = 8 - 13 of expression levels of pathway subset genes. *:p < 0.05, **/##:p < 0.01, ***/###:p < 0.001 compared to the corresponding DIO-NASH Vehicle after correction for gene-wise multiple testing.
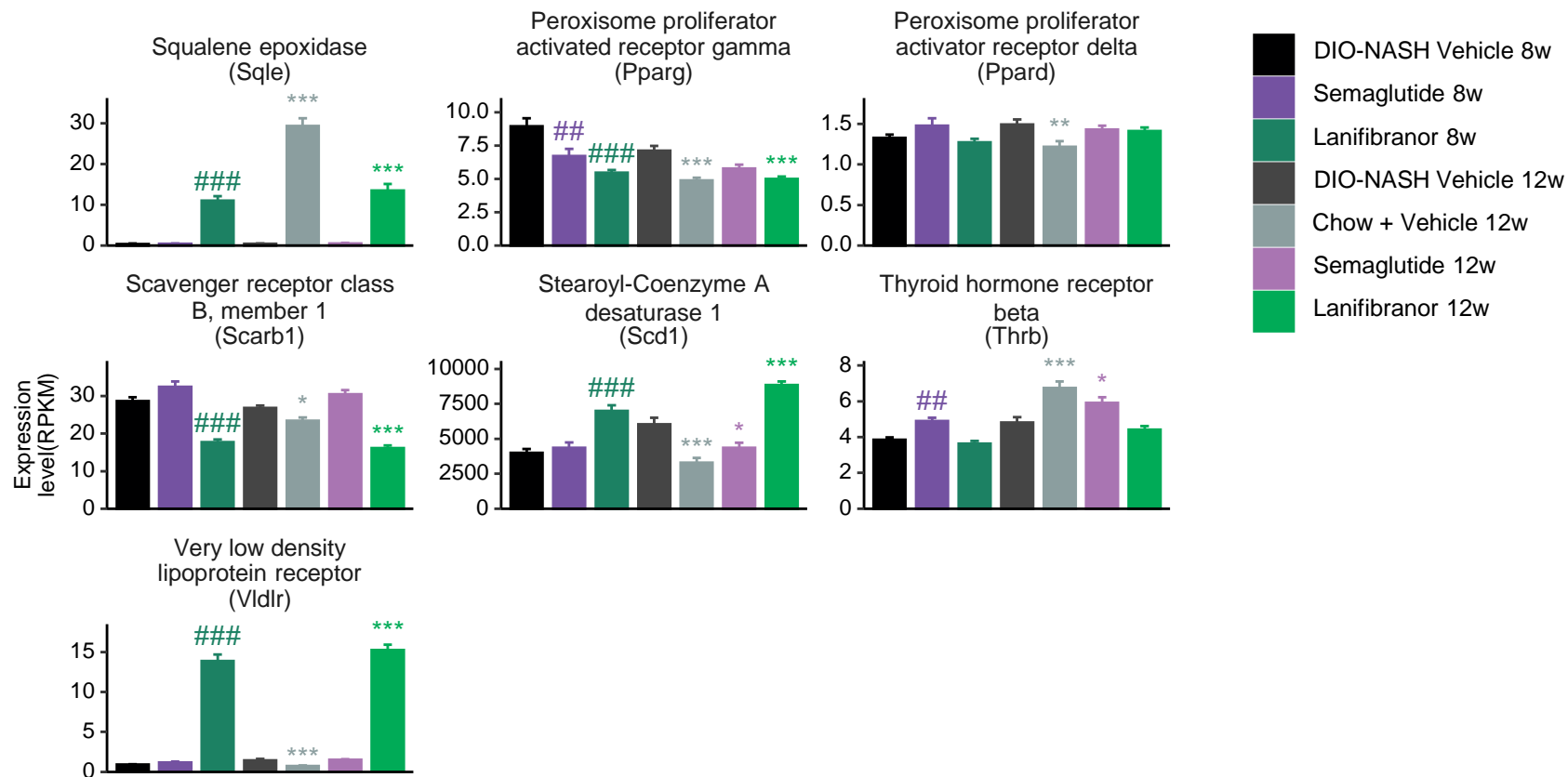
Lipid metabolism

Lipid metabolism - 2/3

Values expressed as mean of n = 8 - 13 of expression levels of pathway subset genes. */#:p < 0.05, **/##:p < 0.01, ***/###:p < 0.001 compared to the corresponding DIO-NASH Vehicle after correction for gene-wise multiple testing.
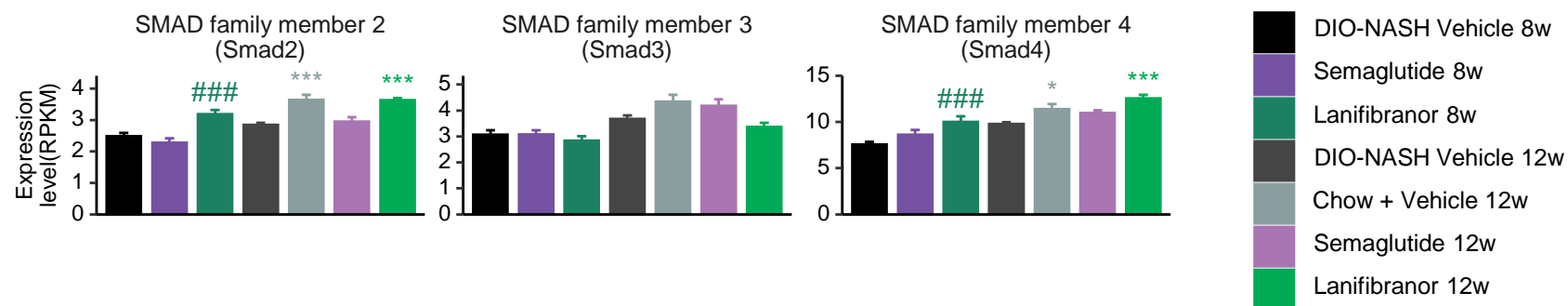
Lipid metabolism

Lipid metabolism - 3/3

Values expressed as mean of n = 8 - 13 of expression levels of pathway subset genes. *:$p < 0.05$, **/##:$p < 0.01$, ***/###:$p < 0.001$ compared to the corresponding DIO-NASH Vehicle after correction for gene-wise multiple testing.

Inflammation signaling

Inflammation signaling

Values expressed as mean of n = 8 - 13 of expression levels of pathway subset genes. *:p < 0.05, ***/###:p < 0.001 compared to the corresponding DIO-NASH Vehicle after correction for gene-wise multiple testing.