

Shared lipidome and proteome signatures of frontotemporal lobar degeneration and Alzheimer's disease

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Running title: Shared lipidome and proteome alterations in FTLN and AD

Supplementary figure legends

Supplementary fig. 1 | Lipidomic alterations in occipital cortex of FTLD compared with neurologically normal controls. **A** PCA of lipidomic profiles from occipital cortex samples demonstrates separation between FTLD and control groups, indicating disease-associated lipid remodeling. **B** Quantification of major lipid classes in occipital cortex from control and FTLD subjects. Bars represent mean $\pm$ SEM, with individual data points shown. Significant differences between groups are indicated by asterisks (* $P < 0.05$, statistical test described in Methods).

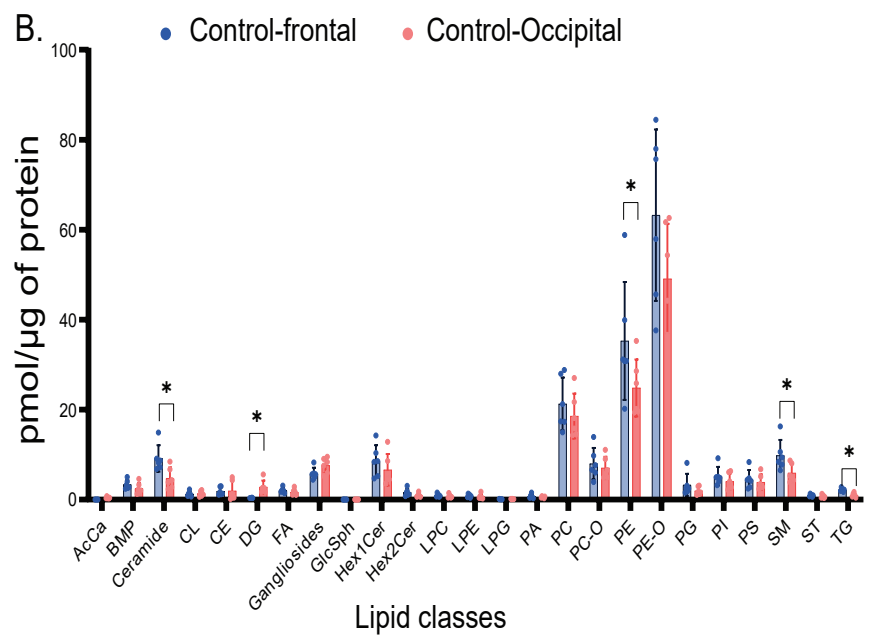
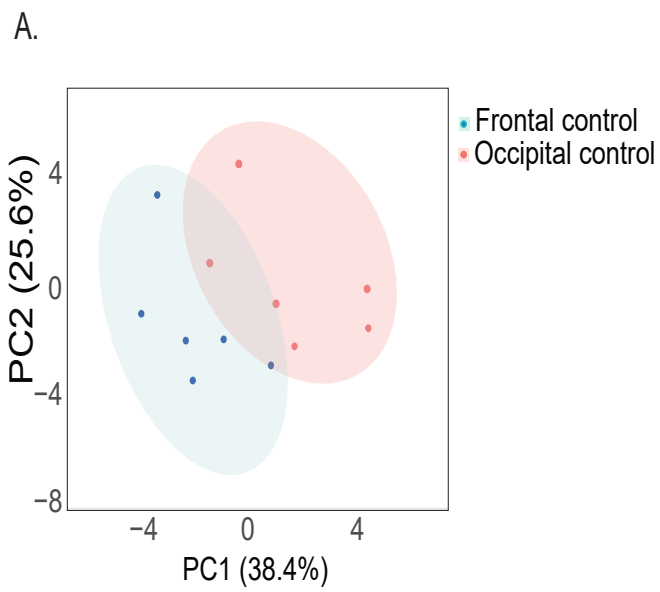
Supplementary fig. 2 | Alterations in BMP molecular species and ganglioside classes in FTLD frontal cortex. **A** Fold-changes of individual BMP molecular species in FTLD relative to controls. **B** Fold-changes of major ganglioside subclasses in FTLD relative to controls. Data are shown as mean $\pm$ SD, with individual samples overlaid. Statistical significance was assessed using multiple unpaired two-tailed Mann-Whitney U tests. * $P < 0.05$; nd, not detected.

Supplementary fig. 3 | Global lipidomic alterations in the occipital cortex of FTLD cases relative to controls. **A** Distribution of log₂ fold-changes for individual lipid species in FTLD relative to controls across lipid classes. Each point represents a single lipid species, illustrating the magnitude and direction of disease-associated lipid alterations. **B** Volcano plot showing differential abundance of lipid species in FTLD occipital cortex compared with controls. The x-axis represents log₂-fold change (FTLD/Control), and the y-axis represents $-\log_{10}(P \text{ value})$. Red and blue points indicate significantly increased and decreased lipid species, respectively, and gray points represent non-significant changes. Selected significantly altered lipid species are annotated. Dashed lines indicate fold-change and significance thresholds.

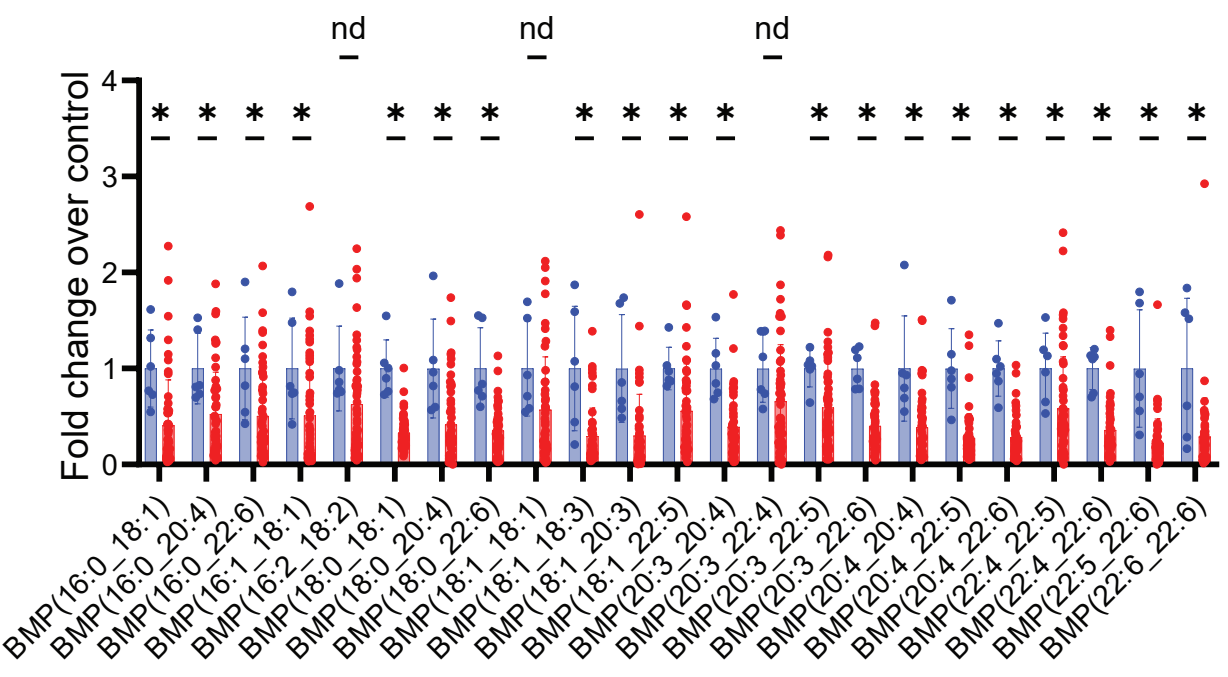
Supplementary fig. 4 | Lipidomic alterations across FTLD subtypes in frontal cortex. **A** Heatmap showing relative abundance of lipid classes across controls and FTLD subtypes **B–F** Volcano plots of differentially abundant lipid species in each FTLD subtype relative to controls, highlighting significantly increased and decreased lipids in FTLD-GRN (**B**), FTLD-C9orf72 (**C**), FTLD-A-Sporadic (**D**), and FTLD-C-Sporadic (**E**) and FTLD-tau-PiD (**F**).

Supplementary fig. 5 | Proteomic alterations in the occipital cortex of FTLD. **A & B** PCA of proteomic profiles from frontal and occipital cortex comparing FTLD and control subjects. **C** Volcano plot showing differentially abundant proteins in FTLD occipital cortex relative to controls. **D** Pathway enrichment analysis of significantly altered proteins, highlighting dysregulated metabolic, lipid metabolic, and lysosomal-related pathways.

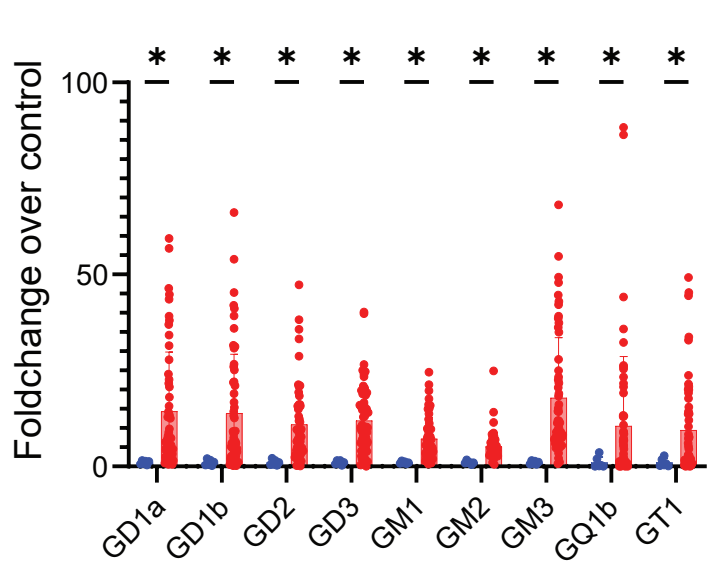
Supplementary fig. 6 | Lipidomic and proteomic alterations in AD. **A** Fold-changes of BMP molecular species in AD frontal cortex relative to controls. **B** Fold-changes of ganglioside classes in AD frontal cortex relative to controls. **C** Distribution of log₂ fold-changes across lipid classes in AD occipital cortex. **D** Volcano plot of differentially abundant lipid species in AD occipital cortex. **E** Volcano plot of differentially abundant proteins in AD occipital cortex. **F** Pathway enrichment analysis of altered proteins. Statistical significance was assessed using multiple unpaired two-tailed Mann-Whitney U tests. * $P < 0.05$; nd, not detected.



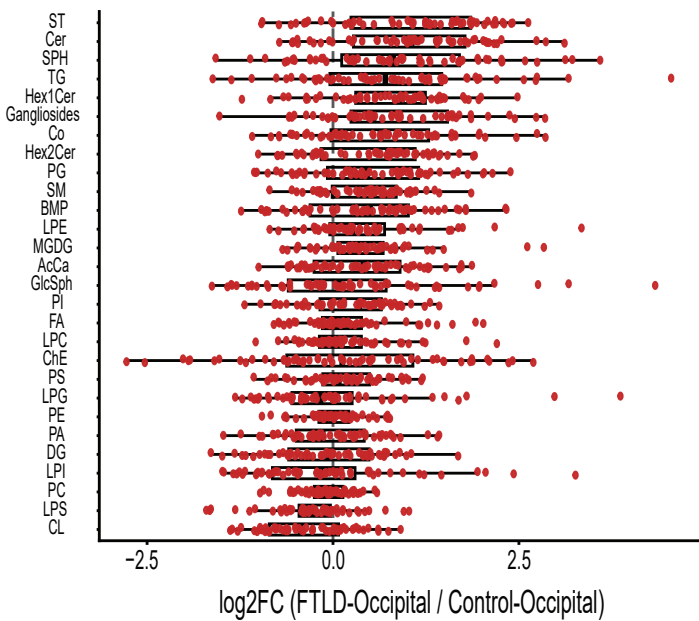
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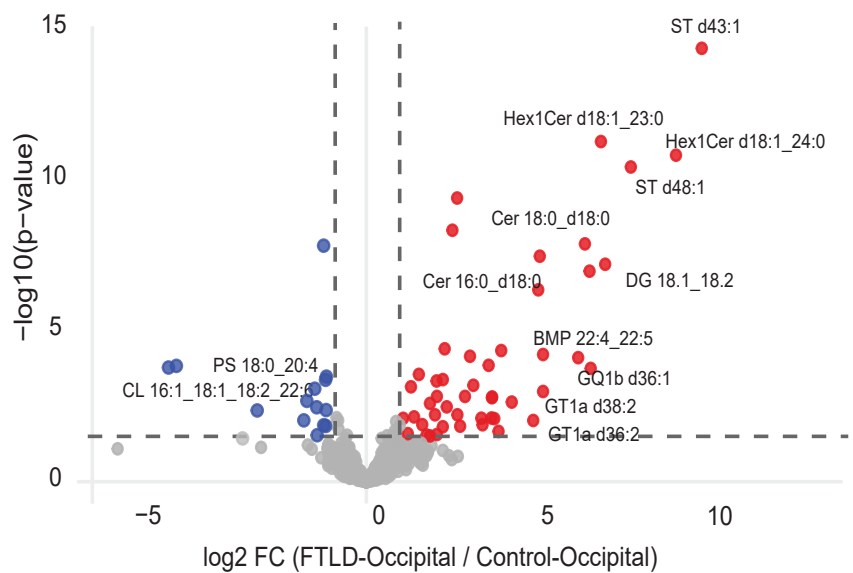
B • Control-frontal • FTLD-frontal



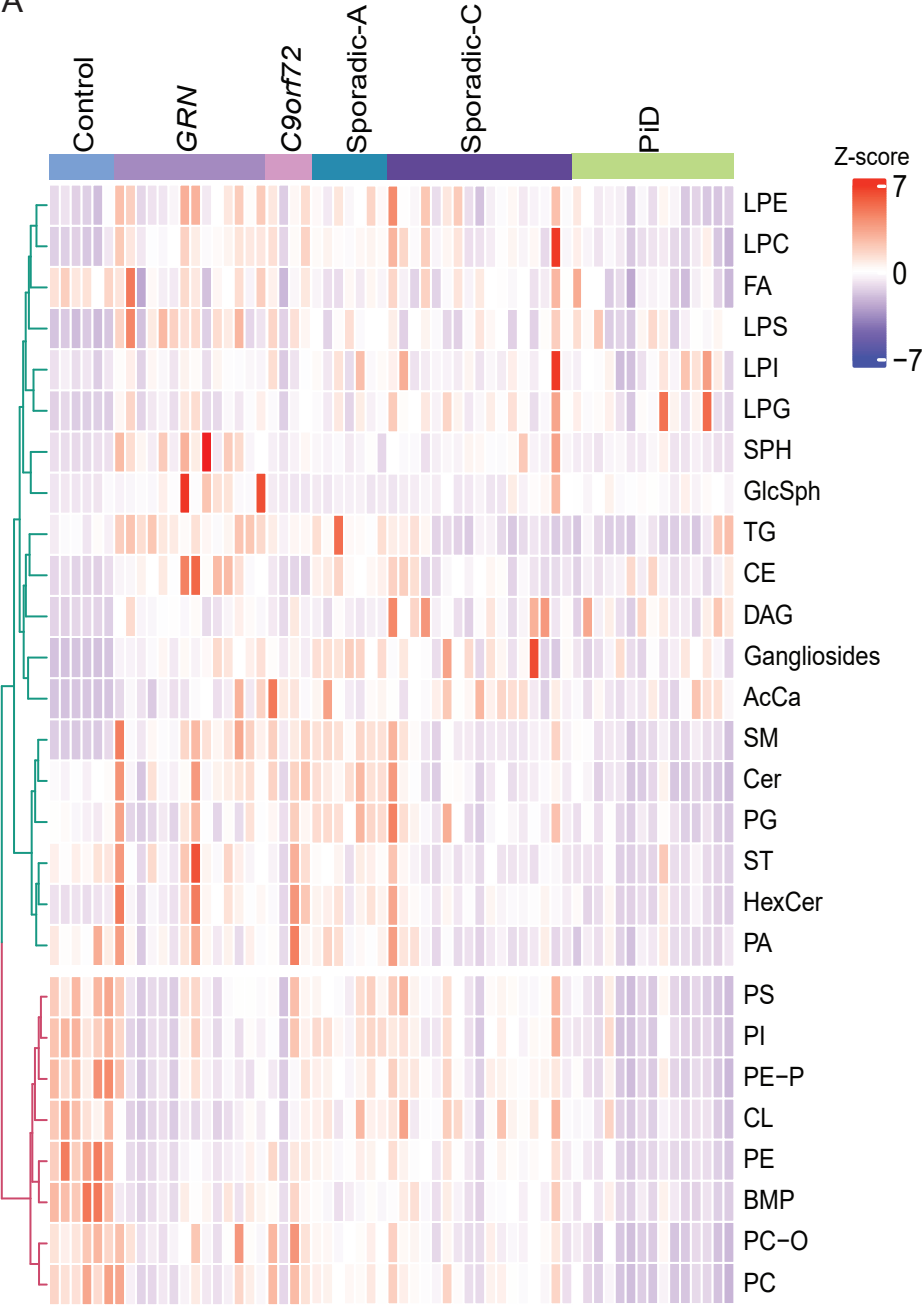
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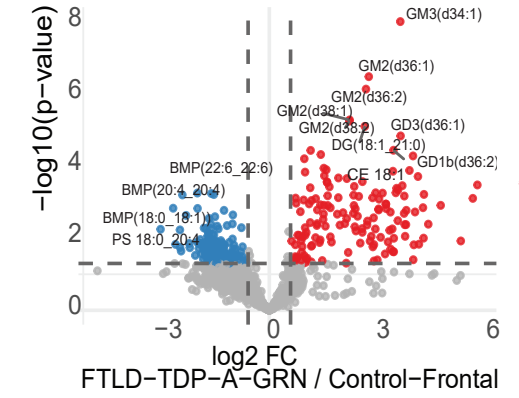
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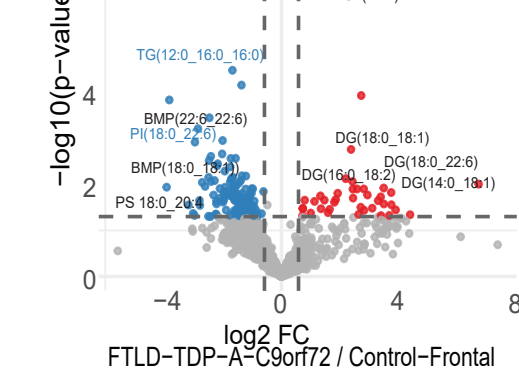
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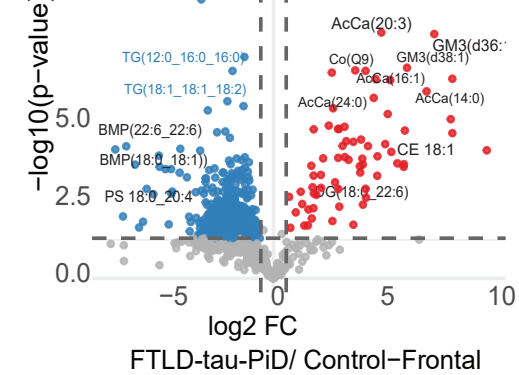
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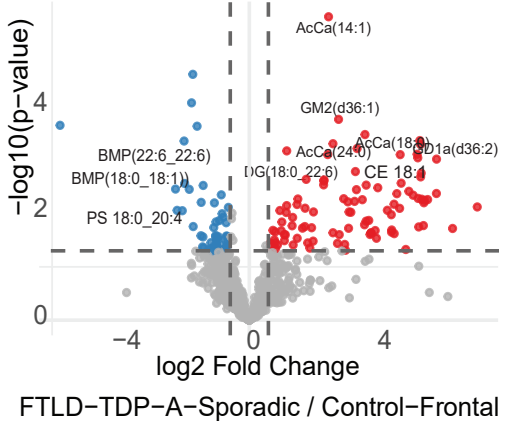
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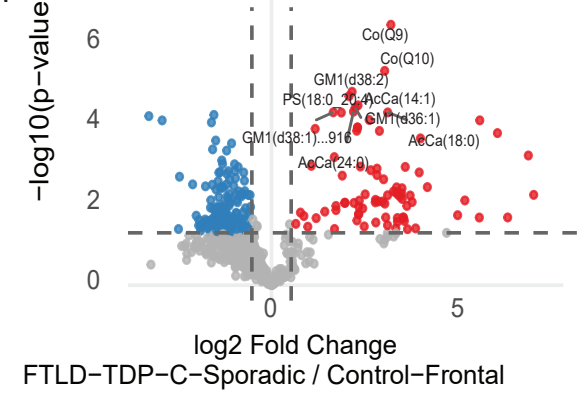
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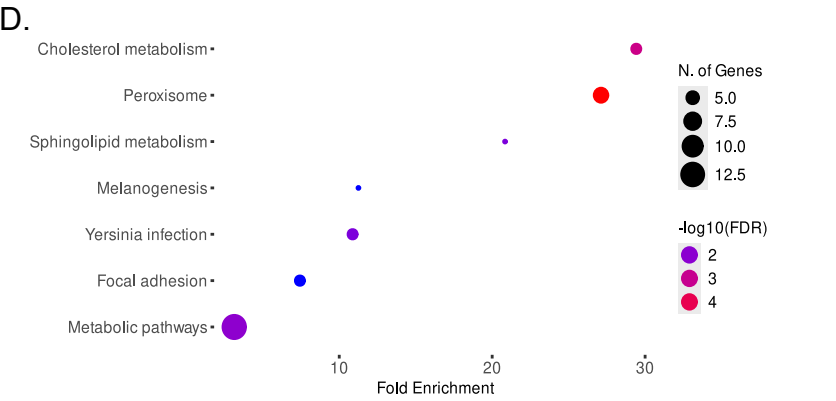
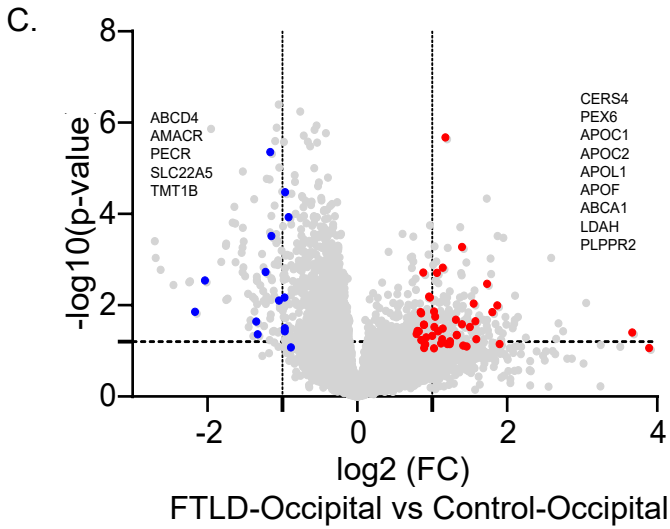
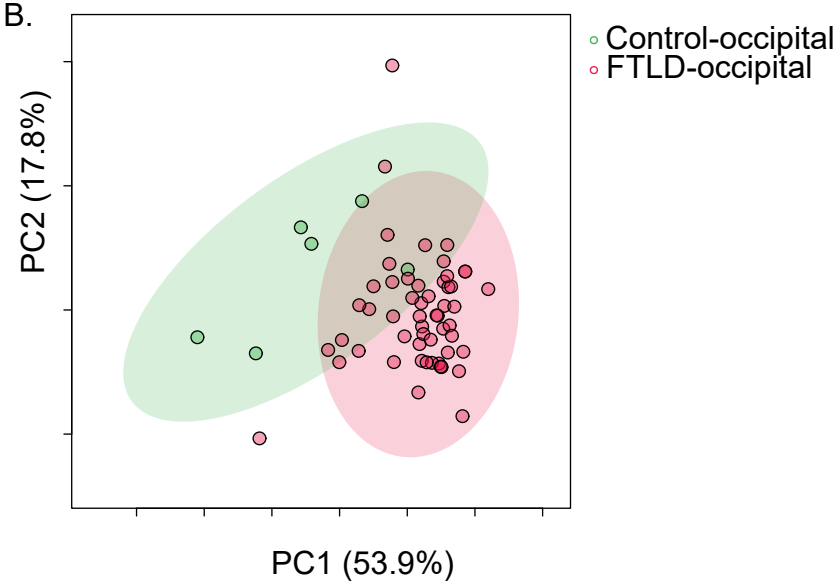
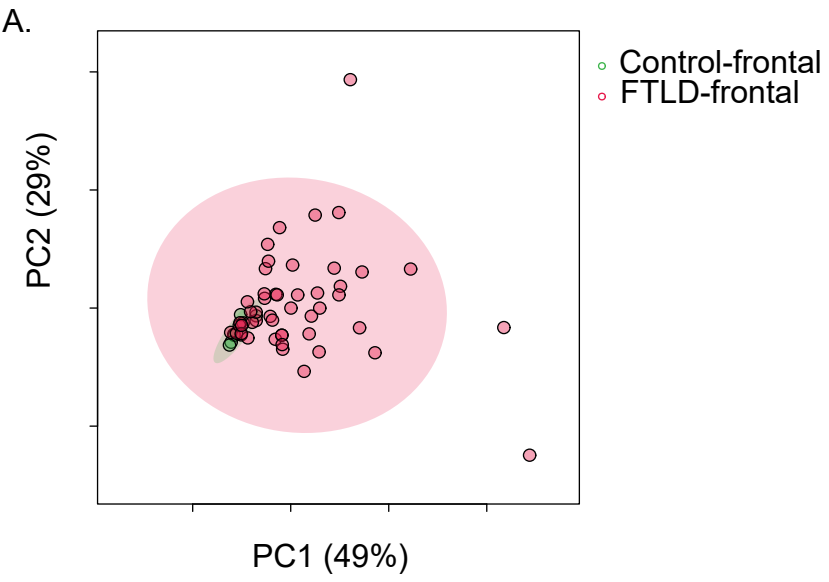


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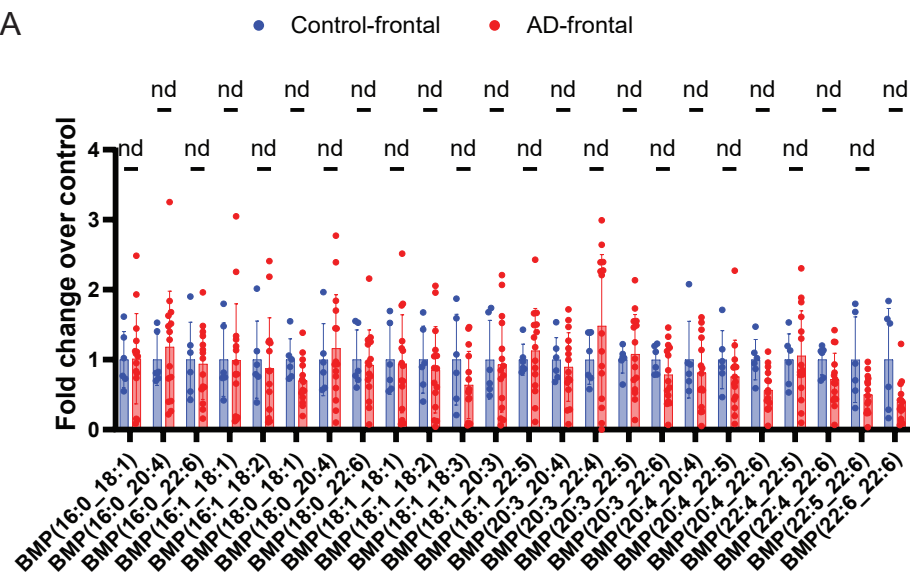


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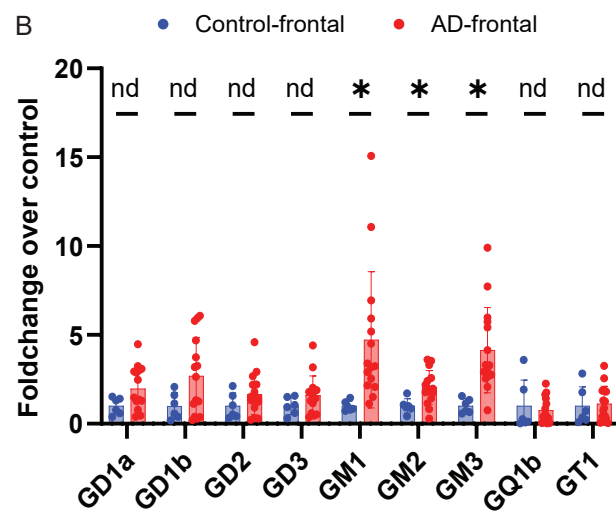




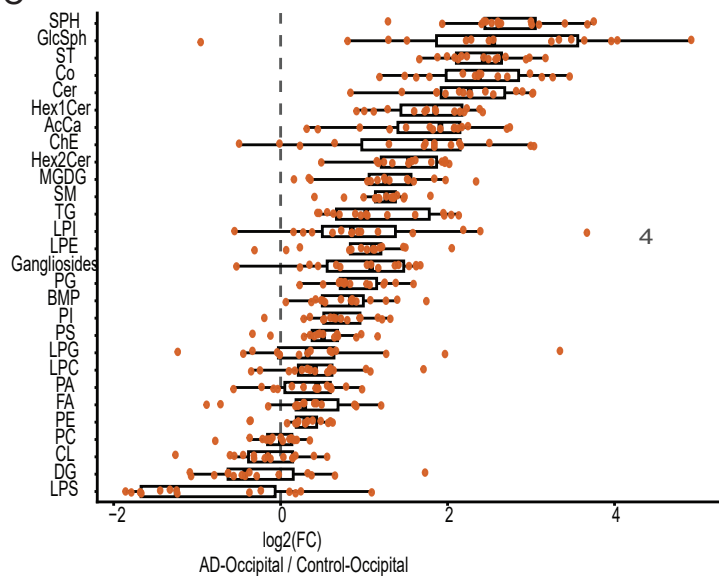
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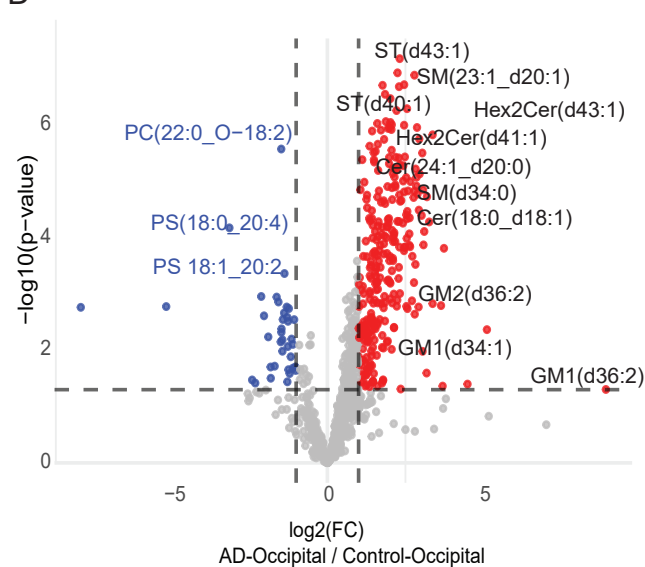
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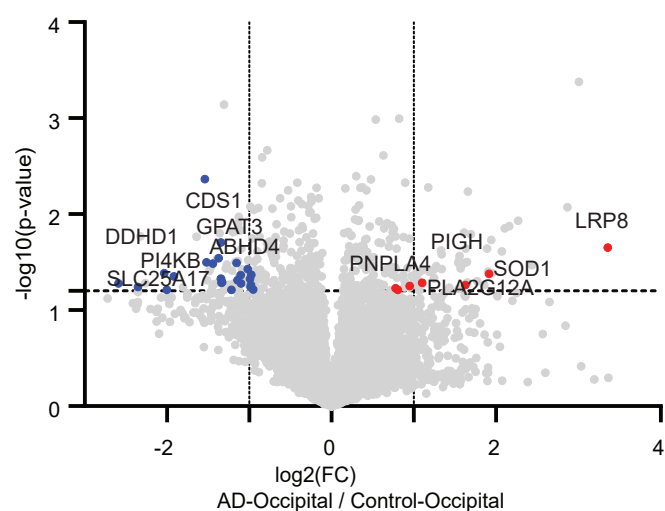
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