

Capturing complex tumour biology *in vitro*: histological and molecular characterisation of precision cut slices

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The PREDECT Consortium - Tissue Slice Platform*

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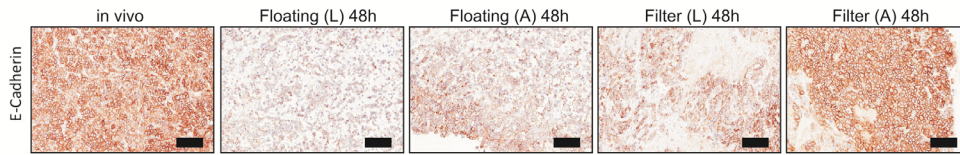
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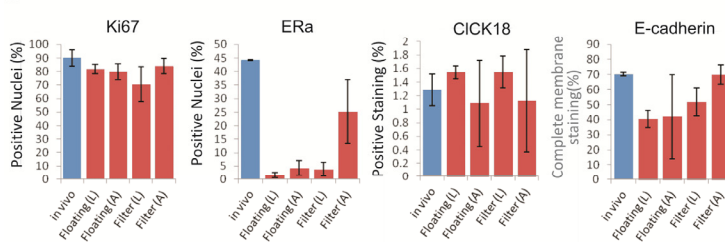
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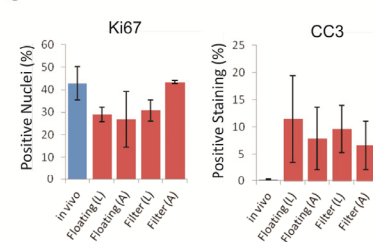
a MCF-7 CDX – 48h



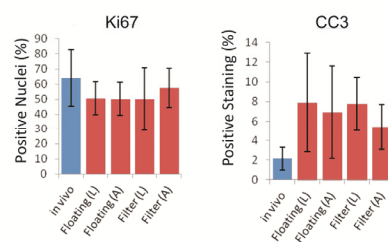
b MCF-7 CDX – 48h



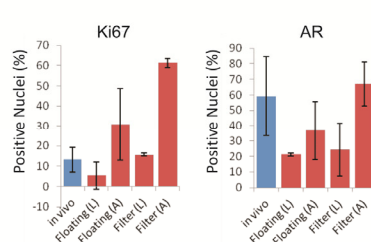
c H1437 CDX – 72h



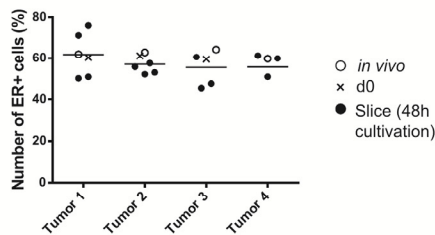
d 1647 PDX – 72h



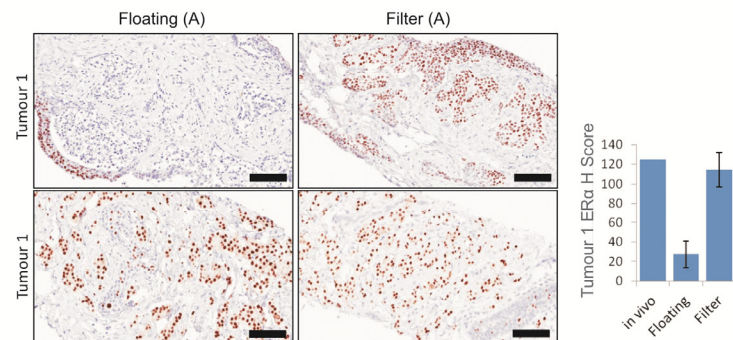
e PC295 PDX – 48h



f MCF-7 CDX – 48h



g ERα - Patient Breast Tumour



Supplementary Figure 1: **Changes in biomarkers according to culture condition.** (a) E-cadherin stained MCF-7 tumour tissue slice sections: retention of complete membranous staining is only observed in tumour slices cultivated on filter supports in atmospheric oxygen. Scale bars represent 100µm. (b-e) Histograms of the quantification of immunohistochemical staining for each of the biomarkers used to generate the heatmaps for each tumour type in Figure 2. Values reflect the means from three independent experiments, error bars represent standard deviations. (f) The total percentage of ER positive cells was quantified in the *in vivo* tumour, the day 0 (d0) samples and in slices cultivated for 48h. Levels of ER positive cells were similar to that found *in vivo*. (g) Slices from two patient breast tumours were cultivated with and without a filter support. Cultivation without a filter support caused a significant loss of ERα positive cells in slices from tumour 1 but had no effect on ERα positive cells in slices from tumour 2. Scale bars represent 100µm.

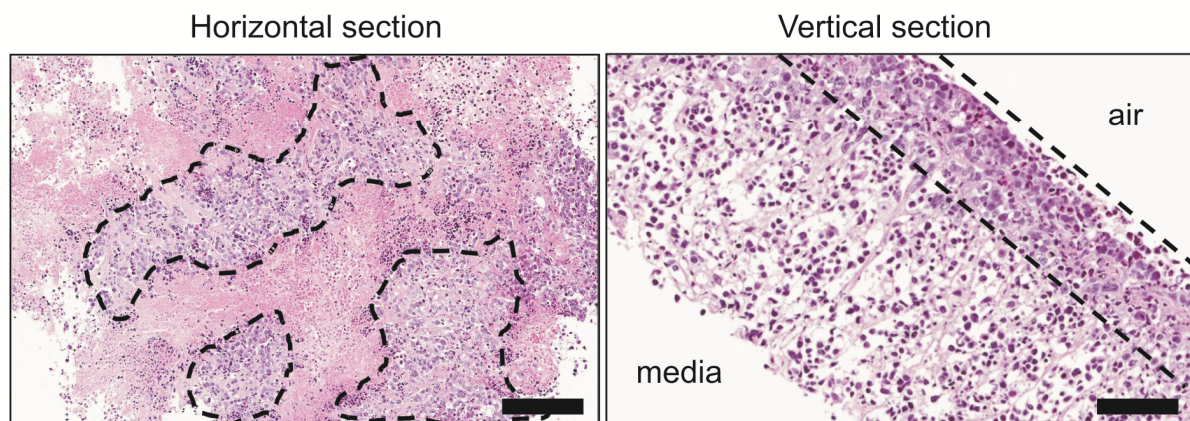
a

oxygen level		A	L	A	L		A	L	A	L
filter-support	d0	+	+	-	-		+	+	-	-
breast MCF-7 CDX	0	6	4	nd	nd	0	22	16	nd	nd

upregulated **downregulated**

b MCF-7 CDX

oxygen level	A	L	A	L	A	L	A	L
filter-support	+	+	-	-	+	+	-	-
apoptosis	1	0	nd	nd	4	1	nd	nd
cell cycle	0	2	nd	nd	10	6	nd	nd
DDR	1	0	nd	nd	5	4	nd	nd
necrosis/autophagy	0	0	nd	nd	0	0	nd	nd
NFkB	0	0	nd	nd	1	2	nd	nd
p38/JNK	0	0	nd	nd	2	1	nd	nd
ROS	2	0	nd	nd	0	1	nd	nd
UPR/ER stress	2	2	nd	nd	0	1	nd	nd

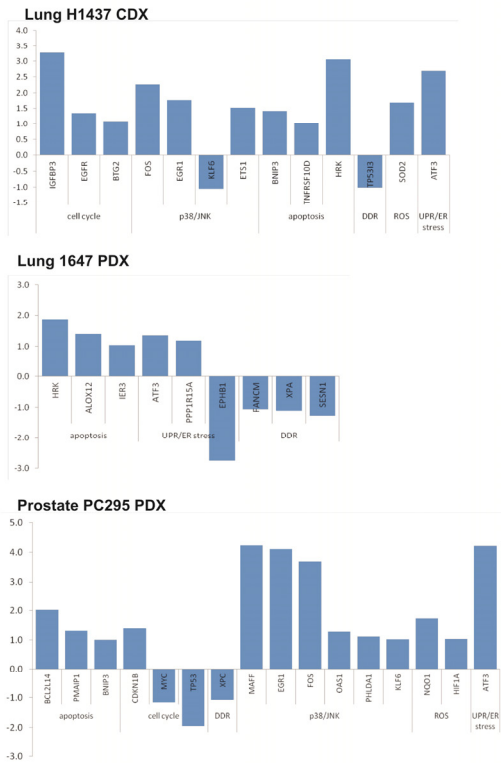
c MCF-7 CDX – Filter, Low Oxygen

Supplementary Figure 2: **Stress biomarker changes in MCF-7 tumour slices.** (a) Total numbers of differentially expressed stress transcripts in MCF-7 tumour slices cultivated on filters in atmospheric and low oxygen conditions. Insufficient RNA could be extracted from MCF-7 tumour slices cultivated under floating conditions. (b) Table of the numbers of differentially expressed genes (DEGs) and their associated functions in MCF-7 tumour slices. Results are from three independent experiments. (c) H&E stained sections of MCF-7 tumour slices cultivated on filters under conditions of low oxygen; dashed line indicates areas of viable cells. Scale bars represent 100µm.

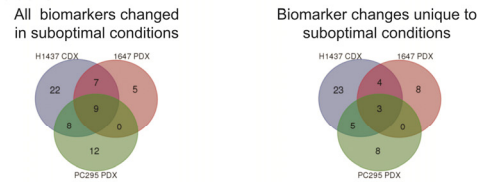
a Biomarker changes in lung and prostate models under optimal culture conditions



b Details of changes under optimal culture conditions



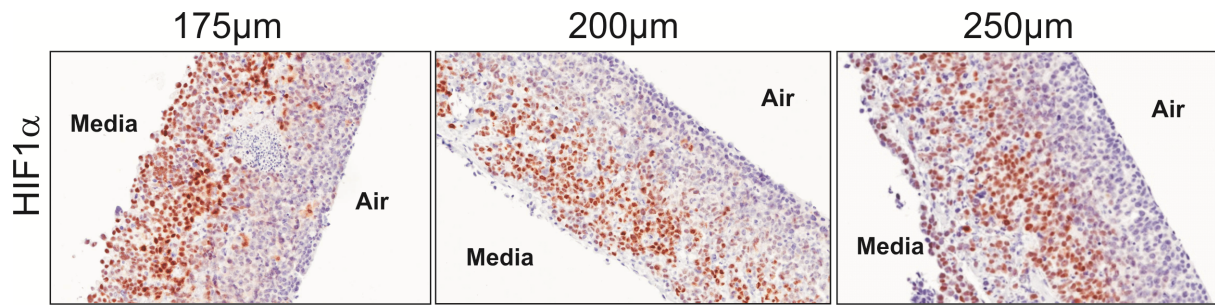
c Biomarker changes in lung and prostate models under suboptimal culture conditions



d Details of changes unique to suboptimal culture conditions



Supplementary Figure 3: **Stress biomarker changes for each model cultivated under either optimal or suboptimal conditions.** The fold-changes in transcriptional biomarkers observed in slices from MCF-7, PC295, H1437 and LXFA 1647 xenografts after cultivation. Red indicates significantly up-regulated genes and green indicates down-regulated genes ($p < 0.05$). (a) Venn diagram showing the stress gene transcripts deregulated in three xenograft models. (b) Details of the individual changes shown in the Venn diagram. (c) Venn diagrams of all biomarker changes observed under suboptimal conditions (floating and low oxygen conditions) and those unique to suboptimal conditions of slice culture. (d) Details of the individual changes in slices from three xenograft models unique to suboptimal conditions. Results are from three independent experiments.



Supplementary Figure 4: **HIF1 α expression in slices of varying thicknesses.** Generation of a gradient of HIF1 α expression after 24h in slices of MCF-7 CDX cut at 175 to 250 μ m and incubated under optimal conditions (filter support, incubation in air, on Millicell Cell Culture inserts (see Methods)).

Supplementary Table 1: A list of the transcripts analysed and their functional classification.

Gene names	Assay (Applied)	Functional Gene Grouping	Upstream pathway/transcription factor	Refs #
ABCB1	Hs00184500_m1	Drug transporter	p53/NFkB	1
ACTB	Hs03023943_g1	housekeeping gene		
AIFM2	Hs01097299_m1	apoptosis	p53	2
ALOX12	Hs00911144_m1	apoptosis	NFkB	3
APAF1	Hs00559440_m1	apoptosis	p53	4
ATF2	Hs01099617_m1	UPR/ER stress	target of stress regulated miR-451	5
ATF3	Hs00231069_m1	UPR/ER stress	p53/p38	6
ATF4	Hs00909569_g1	UPR/ER Stress	UPR target gene	7
ATF6	Hs00232586_m1	UPR/ER Stress	UPR transcription factor	8
ATG12	Hs01047860_g1	necrosis/autophagy	target of ATF4	9
ATG5	Hs01555465_m1	necrosis/autophagy	induced by DNA damage	10
ATG7	Hs00197348_m1	necrosis/autophagy	target of miR17	11
ATM	Hs00175892_m1	DNA damage and repair	BRCA1/E2F1/CtIP	12
ATR	Hs00992132_m1	DNA damage and repair	target of stress regulated miR-185	13
BAK1	Hs00832876_g1	apoptosis	p53	14
BCL2	Hs01048932_g1	apoptosis	NFkB/p53	15, 16
BCL2A1	Hs03405589_m1	apoptosis	p53/NFkB	17, 18
BCL2L1	Hs01067345_g1	apoptosis	NFkB	19
BCL2L11	Hs01083836_m1	apoptosis	NFkB	20
BCL2L13	Hs00209787_m1	apoptosis	prosurvival signals and oncogenes	
BCL2L14	Hs00373302_m1	apoptosis	p53	21
BECN1	Hs01011594_g1	necrosis/autophagy	NFkB	22
BID	Hs00609632_m1	apoptosis	p53	23
BIK	Hs00154189_m1	apoptosis	DNA damage/cytokines	24
BIRC2	Hs01112284_m1	apoptosis	NFkB	25
BLM	Hs01119886_g1	DNA damage and repair	prosurvival signals and oncogenes	26
BNIP3	Hs00969289_m1	apoptosis	NFkB	27
BOK	Hs00261296_m1	apoptosis	p53	28
BRCA1	Hs01556185_m1	DNA damage and repair	regulated by specific factors binding single-stranded DNA	29
BTG2	Hs00198887_m1	proliferation/cell cycle regulation	p53	17

CCNA2	Hs00153138_m1	proliferation/cell cycle regulation	p53	30
CCNB1	Hs01030097_m1	proliferation/cell cycle regulation	p53	31
CCNG1	Hs00171112_m1	proliferation/cell cycle regulation	p53	32
CCNK	Hs01083210_m1	proliferation/cell cycle regulation	p53	33
CDC25C	Hs00156411_m1	proliferation/cell cycle regulation	p53	34
CDK1	Hs00364293_m1	proliferation/cell cycle regulation	p53	35
CDKN1A	Hs99999142_m1	proliferation/cell cycle regulation	p53/NFkB	17 36 ,
CDKN1B	Hs00153277_m1	proliferation/cell cycle regulation	prosurvival signals and oncogenes	37
CFLAR	Hs01116281_m1	apoptosis	NFkB	38
CHEK1	Hs00967510_g1	proliferation/cell cycle regulation	NF-Y-p53	39
DDB2	Hs03044953_m1	DNA damage and repair	p53/BRCA1/AP1	17
DNAJC3	Hs00534489_m1	UPR/ER Stress	UPR target gene	40
EDEM1	Hs00976004_m1	UPR/ER Stress	UPR target gene	40
EDEM2	Hs01076556_m1	UPR/ER Stress	UPR target gene	41
EGFR	Hs01076078_m1	proliferation/cell cycle regulation	p53/NFkB	42 16 ,
EGR1	Hs00152928_m1	p38/JNK	NFkB/p38	43 44 ,
EPHB1	Hs01057855_m1	UPR/ER Stress	UPR target gene	
ERCC1	Hs01012156_m1	DNA damage and repair	AP-1/MZF1	45
ETS1	Hs00901423_m1	p38/JNK	p38	46
FANCA	Hs01116661_m1	DNA damage and repair	target of miR-503	47
FANCD2	Hs00395700_m1	DNA damage and repair	transcriptionally regulated under stress (hypoxia)	48
FANCG	Hs00184947_m1	DNA damage and repair	target of stress responsive miR23a	49
FANCM	Hs00913609_m1	DNA damage and repair	HOXC9	13
FAS	Hs00531110_m1	apoptosis	p53/NFkB	17 50 ,
FASLG	Hs00181226_g1	apoptosis	p53/NFkB	51
FEN1	Hs01099393_g1	DNA damage and repair	p53/AP1	52
FOS	Hs01119266_g1	p38/JNK	p53/p38	44
FOSL1	Hs04187685_m1	p38/JNK	p38	44
FTH1	Hs01000476_g1	ROS	NFkB	53

GRB2	Hs00257910_s1	necrosis/autophagy		
GSTP1	Hs00168310_m1	ROS	NFkB	54
HERPUD1	Hs01124265_m1	UPR/ER Stress	UPR target gene	40
HGF	Hs00900067_m1	proliferation/cell cycle regulation	p53/NFBkB	17 55 ,
HIF1A	Hs00936368_m1	ROS	NFkB/transcriptionally regulated under hypoxia	56 57 ,
HMOX1	Hs01110250_m1	ROS	NFkB	58
HRK	Hs01388767_g1	apoptosis	prosurvival signals and oncogenes	59
HSP90AA1	Hs00743767_sH	UPR/ER Stress	NFkB	60
HSPA5	Hs00946084_g1	UPR/ER Stress	UPR target gene	40
IER3	Hs04187506_g1	apoptosis	p53/NFBkB	16 61 ,
IGFBP3	Hs00426287_m1	proliferation/cell cycle regulation	p53	16
JUN	Hs00277190_s1	p38/JNK	p38	44
JUND	Hs02330233_u1	p38/JNK	p38	62
KLF6	Hs00296661_s1	p38/JNK	p38	44
MAFF	Hs00202412_m1	p38/JNK	p38	44
MAPK8	Hs01548508_m1	p38/JNK	KLF4/FOXM1	63
MCL1	Hs00172036_m1	apoptosis	prosurvival signals and oncogenes	64
MDM2	Hs00234753_m1	proliferation/cell cycle regulation	p53	17
MDM4	Hs00159092_m1	proliferation/cell cycle regulation	p53	17
MET	Hs01565584_m1	proliferation/cell cycle regulation	p53	16
MLH1	Hs00179866_m1	DNA damage and repair	p53/AP1	17
MSH2	Hs00954125_m1	DNA damage and repair	p53/AP1	16
MYC	Hs00905030_m1	proliferation/cell cycle regulation	p53/NFBkB/p38	17 65 44 , ,
NLRP2	Hs01546932_m1	DNA damage and repair	NFkB	66
NOS2A	Hs01075523_m1	apoptosis	NFkB	67
NQO1	Hs00168547_m1	ROS	NFkB	68
OAS1	Hs00242943_m1	p38/JNK	p38	44
P2RY13	Hs01090437_g1	UPR/ER Stress	UPR target gene	
PARP1	Hs00911377_g1	necrosis/autophagy		
PCNA	Hs00696862_m1	proliferation/cell cycle regulation	p53/AP1	17

PGK1	Hs00943178_g1	housekeeping gene		
PHLDA1	Hs00378285_g1	p38/JNK	p38	44
PIDD	Hs01076855_g1	apoptosis	p53	69
PLA2G6	Hs00895666_m1	UPR/ER Stress	UPR target gene	70
PMAIP1	Hs00560402_m1	apoptosis	p53	17
POL2RB	Hs00265358_m1	housekeeping gene		
PPP1R15A	Hs00921550_g1	UPR/ER Stress	UPR target gene	71
PRDX1	Hs03044568_g1	ROS	NRF-2 upon oxidative stress	72
PVR	Hs00197846_m1	necrosis/autophagy	NRF-1 upon oxidative stress	73
RAD51	Hs00947964_m1	DNA damage and repair	transcriptionally regulated under stress (hypoxia)	48
RB1	Hs01078075_m1	proliferation/cell cycle regulation	p53	16
RIPK1	Hs00169407_m1	necrosis/autophagy		
RPA1	Hs01556877_m1	proliferation/cell cycle regulation		
RPLP0	Hs02992885_s1	housekeeping gene		
RRM2B	Hs00968427_m1	DNA damage and repair	p53	74
SENP2	Hs00989703_m1	apoptosis	NFkB	75
SESN1	Hs00902782_m1	DNA damage and repair	p53	17
SFN	Hs00968567_s1	proliferation/cell cycle regulation	p53	76
SHISA5	Hs00429977_m1	apoptosis	p53	77
SIRT1	Hs01009000_m1	DNA damage and repair	target of stress inducible miR34a and HuR	78
SOD1	Hs00916176_m1	ROS	NFkB	79
SOD2	Hs04260076_g1	ROS	NFkB	80
SQSTM1	Hs01061917_g1	ROS	NRF-2 upon oxidative stress	81
SUMO1	Hs00830844_g1	DNA damage and repair	target of stress inducible miR150	
TAP73	Hs01056228_m1	proliferation/cell cycle regulation	p53	82
TBP	Hs00427621_m1	housekeeping gene		
TERT	Hs00972656_m1	proliferation/cell cycle regulation	p53/NFkB	83
TNFRSF10A	Hs00269492_m1	apoptosis	p53/NFkB	84
TNFRSF10B	Hs00366278_m1	apoptosis	p53/NFkB	17
TNFRSF10C	Hs00182570_m1	apoptosis	p53/NFkB	85

TNFRSF10D	Hs04187502_m1	apoptosis	p53/NFBkB	17
TP53	Hs99999147_m1	proliferation/cell cycle regulation	p53/NFBkB	86, 16
TP53AIP1	Hs00986095_m1	apoptosis	p53/NFBkB	87
TP53I3	Hs00936520_m1	DNA damage and repair	p53/NFBkB	17
TP53INP1	Hs00264502_m1	DNA damage and repair	p53/NFBkB	17
TP63	Hs00978342_m1	proliferation/cell cycle regulation	p53/NFBkB	16
TP73	Hs01056230_m1	proliferation/cell cycle regulation	p53/NFBkB	17
TRAF1	Hs01090167_g1	apoptosis	p53/NFBkB	88
TRAF2	Hs00184192_m1	apoptosis	p53/NFBkB	89
TRPM3	Hs01558432_m1	p38/JNK		
TXN	Hs00828652_m1	ROS	NRF-2 upon oxidative stress	90
XBP1	Hs00231936_m1	UPR/ER Stress	UPR target gene	91
XBP1(U)	Hs02856596_m1	UPR/ER Stress	UPR target gene	91
XIAP	Hs00745222_s1	apoptosis	NFkB	92
XPA	Hs00166045_m1	DNA damage and repair	HIF1a	57
XPC	Hs01104213_m1	DNA damage and repair	p53/BRCA1/AP1	17
XRCC1	Hs00959834_m1	DNA damage and repair	E2F1/AP1	93
XRCC3	Hs00193725_m1	DNA damage and repair	transcr inducable by irradiation	94
ZFP36	Hs00185658_m1	p38/JNK	p38	44
ZMAT3	Hs00536976_m1	apoptosis	p53	95

Supplementary Table 2: Part 1: The fold-changes in transcriptional biomarkers observed in slices from H1437 after cultivation.

H1437 lung CDX

filter, atmospheric oxygen vs in vivo				
process	ID	logFC	P.Value	adj.P.Val
apoptosis	HRK	3.06	2.21E-03	1.91E-02
apoptosis	BNIP3	1.41	5.53E-04	6.09E-03
apoptosis	TNFRSF10C	1.00	1.83E-04	3.16E-03
cell cycle	IGFBP3	3.29	1.08E-03	1.09E-02
cell cycle	EGFR	1.35	4.91E-03	3.64E-02
cell cycle	BTG2	1.09	7.47E-03	4.76E-02
DDR	TP53I3	-1.02	5.11E-03	3.64E-02
p38/JNK	FOS	2.26	2.38E-06	1.44E-04
p38/JNK	EGR1	1.76	3.43E-05	1.06E-03
p38/JNK	ETS1	1.52	6.18E-05	1.25E-03
p38/JNK	KLF6	-1.06	3.79E-05	1.06E-03
ROS	SOD2	1.69	4.37E-05	1.06E-03
UPR/ER str	ATF3	2.70	2.36E-07	2.85E-05

filter, low oxygen vs in vivo				
process	ID	logFC	P.Value	adj.P.Val
apoptosis	BCL2A1	3.01	1.16E-03	2.86E-03
apoptosis	MCL1	2.76	1.12E-07	1.23E-06
apoptosis	IER3	2.72	7.86E-04	2.21E-03
apoptosis	TNFRSF10C	2.51	1.01E-08	2.05E-07
apoptosis	BNIP3	2.23	7.72E-06	4.45E-05
apoptosis	TRAF1	2.12	8.58E-05	3.35E-04
apoptosis	BCL2L1	1.88	6.87E-08	3.35E-07
apoptosis	TNFRSF10C	1.88	6.87E-08	3.35E-07
apoptosis	BCL2L1	1.39	1.39E-03	3.16E-04
apoptosis	PMAIP1	1.29	3.59E-06	2.29E-05
apoptosis	XIAP	1.28	8.55E-06	4.50E-05
apoptosis	TNFRSF10C	1.04	4.07E-03	8.48E-03
apoptosis	FAS	-1.11	7.57E-03	1.40E-02
apoptosis	ZMAT3	-1.14	1.06E-03	2.71E-03
cell cycle	IGFBP3	4.36	9.71E-05	3.56E-04
cell cycle	TP73	3.55	2.69E-04	8.33E-04
cell cycle	Tap73	3.32	1.19E-03	2.88E-03
cell cycle	BTG2	3.27	3.68E-07	3.18E-06
cell cycle	EGFR	2.84	8.32E-06	4.50E-05
cell cycle	CDKN1A	2.81	1.17E-06	8.31E-06
cell cycle	MET	1.96	1.96E-07	1.82E-06
cell cycle	CDKN1B	1.49	1.04E-06	7.88E-06
cell cycle	TP63	1.25	1.14E-02	1.19E-02
cell cycle	PCNA	-1.56	2.09E-04	6.82E-04
cell cycle	CDC25C	-1.71	6.22E-04	1.84E-03
cell cycle	CEN2A	-1.84	1.30E-03	3.03E-03
cell cycle	CCNB1	-1.89	1.93E-04	6.65E-04
cell cycle	CHEK1	-2.06	1.12E-04	3.97E-04
cell cycle	HGF	-2.21	2.55E-02	4.17E-02
cell cycle	CDK1	-2.84	4.23E-06	2.56E-05
DDR	ERCC1	1.44	8.76E-04	2.36E-03
DDR	TP53INP1	1.07	3.18E-03	6.75E-03
DDR	MSH2	-1.08	1.98E-04	6.65E-04
DDR	SESN1	-1.09	1.21E-05	5.84E-05
DDR	XRCC3	-1.93	2.22E-04	7.06E-04
DDR	FANCD2	-2.01	1.20E-05	5.84E-05
DDR	ATR	-2.15	6.90E-08	8.35E-07
DDR	BLM	-2.24	8.92E-05	3.37E-04
DDR	FANCM	-2.26	1.87E-07	1.82E-06
DDR	BRCA1	-2.68	5.57E-07	4.50E-06
DDR	RAD51	-2.73	6.31E-05	2.63E-04
apoptosis	PARP1	-1.00	5.35E-03	1.08E-02
p38/JNK	ETS1	4.72	1.72E-10	1.04E-08
p38/JNK	EGR1	4.02	3.53E-09	1.43E-07
p38/JNK	FOS	3.84	5.40E-09	1.63E-07
p38/JNK	MAFF	3.52	2.69E-05	1.21E-04
p38/JNK	FOSL1	2.89	1.07E-03	2.71E-03
p38/JNK	JUN	2.73	6.93E-04	2.00E-03
p38/JNK	ZFP36	2.42	4.61E-03	9.45E-03
p38/JNK	PHLDA1	2.34	2.17E-06	1.46E-05
p38/JNK	KLF6	1.93	5.53E-08	8.35E-07
ROS	SOD2	3.67	8.25E-09	2.00E-07
ROS	NQO1	-1.41	7.61E-03	1.40E-02
UPR/ER str	ATF3	5.94	1.76E-11	2.13E-09
UPR/ER str	PPP1R15A	4.56	4.71E-05	2.04E-04
UPR/ER str	HSPA5	1.87	1.41E-08	2.44E-07
UPR/ER str	HERPUD1	1.65	2.44E-05	1.13E-04
UPR/ER str	PLA2G6	1.04	1.77E-02	3.01E-02
UPR/ER str	EDEM1	1.02	8.56E-05	3.35E-04
UPR/ER str	XBP1	-1.36	2.69E-03	5.80E-03
UPR/ER str	XBP1(U)	-1.44	1.68E-03	3.76E-03

floating, atmospheric oxygen vs in vivo				
process	ID	logFC	P.Value	adj.P.Val
apoptosis	BCL2A1	3.74	3.86E-04	1.20E-03
apoptosis	MCL1	3.03	3.78E-08	5.08E-07
apoptosis	TNFRSF10C	2.83	2.32E-09	9.36E-08
apoptosis	BNIP3	2.81	6.33E-07	4.50E-06
apoptosis	TRAF1	2.31	3.69E-05	1.59E-04
apoptosis	IER3	2.24	3.34E-03	7.93E-03
apoptosis	BOK	2.16	1.85E-02	3.20E-02
apoptosis	TNFRSF10C	2.11	1.79E-08	2.71E-07
apoptosis	PMAIP1	1.51	6.07E-07	4.50E-06
apoptosis	BCL2L1	1.30	2.30E-03	5.67E-03
apoptosis	BIK	1.06	2.44E-02	3.94E-02
apoptosis	BAK1	1.01	2.09E-02	3.46E-02
apoptosis	FAS	-1.07	9.06E-03	1.78E-02
cell cycle	IGFBP3	5.52	9.58E-06	5.52E-05
cell cycle	TP73	4.13	7.13E-05	2.70E-04
cell cycle	Tap73	3.59	6.48E-04	1.91E-03
cell cycle	CDKN1A	3.41	1.33E-07	1.46E-06
cell cycle	EGFR	2.86	7.62E-06	4.61E-05
cell cycle	MET	2.44	1.53E-08	2.71E-07
cell cycle	BTG2	2.19	2.60E-05	1.31E-04
cell cycle	CDKN1B	1.66	3.01E-07	2.92E-06
cell cycle	CHEK1	-1.15	9.25E-03	1.78E-02
cell cycle	CDK1	-1.23	5.92E-03	1.26E-02
cell cycle	HGF	-1.64	2.70E-02	4.18E-02
DDR	ERCC1	2.10	2.97E-05	1.38E-04
DDR	TP53INP1	1.40	4.14E-04	1.25E-03
DDR	SIRT1	1.22	1.09E-04	3.76E-04
DDR	FANCD2	-1.04	3.50E-03	8.14E-03
DDR	BRCA1	-1.27	8.15E-04	2.34E-03
DDR	BLM	-1.28	7.12E-03	1.46E-02
DDR	RAD51	-1.75	4.95E-03	1.11E-02
DDR	ATR	-1.88	3.14E-07	2.92E-06
DDR	FANCM	-2.06	5.37E-07	4.33E-06
necrosis	PVR	1.99	5.67E-03	1.23E-02
necrosis	ATG5	1.20	1.85E-05	9.71E-05
necrosis	ATG7	1.07	6.02E-05	2.43E-04
p38/JNK	MAFF	4.76	1.16E-06	7.78E-06
p38/JNK	ETS1	4.70	1.83E-10	1.11E-08
p38/JNK	FOSL1	3.96	7.11E-05	2.70E-04
p38/JNK	EGR1	3.65	1.11E-08	2.70E-07
p38/JNK	JUN	3.47	8.70E-05	3.09E-04
p38/JNK	FOS	3.18	5.09E-08	6.15E-07
p38/JNK	ZFP36	2.80	1.64E-03	4.22E-03
p38/JNK	PHLDA1	2.42	1.53E-06	9.75E-06
p38/JNK	KLF6	1.59	5.01E-07	4.33E-06
p38/JNK	MAPK8	1.06	1.37E-02	2.48E-02
ROS	SOD2	3.44	1.78E-08	2.71E-07
ROS	SQSTM1	1.47	1.09E-03	3.01E-03
ROS	HMOX1	1.29	2.00E-02	3.36E-02
ROS	NQO1	-1.08	3.15E-02	4.82E-02
ROS	HIF1A	-1.22	3.32E-05	1.49E-04
UPR/ER str	PPP1R15A	5.32	1.01E-05	5.58E-05
UPR/ER str	ATF3	5.22	8.82E-11	1.07E-08
UPR/ER str	HSPA5	1.92	1.06E-08	2.70E-07
UPR/ER str	PLA2G6	1.44	2.46E-03	5.96E-03
UPR/ER str	HERPUD1	1.36	1.55E-04	5.22E-04
UPR/ER str	EDEM1	1.13	2.95E-05	1.38E-04
UPR/ER str	XBP1(U)	-1.12	9.12E-03	1.78E-02

floating, low oxygen vs in vivo				
process	ID	logFC	P.Value	adj.P.Val
apoptosis	BCL2A1	3.55	4.90E-04	9.72E-04
apoptosis	MCL1	3.29	1.42E-08	1.71E-07
apoptosis	TNFRSF10C	3.14	6.63E-10	2.01E-08
apoptosis	BNIP3	3.12	1.96E-07	1.25E-06
apoptosis	TRAF1	2.25	4.88E-05	1.34E-04
apoptosis	TNFRSF10C	2.16	1.35E-08	1.71E-07
apoptosis	IER3	2.14	4.48E-03	6.69E-03
apoptosis	PMAIP1	2.12	1.23E-08	1.71E-07
apoptosis	XIAP	1.74	2.95E-07	1.79E-06
apoptosis	BCL2L1	1.69	2.73E-04	5.60E-04
apoptosis	TNFRSF10C	1.11	2.50E-03	4.03E-03
apoptosis	BID	-1.36	4.44E-03	6.69E-03
apoptosis	ZMAT3	-1.50	1.05E-04	2.49E-04
apoptosis	FAS	-1.59	5.87E-04	1.11E-03
cell cycle	IGFBP3	5.94	4.41E-06	1.69E-05
cell cycle	TP73	4.78	1.85E-05	6.06E-05
cell cycle	Tap73	4.19	1.84E-04	3.90E-04
cell cycle	EGFR	3.58	6.83E-07	3.44E-06
cell cycle	CDKN1A	3.50	9.89E-08	7.04E-07
cell cycle	BTG2	2.91	1.38E-06	6.40E-06
cell cycle	MET	2.52	1.07E-08	1.71E-07
cell cycle	TP63	1.91	5.88E-04	1.11E-03
cell cycle	CDKN1B	1.87	7.50E-08	6.48E-07
cell cycle	RB1	1.21	4.42E-06	1.69E-05
cell cycle	MDM4	1.05	1.76E-04	3.80E-04
cell cycle	MYC	-1.53	2.56E-03	4.08E-03
cell cycle	PCNA	-1.65	1.30E-04	2.97E-04
cell cycle	CHEK1	-2.12	8.64E-05	2.13E-04
cell cycle	CDC25C	-2.41	2.80E-05	8.47E-05
cell cycle	CCNB1	-2.78	4.48E-06	1.69E-05
cell cycle	CEN2A	-2.93	2.08E-05	6.45E-05
cell cycle	CDK1	-4.04	8.22E-08	6.63E-07
DDR	ERCC1	1.92	7.25E-05	1.91E-04
DDR	TP53INP1	1.33	6.43E-04	1.20E-03
DDR	DBP2	1.01	6.90E-03	1.01E-02
DDR	MSH2	-1.33	2.90E-05	8.56E-05
DDR	XRCC3	-1.56	1.26E-03	2.21E-03
DDR	SESN1	-1.61	1.78E-07	1.20E-06
DDR	FANCA	-2.11	4.98E-04	9.73E-04
DDR	FANCM	-2.14	3.48E-07	2.00E-06
DDR	ATR	-2.38	2.04E-08	2.06E-07
DDR	FANCD2	-2.61	7.44E-07	3.60E-06
DDR	BRCA1	-2.65	6.42E-07	3.38E-06
DDR	BLM	-3.30	1.80E-06	8.05E-06
DDR	RAD51	-3.41	8.63E-06	2.90E-05
necrosis	PVR	1.85	8.79E-03	1.21E-02
necrosis	ATG5	1.37	4.68E-06	1.71E-05
necrosis	ATG7	1.16	8.88E-05	2.15E-04
necrosis	ATG7	1.14	3.49E-05	1.01E-04
necrosis	RIPK1	1.02	5.02E-05	1.35E-04
necrosis	PARP1	-1.82	4.34E-05	1.22E-04
p38/JNK	ETS1	5.53	2.43E-11	1.47E-09
p38/JNK	MAFF	4.22	4.18E-06	1.69E-05
p38/JNK	JUN	4.04	1.98E-05	6.31E-05
p38/JNK	EGR1	3.85	6.05E-09	1.22E-07
p38/JNK	FOSL1	3.71	1.28E-04	2.97E-04
p38/JNK	FOS	3.45	1.94E-08	2.06E-07
p38/JNK	KLF6	2.36	5.15E-09	1.22E-07
p38/JNK	PHLDA1	2.30	2.61E-06	1.13E-05
p38/JNK	ZFP36	2.18	8.70E-03	1.21E-02
p38/JNK	MAPK8	1.15	8.46E-03	1.20E-02
ROS	SOD2	2.98	9.67E-08	7.04E-07
ROS	SQSTM1	1.22	4.07E-03	6.23E-03
ROS	PRDX1	-1.06	1.83E-03	3.00E-03
ROS	SOD1	-1.06	1.67E-03	2.80E-03
ROS	HIF1A	-1.40	8.63E-06	2.90E-05
ROS	GSTP1	-1.63	1.57E-03	2.71E-03
ROS	NQO1	-2.38	1.44E-04	3.22E-04
UPR/ER str	ATF3	6.14	1.17E-11	1.41E-09
UPR/ER str	PPP1R15A	5.63	5.59E-06	1.99E-05
UPR/ER str	HSPA5	3.02	4.25E-11	1.71E-09
UPR/ER str	HERPUD1	2.37	5.20E-07	2.86E-06
UPR/ER str	EDEM1	2.00	6.19E-08	5.76E-07
UPR/ER str	PLA2G6	1.41	2.86E-03	4.49E-03
UPR/ER str	ATF4	1.30	8.48E-05	2.13E-04
UPR/ER str	XBP1	-1.77	3.57E-04	7.20E-04
UPR/ER str	XBP1(U)	-2.06	8.37E-05	2.13E-04

Red indicates significantly up-regulated genes, and green indicates down-regulated genes ($p < 0.05$). The different stress pathways are indicated by different colors.

Supplementary Table 2: Part 2: The fold-changes in transcriptional biomarkers observed in slices from 1647 lung PDX after cultivation.

1647 lung PDX

filter, atmospheric oxygen vs in vivo

process	ID	logFC	P.Value	adj.P.Val
apoptosis	HRK	1.87	2.77E-05	4.12E-04
apoptosis	ALOX12	1.41	9.71E-06	1.93E-04
apoptosis	IER3	1.03	1.37E-04	1.36E-03
DDR	FANCM	-1.06	8.13E-06	1.93E-04
DDR	XPA	-1.10	6.15E-05	6.65E-04
DDR	SES1	-1.26	1.66E-05	2.83E-04
UPR/ER stress	ATF3	1.37	1.44E-07	1.71E-05
UPR/ER Stress	PPP1R15A	1.19	5.41E-06	1.93E-04
UPR/ER Stress	EPHB1	-2.76	8.01E-06	1.93E-04

filter, low oxygen vs in vivo

process	ID	logFC	P.Value	adj.P.Val
apoptosis	HRK	2.13	6.05E-06	4.24E-05
apoptosis	TNFRSF10D	1.99	1.24E-09	3.68E-08
apoptosis	ALOX12	1.95	1.35E-07	2.30E-06
apoptosis	IER3	1.81	1.27E-07	2.30E-06
apoptosis	BNIP3	1.41	8.46E-07	8.39E-06
apoptosis	TNFRSF10B	1.32	6.19E-07	6.70E-06
apoptosis	BCL2L11	1.16	1.45E-05	7.91E-05
cell cycle	IGFBP3	2.36	8.48E-11	5.05E-09
cell cycle	CDKN1B	1.45	1.27E-06	1.16E-05
cell cycle	MET	1.37	5.09E-07	6.06E-06
cell cycle	CDKN1A	1.12	9.49E-06	5.94E-05
cell cycle	TP73	1.04	7.66E-05	2.94E-04
cell cycle	EGFR	1.04	1.32E-05	7.86E-05
DDR	BLM	-1.06	1.72E-05	8.51E-05
DDR	BRCA1	-1.07	2.76E-06	2.34E-05
DDR	SES1	-1.26	1.61E-05	8.31E-05
DDR	FANCM	-1.45	1.22E-07	2.30E-06
necrosis/autoph.	PVR	1.27	7.49E-06	4.95E-05
p38/JNK	MAFF	1.80	4.55E-07	6.01E-06
p38/JNK	FOS	1.51	1.46E-05	7.91E-05
p38/JNK	ZFP36	1.33	5.50E-06	4.09E-05
p38/JNK	ETS1	1.29	2.62E-05	1.25E-04
ROS	SOD2	1.19	5.01E-06	3.97E-05
ROS	HMOX1	1.35	4.54E-04	1.38E-03
UPR/ER stress	ATF3	2.76	2.55E-12	3.04E-10
UPR/ER Stress	PPP1R15A	2.17	9.91E-10	3.68E-08
UPR/ER Stress	PLA2G6	1.58	3.80E-07	5.65E-06
UPR/ER Stress	HERPUD1	1.08	1.39E-04	5.01E-04

floating, atmospheric oxygen vs in vivo

process	ID	logFC	P.Value	adj.P.Val
apoptosis	HRK	2.76	1.85E-07	2.76E-06
apoptosis	TNFRSF10D	1.96	1.58E-09	5.92E-08
apoptosis	BNIP3	1.54	2.45E-07	3.24E-06
apoptosis	IER3	1.48	1.99E-06	1.69E-05
apoptosis	ALOX12	1.44	7.20E-06	4.29E-05
apoptosis	TNFRSF10B	1.38	3.33E-07	3.96E-06
apoptosis	BCL2L11	1.31	3.40E-06	2.40E-05
cell cycle	IGFBP3	2.30	1.34E-10	7.98E-09
cell cycle	CDKN1B	1.68	1.67E-07	2.76E-06
cell cycle	MET	1.08	9.12E-06	5.17E-05
cell cycle	EGFR	1.04	1.26E-05	6.83E-05
cell cycle	TP63	-1.22	9.85E-05	4.34E-04
DDR	MSH2	-1.02	3.01E-06	2.39E-05
DDR	RAD51	-1.09	2.80E-03	7.58E-03
DDR	SES1	-1.11	7.23E-05	3.31E-04
DDR	BLM	-1.31	1.25E-06	1.24E-05
DDR	BRCA1	-1.38	9.00E-08	1.79E-06
DDR	FANCM	-1.61	2.68E-08	6.39E-07
necrosis/autoph.	PVR	1.33	3.87E-06	2.56E-05
p38/JNK	MAFF	1.73	7.91E-07	8.56E-06
p38/JNK	FOS	1.44	2.59E-05	1.28E-04
ROS	HMOX1	1.15	1.78E-03	5.16E-03
UPR/ER stress	ATF3	3.01	6.04E-13	7.19E-11
UPR/ER Stress	PPP1R15A	2.08	1.99E-09	5.92E-08
UPR/ER Stress	HERPUD1	1.57	1.62E-06	1.48E-05
UPR/ER Stress	HSPA5	1.35	3.43E-06	2.40E-05
UPR/ER Stress	PLA2G6	1.28	6.01E-06	3.76E-05

floating, low oxygen vs in vivo

process	ID	logFC	P.Value	adj.P.Val
apoptosis	HRK	2.97	6.54E-08	5.56E-07
apoptosis	TNFRSF10D	2.47	4.19E-11	2.36E-09
apoptosis	TNFRSF10B	1.63	3.01E-08	3.58E-07
apoptosis	BNIP3	1.43	7.02E-07	4.40E-06
apoptosis	BCL2L11	1.35	2.27E-06	1.08E-05
apoptosis	IER3	1.23	1.91E-05	6.68E-05
apoptosis	CFLAR	-1.04	1.07E-05	3.99E-05
cell cycle	IGFBP3	2.21	2.53E-10	5.03E-09
cell cycle	CDKN1B	1.68	1.70E-07	1.27E-06
cell cycle	EGFR	1.09	7.09E-06	2.91E-05
cell cycle	CDK1	-1.17	3.19E-06	1.41E-05
cell cycle	CHEK1	-1.23	5.83E-07	3.85E-06
cell cycle	CCNB1	-1.29	2.09E-06	1.04E-05
cell cycle	TP63	-3.08	3.44E-10	5.85E-09
DDR	ATR	-1.02	8.73E-06	3.35E-05
DDR	XRCC3	-1.07	7.97E-06	3.16E-05
DDR	SES1	-1.19	3.31E-05	1.07E-04
DDR	MSH2	-1.33	8.46E-08	6.71E-07
DDR	FANCD2	-1.51	4.29E-08	4.64E-07
DDR	RAD51	-1.61	1.87E-05	6.68E-05
DDR	BRCA1	-2.19	7.93E-11	2.36E-09
DDR	BLM	-2.23	5.26E-10	7.83E-09
DDR	FANCM	-2.26	1.38E-10	3.27E-09
necrosis/autoph.	PVR	1.16	2.06E-05	6.81E-05
p38/JNK	MAFF	1.73	8.04E-07	4.55E-06
p38/JNK	FOS	1.29	8.29E-05	2.47E-04
p38/JNK	EGR1	-1.43	1.89E-07	1.32E-06
p38/JNK	OAS1	-1.76	7.55E-07	4.50E-06
ROS	HMOX1	2.17	2.10E-06	1.04E-05
ROS	HIF1A	-1.27	1.81E-06	9.78E-06
UPR/ER stress	ATF3	3.27	1.51E-13	1.80E-11
UPR/ER Stress	PPP1R15A	2.55	7.75E-11	2.36E-09
UPR/ER Stress	HERPUD1	2.00	5.90E-08	5.48E-07
UPR/ER Stress	HSPA5	1.98	1.71E-08	2.26E-07
UPR/ER Stress	PLA2G6	1.80	5.99E-08	5.48E-07
UPR/ER Stress	EPHB1	-2.18	2.52E-06	1.15E-05

Red indicates significantly up-regulated genes, and green indicates down-regulated genes (p < 0.05). The different stress pathways are indicated by different colors.

Supplementary Table 2: Part 3: The fold-changes in transcriptional biomarkers observed in slices from PC295 prostate PDX after cultivation.

PC295 prostate PDX

filter, atmospheric oxygen vs in vivo

process	ID	logFC	P.Value	adj.P.Val
apoptosis	BCL2L14	2.02	5.07E-06	8.33E-05
apoptosis	PMAIP1	1.30	3.58E-06	8.22E-05
apoptosis	BNIP3	1.00	2.23E-03	1.02E-02
cell cycle	CDKN1B	1.39	3.36E-04	2.97E-03
cell cycle	MYC	-1.16	8.20E-04	4.49E-03
cell cycle	TP53	-1.95	2.08E-06	5.98E-05
DDR	XPC	-1.07	6.12E-04	4.15E-03
p38/JNK	MAFF	4.23	7.93E-07	3.04E-05
p38/JNK	ESR1	4.11	1.76E-07	1.01E-05
p38/JNK	FOS	3.69	7.28E-04	4.19E-03
p38/JNK	OAS1	1.28	1.41E-02	4.52E-02
p38/JNK	PHLDA1	1.11	1.41E-02	4.52E-02
p38/JNK	KLf6	1.02	1.26E-04	1.32E-03
ROS	NQO1	1.73	4.55E-06	8.33E-05
ROS	HIF1A	1.03	6.35E-06	9.12E-05
UPR/ER stress	ATF3	4.22	1.15E-09	1.33E-07

filter, low oxygen vs in vivo

process	ID	logFC	P.Value	adj.P.Val
apoptosis	PMAIP1	2.14	1.42E-08	4.09E-07
apoptosis	BNIP3	1.25	3.95E-04	1.30E-03
apoptosis	ZMAT3	-1.02	5.32E-04	1.61E-03
apoptosis	BIK	-1.03	1.46E-03	3.83E-03
apoptosis	TRAF1	-1.25	1.21E-02	2.24E-02
apoptosis	SHISA5	-2.08	1.03E-02	1.97E-02
cell cycle	CDKN1B	1.33	4.67E-04	1.45E-03
cell cycle	BTG2	-1.17	3.92E-03	9.38E-03
cell cycle	PCNA	-1.61	8.25E-07	8.63E-06
cell cycle	TP53	-2.17	6.63E-07	7.62E-06
cell cycle	TERT	-2.45	1.56E-02	2.80E-02
cell cycle	MYC	-2.97	7.53E-08	1.61E-06
DDR	FANCM	-1.24	6.02E-06	3.84E-05
DDR	XRCC1	-1.25	1.02E-03	3.01E-03
DDR	MLH1	-1.34	1.19E-07	1.95E-06
DDR	DDR2	-1.36	1.75E-05	9.61E-05
DDR	RAD51	-1.41	2.72E-06	2.09E-05
DDR	NLRP2	-1.41	8.39E-08	1.61E-06
DDR	XRCC3	-1.43	2.80E-02	4.67E-02
DDR	MSH2	-1.44	4.94E-07	6.31E-06
DDR	ATM	-1.54	1.10E-05	6.34E-05
DDR	FEN1	-1.58	6.25E-05	2.99E-04
DDR	BLM	-1.66	4.37E-06	3.14E-05
DDR	BRCA1	-1.69	2.14E-06	1.84E-05
DDR	FANCG	-1.76	1.15E-03	3.16E-03
DDR	XPC	-1.94	2.24E-06	1.84E-05
DDR	ATR	-2.02	5.97E-09	3.43E-07
necrosis/autoph.	ATG7	-1.07	9.78E-05	4.02E-04
p38/JNK	EGR1	5.24	1.09E-08	4.09E-07
p38/JNK	MAFF	4.50	4.17E-07	5.99E-06
p38/JNK	FOS	4.46	1.48E-04	5.68E-04
p38/JNK	ZFP36	2.71	1.82E-03	4.55E-03
p38/JNK	KLf6	1.62	1.33E-06	1.28E-05
p38/JNK	OAS1	1.49	6.37E-03	1.36E-02
p38/JNK	PHLDA1	1.06	1.83E-02	3.24E-02
ROS	NQO1	1.30	7.90E-05	3.53E-04
UPR/ER stress	ATF3	5.14	1.29E-10	1.48E-08
UPR/ER Stress	HERPUD1	1.59	5.03E-06	3.41E-05
UPR/ER Stress	ATF4	1.46	8.91E-06	5.39E-05
UPR/ER Stress	HSPA5	1.05	1.72E-04	6.37E-04
UPR/ER Stress	PLAZG6	-1.34	6.02E-03	1.31E-02

floating, atmospheric oxygen vs in vivo

process	ID	logFC	P.Value	adj.P.Val
apoptosis	PMAIP1	2.33	5.35E-09	1.54E-07
apoptosis	BNIP3	1.37	1.85E-04	6.46E-04
apoptosis	MCL1	1.13	5.15E-03	1.04E-02
apoptosis	AIFM2	1.02	2.86E-03	6.86E-03
cell cycle	CDKN1B	1.82	2.91E-05	1.34E-04
cell cycle	EGFR	1.50	1.14E-05	7.27E-05
cell cycle	CDKN1A	1.27	1.64E-03	4.23E-03
cell cycle	CHEK1	-1.01	8.92E-04	2.44E-03
cell cycle	PCNA	-1.14	2.77E-05	1.33E-04
cell cycle	TP53	-1.60	1.58E-05	9.56E-05
cell cycle	MYC	-2.33	1.12E-06	1.17E-05
DDR	MLH1	-1.08	1.28E-06	1.23E-05
DDR	FANCG	-1.24	1.20E-02	2.33E-02
DDR	FEN1	-1.35	2.66E-04	8.48E-04
DDR	NLRP2	-1.36	1.28E-07	2.46E-06
DDR	ATM	-1.37	3.39E-05	1.50E-04
DDR	XPC	-1.40	5.90E-05	2.39E-04
DDR	RAD51	-1.41	2.78E-06	2.28E-05
DDR	FANCM	-1.52	7.09E-07	8.16E-06
DDR	MSH2	-1.53	2.55E-07	4.19E-06
DDR	BRCA1	-1.56	4.89E-06	3.51E-05
DDR	BLM	-1.65	4.80E-06	3.51E-05
DDR	ATR	-2.20	2.24E-09	8.58E-08
necrosis/autophagy	PARP1	-1.11	2.75E-05	1.33E-04
p38/JNK	EGR1	6.61	7.23E-10	4.16E-08
p38/JNK	MAFF	6.29	1.21E-08	2.78E-07
p38/JNK	FOS	5.46	2.22E-05	1.16E-04
p38/JNK	ZFP36	4.58	2.02E-05	1.10E-04
p38/JNK	JUN	2.62	2.67E-03	6.67E-03
p38/JNK	OAS1	2.49	2.08E-04	7.04E-04
p38/JNK	PHLDA1	2.25	8.13E-05	3.12E-04
p38/JNK	KLf6	1.81	3.94E-07	5.67E-06
ROS	HMOX1	4.01	3.02E-03	6.93E-03
ROS	NQO1	1.88	1.93E-06	1.71E-05
UPR/ER stress	ATF3	5.89	2.87E-11	3.30E-09
UPR/ER Stress	PPP1R15A	5.20	1.12E-04	4.16E-04
UPR/ER Stress	HERPUD1	1.98	4.90E-07	6.26E-06
UPR/ER Stress	HSPA5	1.40	1.07E-05	7.24E-05
UPR/ER Stress	ATF4	1.20	6.02E-05	2.39E-04

floating, low oxygen vs in vivo

process	ID	logFC	P.Value	adj.P.Val
apoptosis	PMAIP1	2.99	2.80E-10	1.61E-08
apoptosis	TNFRSF10B	1.22	1.52E-04	4.61E-04
apoptosis	MCL1	1.21	3.36E-03	6.43E-03
apoptosis	BNIP3	1.00	2.19E-03	4.50E-03
apoptosis	ZMAT3	-1.10	2.75E-04	7.72E-04
apoptosis	TNFRSF10A	-1.31	7.15E-05	2.42E-04
apoptosis	PIDD	-1.58	1.06E-02	1.84E-02
cell cycle	CDKN1B	1.93	1.59E-05	6.31E-05
cell cycle	CDKN1A	1.14	3.49E-03	6.58E-03
cell cycle	TP73	-1.09	2.73E-02	4.19E-02
cell cycle	CCNA2	-1.10	1.77E-03	3.83E-03
cell cycle	CDC25C	-1.12	3.53E-04	9.68E-04
cell cycle	RPA1	-1.13	1.26E-05	5.54E-05
cell cycle	CDK1	-1.25	3.93E-06	2.15E-05
cell cycle	BTG2	-1.26	2.39E-03	4.82E-03
cell cycle	TP53	-1.78	5.57E-06	2.67E-05
cell cycle	PCNA	-1.87	1.60E-07	1.53E-06
cell cycle	TERT	-2.60	1.59E-02	2.65E-02
cell cycle	MVC	-2.99	6.88E-08	7.92E-07
DDR	XRCC1	-1.90	4.78E-03	8.60E-03
DDR	DDR2	-1.21	5.58E-05	1.94E-04
DDR	ATM	-1.26	7.61E-05	2.50E-04
DDR	SESN1	-1.29	4.54E-06	2.27E-05
DDR	MLH1	-1.43	5.68E-08	7.54E-07
DDR	XRCC3	-1.44	2.69E-02	4.18E-02
DDR	RAD51	-1.45	2.09E-06	1.34E-05
DDR	BLM	-1.49	1.39E-05	5.70E-05
DDR	FANCM	-1.54	6.12E-07	5.41E-06
DDR	BRCA1	-1.65	2.83E-06	1.63E-05
DDR	MSH2	-1.67	9.37E-08	9.80E-07
DDR	FANCG	-1.79	1.04E-03	2.43E-03
DDR	NLRP2	-1.98	1.69E-09	3.88E-08
DDR	FEN1	-1.99	6.66E-06	3.06E-05
DDR	XPC	-2.02	1.45E-06	1.04E-05
DDR	ATR	-2.43	7.01E-10	2.01E-08
necrosis/autoph.	PARP1	-1.52	1.13E-06	8.68E-06
necrosis/autoph.	RIPK1	-1.97	2.75E-06	1.63E-05
p38/JNK	EGR1	6.89	4.35E-10	1.67E-08
p38/JNK	MAFF	6.47	8.93E-09	1.47E-07
p38/JNK	FOS	5.96	1.85E-05	6.84E-05
p38/JNK	ZFP36	4.78	1.30E-05	5.54E-05
p38/JNK	OAS1	3.23	8.06E-05	2.50E-04
p38/JNK	PHLDA1	2.62	1.90E-05	6.84E-05
p38/JNK	KLf6	2.14	5.90E-08	7.54E-07
p38/JNK	JUN	2.02	1.32E-02	2.27E-02
ROS	HMOX1	3.36	9.14E-03	1.62E-02
UPR/ER stress	ATF3	6.38	1.16E-11	1.33E-09
UPR/ER Stress	PPP1R15A	4.18	8.25E-04	1.98E-03
UPR/ER Stress	HERPUD1	2.86	7.72E-09	1.47E-07
UPR/ER Stress	HSPA5	1.77	9.57E-07	7.86E-06
UPR/ER Stress	ATF4	1.57	4.16E-06	2.18E-05
UPR/ER Stress	XBP1(U)	-1.04	2.16E-04	6.38E-04
UPR/ER Stress	EDEM2	-1.07	1.73E-05	6.63E-05

Red indicates significantly up-regulated genes, and green indicates down-regulated genes (p < 0.05). The different stress pathways are indicated by different colors.

Supplementary Table 2: Part 4: The fold-changes in transcriptional biomarkers observed in slices from MCF-7 breast CDX after cultivation.

MCF-7 breast CDX

filter, atmospheric oxygen vs in vivo

process	ID	logFC	P.Value	adj.P.Val
apoptosis	HRK	1.31	2.78E-03	8.42E-03
apoptosis	BID	-1.02	3.72E-03	1.07E-02
apoptosis	BCL2L1	-1.17	6.78E-05	4.33E-04
apoptosis	PIDD	-1.99	4.15E-03	1.14E-02
apoptosis	TP53AIP1	-2.10	6.97E-06	8.02E-05
cell cycle	CCNB1	-1.03	1.22E-04	7.00E-04
cell cycle	CHEK1	-1.03	1.49E-05	1.32E-04
cell cycle	BTG2	-1.08	1.24E-02	2.91E-02
cell cycle	CDC25C	-1.22	2.41E-07	4.61E-06
cell cycle	CCNA2	-1.32	2.74E-05	1.97E-04
cell cycle	TERT	-1.35	8.48E-03	2.17E-02
cell cycle	SFN	-1.95	7.43E-05	4.50E-04
cell cycle	TP63	-2.81	1.84E-08	1.77E-06
cell cycle	TAp73	-2.89	5.49E-05	3.71E-04
cell cycle	TP73	-3.28	2.81E-07	4.61E-06
DDR	ATR	1.07	7.60E-04	2.91E-03
DDR	XPA	-1.05	2.11E-04	1.16E-03
DDR	BRCA1	-1.19	8.44E-08	2.43E-06
DDR	BLM	-1.47	1.88E-07	4.32E-06
DDR	DDB2	-1.49	4.61E-08	1.77E-06
DDR	RAD51	-1.76	3.18E-04	1.52E-03
p38/JNK	OAS1	-1.06	4.07E-03	1.14E-02
p38/JNK	EGR1	-2.28	9.28E-06	8.89E-05
ROS	HMOX1	1.77	9.44E-07	1.36E-05
ROS	SQSTM1	1.02	6.85E-04	2.81E-03
ROS	SOD2	-1.15	4.34E-06	5.55E-05
UPR/ER Stress	HERPUD1	2.08	3.40E-08	1.77E-06
UPR/ER Stress	HSPA5	1.40	2.61E-05	1.97E-04

filter, low oxygen vs in vivo

process	ID	logFC	P.Value	adj.P.Val
apoptosis	TP53AIP1	-1.36	9.84E-04	4.92E-03
cell cycle	CCNB1	-1.20	2.00E-05	1.92E-04
cell cycle	CCNA2	-1.37	1.84E-05	1.92E-04
cell cycle	TERT	-1.41	6.32E-03	2.20E-02
cell cycle	SFN	-1.51	1.07E-03	5.12E-03
cell cycle	CDC25C	-1.56	3.93E-09	4.52E-07
cell cycle	TAp73	-1.73	7.20E-03	2.44E-02
cell cycle	TP73	-1.91	3.35E-04	1.92E-03
cell cycle	TP63	-2.10	1.89E-06	2.72E-05
DDR	BRCA1	-1.03	8.42E-07	1.61E-05
DDR	BLM	-1.27	1.76E-06	2.72E-05
DDR	RAD51	-1.44	2.00E-05	1.92E-04
DDR	DDB2	-1.54	2.74E-08	7.88E-07
p38/JNK	EGR1	-2.10	2.69E-05	2.38E-04
ROS	HIF1A	1.18	1.97E-03	8.40E-03
ROS	SOD1	-1.02	5.06E-05	3.64E-04
ROS	SOD2	-1.64	1.59E-08	7.88E-07
UPR/ER Stress	HERPUD1	2.12	2.52E-08	7.88E-07
UPR/ER Stress	HSPA5	1.58	4.83E-06	6.17E-05
UPR/ER Stress	DNAJC3	1.35	4.38E-08	1.01E-06

Red indicates significantly up-regulated genes, and green indicates down-regulated genes (p < 0.05).
The different stress pathways are indicated by different colors.

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