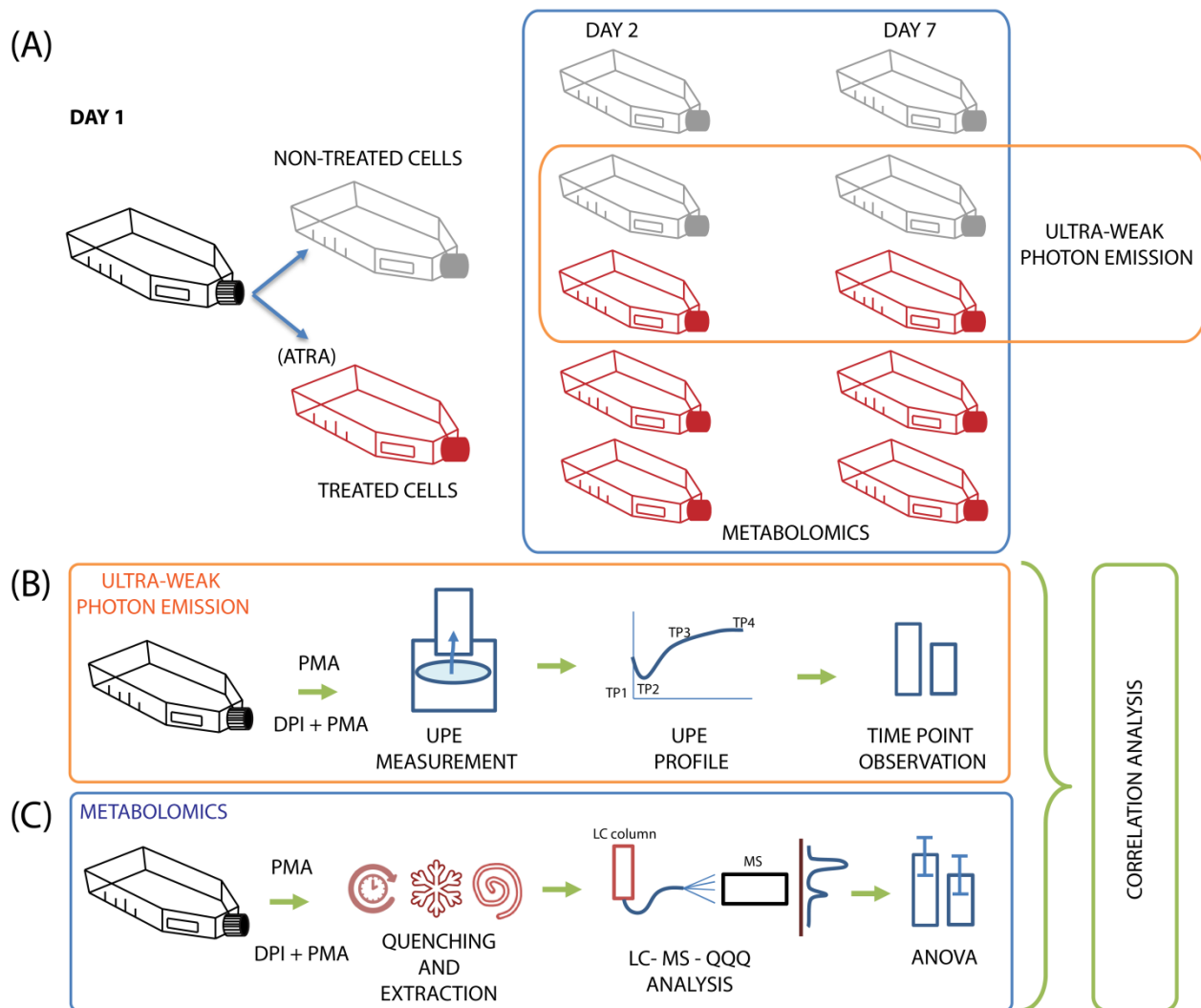


Supplementary Information

Ultra-weak photon emission as a dynamic tool for monitoring oxidative stress metabolism.

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Supplementary Figure S1: Experimental design. (A) Cultured HL-60 cells were split into 10 flasks; six flasks were treated with ATRA (red), and four flasks received only vehicle (grey). (B) Ultra-weak photon emission (UPE) was measured on days 2 and 7. PMA or DPI+PMA was applied to each flask to induce respiratory burst, and UPE was recorded for 9000 seconds. (C) Samples were collected for metabolomics analyses at the specified time points (TP1, TP2, TP3, and TP4) indicated in (B). TP1 samples were collected prior to the addition of PMA/ DPI. After sample collection, liquid-liquid extraction was used to obtain cell extracts and medium extracts. The metabolic profile was recorded using LC-MS-QQQ. The metabolic data were analysed using an ANOVA, and Spearman's correlation coefficient was calculated in order to analyse the relationship between the UPE data and metabolic profiles.

Supplementary Table S1: List of metabolites detected in the intracellular (cell lysates) and extracellular (culture medium) samples.

METABOLITE	INTRACELLULAR ANALYSIS	EXTRACELLULAR ANALYSIS
8-iso-PGE ₂	Detected	Not detected
8-iso-PGE ₁	Detected	Not detected
PGE ₂	Detected	Detected
PGE ₁	Detected	Detected
PGD ₂	Not detected	Detected
PGF _{2a}	Detected	Detected
(±)5-iPF2a-IV	Not detected	Detected
8-iso-PGA ₁	Detected	Detected
PGA ₂	Detected	Detected
8-12-iPF2a-IV	Detected	Detected
Sph C18_1	Detected	Not detected
Spha C18_0	Detected	Detected
NO ₂ -LA	Not detected	Detected

PGE, prostaglandin E; PGD, prostaglandin D; PGF, prostaglandin F; iPF, isoprostane F; PGA, prostaglandin A; Sph, sphingosine C18:1; Spha, sphinganine C18:0; NO₂-LA, nitro-linoleic acid.

Supplementary Table S2: Intracellular metabolites with significant changes during PMA and DPI+PMA treatment (n=3/ TP) collected on Day 7.

Sample Treatment	Compound	ANOVA			SPEARMAN'S CORRELATION	
		p-value	FDR ^a	Fisher's LSD ^b	Corr. Coefficient	p-value
PMA	Sphinganine C18:0	3.93E ⁻⁰⁵	0.00017	TP3 vs TP1; TP4 vs TP1; TP3 vs TP2; TP4 vs TP2; TP4 vs TP3	0.60	0.40
	8-iso-PGE1	4.23E ⁻⁰⁵	0.00017	TP3 vs TP1; TP4 vs TP1; TP3 vs TP2; TP4 vs TP2	0.80	0.20
	8-iso-PGE2	4.51E ⁻⁰⁵	0.00017	TP2 vs TP1; TP3 vs TP1; TP4 vs TP1; TP3 vs TP2; TP4 vs TP2	1.0	0.01
	PGE1	0.00097	0.00232	TP3 vs TP1; TP4 vs TP1; TP3 vs TP2; TP4 vs TP2	1.0	0.01
	Sphingosine C18:1	0.024	0.04847	TP1 vs TP3; TP2 vs TP3	-1.0	0.01
DPI + PMA	8-iso-PGE1	0.00017	0.00180	TP3 vs TP1; TP4 vs TP1; TP3 vs TP2; TP4 vs TP2	1.0	0.01
	8-iso-PGE2	0.0003	0.00180	TP3 vs TP1; TP4 vs TP1; TP3 vs TP2; TP4 vs TP2	1.0	0.01
	PGE1	0.018	0.07216	TP3 vs TP1; TP4 vs TP1; TP3 vs TP2; TP4 vs TP2	0.60	0.40

^a FDR: false discovery rate.

^b Fisher's LSD: significance between the Time Points (TP) indicated (*p-value*<0.05).

Supplementary Table S3: Extracellular metabolites with significant changes during PMA and DPI+PMA treatment (n=3 samples/group) collected on Day 7.

Sample Treatment	Compound	ANOVA			SPEARMAN'S CORRELATION	
		p-value	FDR ^a	Fisher's LSD ^b	Corr. Coefficient	p-value
PMA	(±)5-iPF2α-IV	9.25E ⁻⁰⁹	1.02E-07	TP3 vs TP1; TP4 vs TP1; TP3 vs TP2; TP4 vs TP2; TP4 vs TP3	0.74	0.26
	PGD2	5.28E ⁻⁰⁶	2.90E-05	TP3 vs TP1; TP4 vs TP1; TP3 vs TP2; TP4 vs TP2; TP4 vs TP3	0.80	0.20
	8-12-iPF2α-IV	0.000158	0.00058	TP3 vs TP1; TP4 vs TP1; TP3 vs TP2; TP4 vs TP2; TP4 vs TP3	0.80	0.20
	PGE2	0.018996	0.05223	TP4 vs TP1; TP4 vs TP2	0.80	0.20
DPI + PMA	PGD2	2.04E ⁻⁰⁷	2.24E-06	TP3 vs TP1; TP4 vs TP1; TP3 vs TP2; TP4 vs TP2; TP4 vs TP3	0.60	0.40
	PGE2	3.69E ⁻⁰⁶	2.03E-05	TP3 vs TP1; TP4 vs TP1; TP3 vs TP2; TP4 vs TP2; TP4 vs TP3	0.80	0.20
	(±)5-iPF2α-IV	3.11E ⁻⁰⁵	0.00011	TP1 vs TP2; TP3 vs TP1; TP4 vs TP1; TP3 vs TP2; TP4 vs TP2; TP4 vs TP3	0.60	0.40
	8-12-iPF2α-IV	0.00027	0.00074	TP1 vs TP3; TP2 vs TP3; TP4 vs TP3	0.60	0.40

^a FDR: false discovery rate.

^b Fisher LSD: significance between the Time Points (TP) indicated (*p-value*<0.05).