# Supplementary Materials

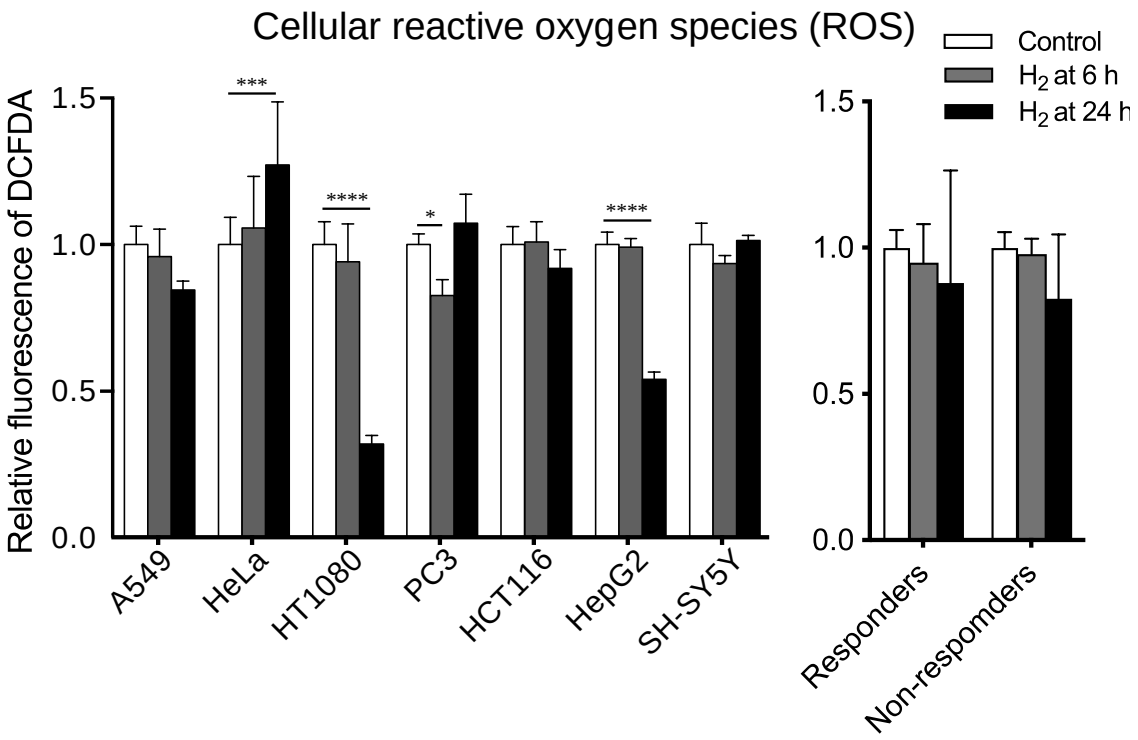
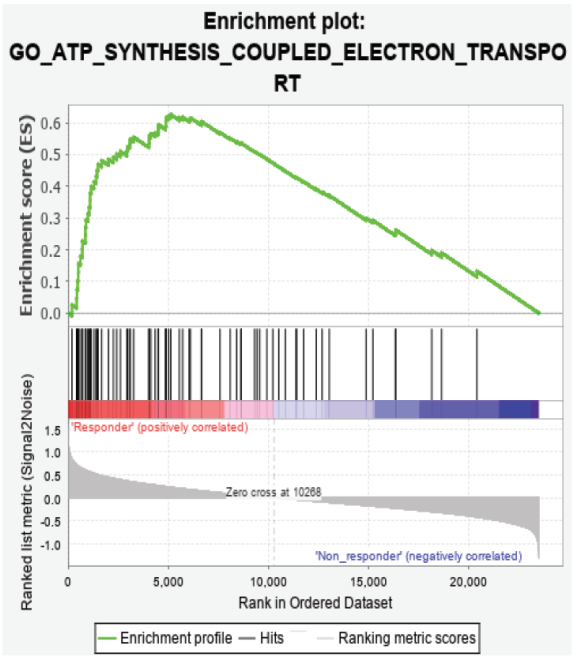



**Figure S1.** Change of cellular ROS levels by hydrogen gas. Relative fluorescence of DCFDA was measured using flowcytometry at 6 and 24 h under 1% hydrogen gas. Mean and SD are indicated ($n$ = 3 culture dishes). *$p$ < 0.05, **$p$ < 0.01, ***$p$ < 0.001 and ****$p$ < 0.0001 by two-way repeated measures ANOVA followed by Dunnett's multiple comparison test compared to control.

a




b

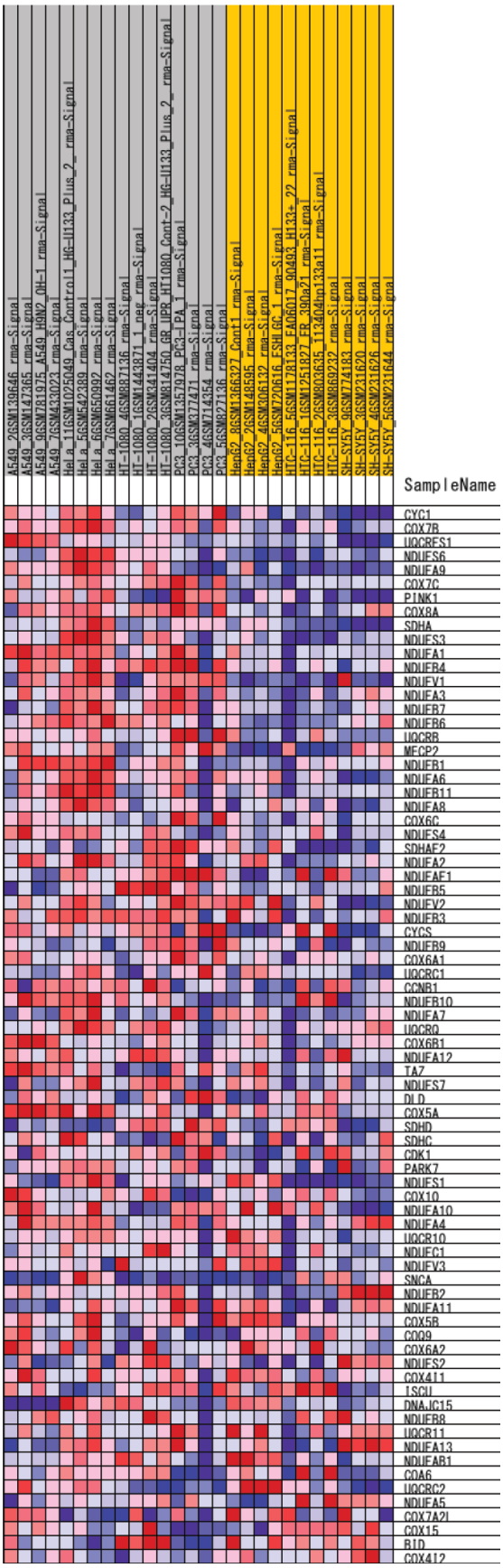



**Figure S2.** Gene sets enriched in the responders. An enrichment plot (**a**) and a heatmap (**b**) of "ATP synthesis coupled electron transport" that was the most enriched gene set in the responders (see Figure 3a).

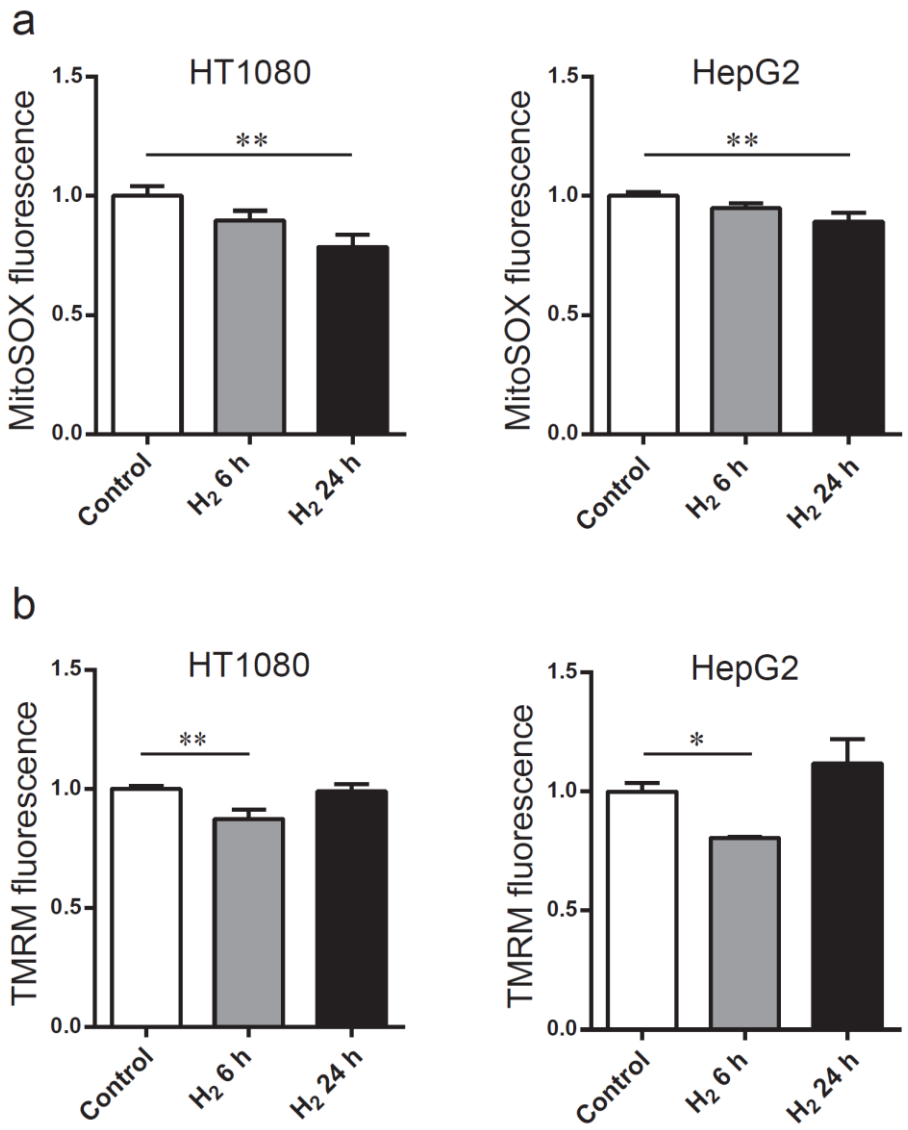



**Figure S3.** Mitochondrial superoxide (MitoSOX) and mitochondrial membrane potential (TMRM) in HT1080 cells (a responder) and HepG2 cells (a non-responder) under 10% hydrogen gas. Relative fluorescence of MitoSOX (**a**) and TMRM (**b**) was measured using flowcytometry after 6- and 24-h incubation under 10% hydrogen gas. Mean and SD are indicated (n = 3 culture dishes). *$p < 0.05$ and **$p < 0.01$, by one-way ANOVA followed by Dunnett's multiple comparison test compared to control.

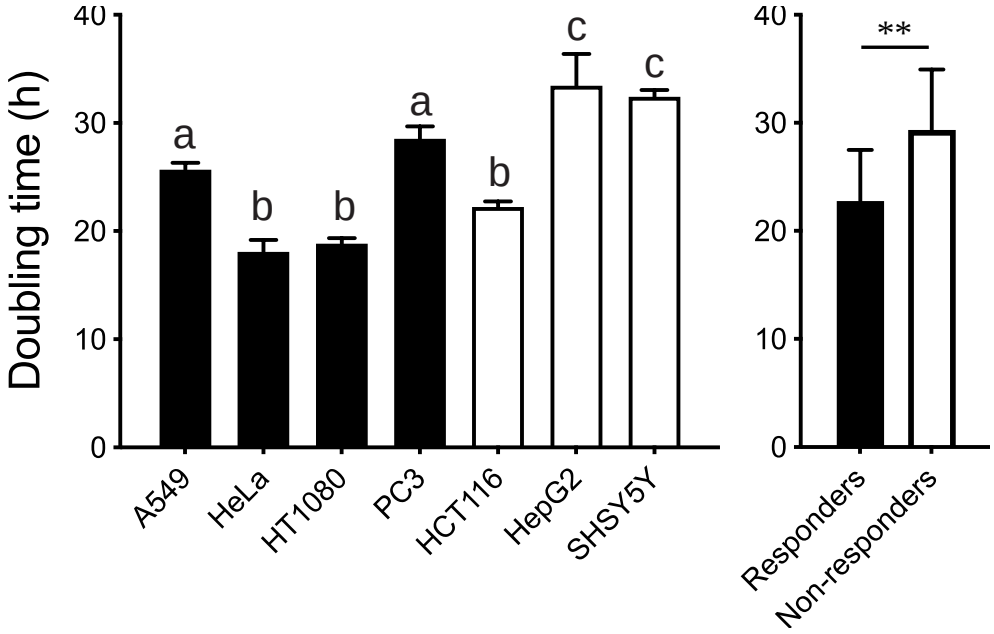



**Figure S4.** Doubling time of seven cell lines. Mean and SD are indicated ($n$ = 3 culture dishes). Single letter labels indicate $p < 0.05$ by one-way ANOVA followed by Tukey's multiple comparison test. Values in the same label (for example, two "a's") are not statistically different each other. **$p < 0.01$ by Student's $t$-test between the responders and non-responders.

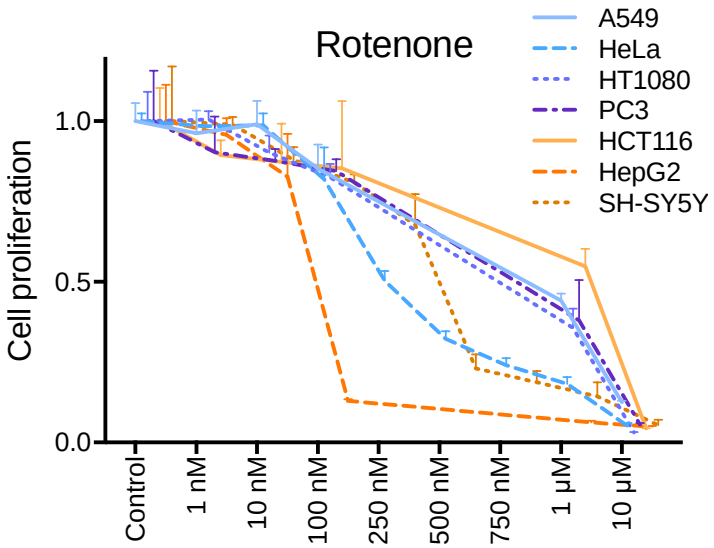



**Figure S5.** Calibration of proliferation inhibition by rotenone. Relative amount of incorporated BrdU in the seven cell lines under the indicated concentrations of rotenone. The values were normalized for that without rotenone (control). Mean and SD are indicated ($n$ = 3 culture dishes).

**Table S1.** Antibodies for Western blotting.

| Molecule | Manufacturer | Host | Cat. No. | Dilution |
|---|---|---|---|---|
| HSP60 | Cell Signaling Technology | Rabbit polyclonal | D307 | 1:1000 |
| VDAC1 | Abcam | Mouse monoclonal | ab14734 | 1:1000 |
| Phospho-eIf2α (Ser51) | Cell Signaling Technology | Rabbit polyclonal | 9721 | 1:1000 |
| ATF5 | Abcam | Rabbit monoclonal | ab184923 | 1:1000 |
| β-actin | Santa Cruz | Mouse monoclonal | sc-47778 | 1:1000 |

**Table S2.** GEO microarray datasets for gene set enrichment analyses.

| Cells | Accession number |
|---|---|
| A549 | 2GSM139646 |
| A549 | 3GSM147365 |
| A549 | 6GSM335974 |
| A549 | 9GSM781975_A549_H9N2_0H-1 |
| HeLa | 3GSM463942 |
| HeLa | 5GSM542389 |
| HeLa | 7GSM661462 |
| HeLa | 9GSM930228_Cnt_1 |
| HepG2 | 1GSM1692555_Cont1_HG-U133_Plus_2_ |
| HepG2 | 5GSM720616_FSHLGC_1 |
| HepG2 | 6GSM726069_HepG2_APRIL_0h |
| HepG2 | 8GSM1366327_Cont1 |
| HT1080 | 1GSM1443871_1_neg |
| HT1080 | 2GSM341404 |
| HT1080 | 3GSM814750_GR_UPR_HT1080_Cont-2_HG-U133_Plus_2_ |
| HT1080 | 4GSM887136 |
| HCT116 | 1GSM1251827_FR_390a21 |
| HCT116 | 2GSM803635_113404hp133a11 |
| HCT116 | 4GSM1017469_mRNA_6a_041206 |
| HCT116 | 5GSM1178133_EA06017_90493_H133+_22 |
| PC3 | 3GSM377471 |
| PC3 | 4GSM714354 |
| PC3 | 5GSM827136 |
| PC3 | 10GSM1357978_PC3-LPA_1 |
| SH-SY5Y | 3GSM231620 |
| SH-SY5Y | 5GSM231644 |
| SH-SY5Y | 6GSM231654 |
| SH-SY5Y | 7GSM231664 |