Supporting Information

Chronic PFOA and PFOS Exposure Triggers Cellular Oxidative Stress and Alters Lipid Levels as Revealed Through Multi-omics Analysis

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Table S1. Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS) analysis parameters.

PFAS	Adduct	Precursor Ion (*m/z*)	Product ions (*m/z*)	Collision Energy	Surrogate
PFOA	[M-H]$^-$	412.800	368.9	12	$^{13}C_8$-PFOA
			168.9	19	
PFOS	[M-H]$^-$	498.800	98.8	44	$^{13}C_8$-PFOS
			79.9	50	

Table S2. Matrix limit of detections (LODs) and limit of quantifications (LOQs) for hTERT RPE-1. LODs and LOQs were calculated using the formula LOD = 3(Sy/S) and LOQ = 10(Sy/S) and reported in ppb and ng/mg protein units. The standard deviation of the response (Sy) was obtained from the lowest concentration (n=7) while the slope (S) was obtained from the calibration curve shown in Figure S1.

PFAS	LOD		LOQ	
	ppb	ng/mg protein	ppb	ng/mg protein
PFOA	0.8634	0.7508	2.8780	2.5026
PFOS	0.0709	0.0616	0.2362	0.2054

Table S3. (separated file)

Targeted lipidomics of PFOA and PFOS-treated cells. Relative abundance was calculated as the ratio of each lipid's abundance to the mean abundance of the control group at the corresponding time point. The $\log_2$ of this ratio was then used to compute the $\log_2$ fold change. This is provided as a separate excel sheet.

Excel File: Table S3

Table S4. Average PFOA and PFOS uptake results +/- standard deviation in hTERT RPE-1 cells. Data are obtained from three independent replicates.

Time Points	PFOA, ng/mg protein	PFOS, ng/mg protein
24 hours	< LOD	0.39 ± 0.06
7 weeks	< LOD	0.38 ± 0.06
17 weeks	< LOD	0.26 ± 0.05
24 weeks	< LOD	0.42 ± 0.01

Table S5. (separated file)

Comprehensive summary table containing all differential expression results from transcriptomic analyses comparing PFOA and PFOS exposures to MeOH controls across multiple time points. Provided as a separate Excel file.

Excel File: Table S5

Table S6. (separated file)

Gene ontology (GO) enrichment results for differentially expressed genes ($|\log_2\text{FoldChange}| > 1$, $p < 0.05$) from both PFOA vs. MeOH and PFOS vs. MeOH comparisons at the 24-week time point. Results are merged into a separate excel file.

Excel File: Table S6

Table S7. (separated file)

Highly differentially expressed genes (DEGs) with their corresponding Gene ontology (GO) enrichment results ($|\log_2\text{FoldChange}| > 1$, $p < 0.05$) from PFOA vs PFOS comparison at the 24-week time point.
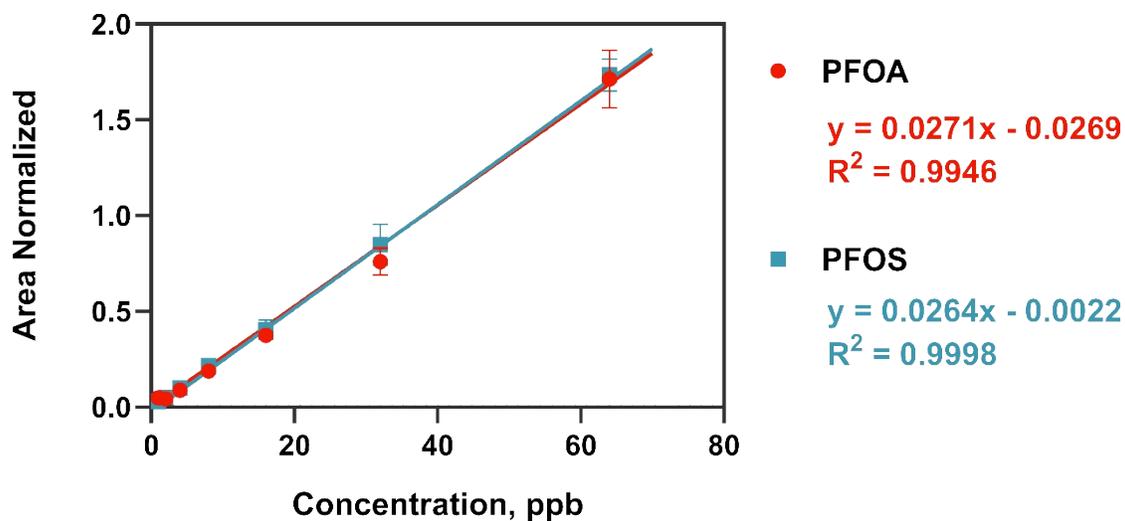
Excel File: Table S7

Figure S1. Matrix-matched calibration curves for PFOA and PFOS in hTERT RPE-1 cells. Seven-point calibration with replicates (n=3) were independently prepared for PFOA and PFOS using serial dilution of the highest concentration solution to cover 1 ppb to 64 ppb standards in matrix diluent containing 50 ppb of the corresponding isotopically labeled internal standard (M8PFOA for PFOA and M8PFOS for PFOS) for normalization.
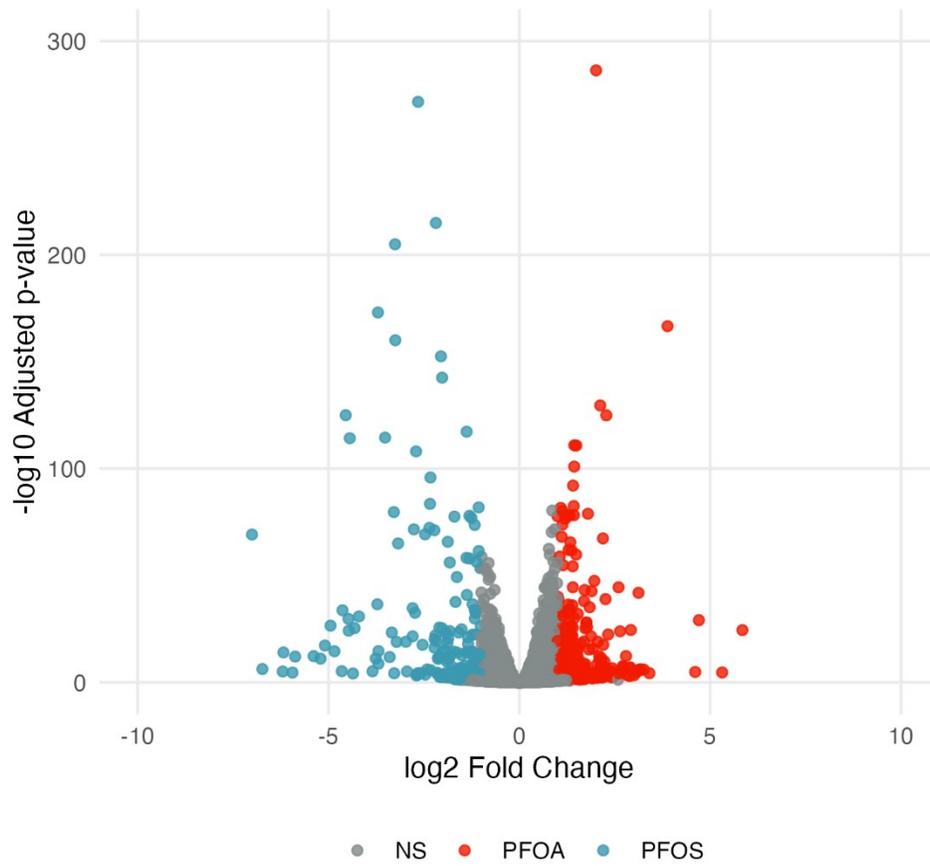
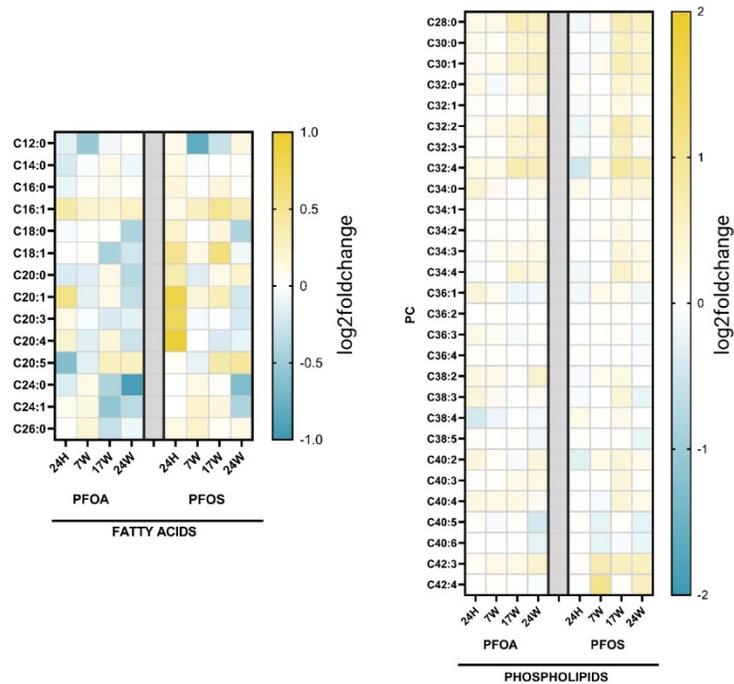**Figure S2**. Volcano plot showing the highly expressed genes in PFOA and PFOS at 24 weeks.

Figure S3. Heatmap of fatty acid (FA) and phosphatidylcholines (PC) alterations in hTERT RPE-1 cells after prolonged PFOA and PFOS exposure. Data are shown as log2foldchanges with respect to corresponding control group per time point.