

Identification of Gene Expression Biomarkers for Predicting Radiation Exposure

Tzu-Pin Lu,^{1,2} Yi-Yao Hsu,³ Liang-Chuan Lai,^{4,5} Mong-Hsun Tsai,^{4,6,*} and Eric Y. Chuang,^{3,4,*}

¹Department of Public Health, National Taiwan University, Taipei, Taiwan

²Institute of Epidemiology and Preventative Medicine, National Taiwan University, Taiwan

³Graduate Institute of Biomedical Electronics and Bioinformatics and Department of Electrical Engineering, National Taiwan University, Taipei, Taiwan

⁴Bioinformatics and Biostatistics Core, Center of Genomic Medicine, National Taiwan University, Taipei, Taiwan

⁵Graduate Institute of Physiology, National Taiwan University, Taipei, Taiwan

⁶Institute of Biotechnology, National Taiwan University, Taipei, Taiwan

Supplementary Tables

Table S1. Characteristics of testing samples.

Accession[*]	Sample number	Cell type	Dose (Gy)	Time (h)
GSE762	1	LNCap C4-2	10	6
GSE7505	63	NCI60, ML-1, TK6, NH32	8	4
GSE20549	6	H1299, H460	2	4
GSE6978	24	Lymphocyte	0.05, 0.5	3
GSE8917	15	Peripheral blood	0.5, 2, 8	24
GSE25772	4	Fibroblast	2	24
GSE6971	4	Fibroblast	1.5	24
GSE20549	6	H1299, H460	2	24
GSE6978	42	Lymphocyte	0.05 & 0.5	24

^{*} GEO accession number

Table S2. Biomarkers for predicting radiation doses.

Source (Gene No.)	Gene symbol
Paul <i>et al.</i> [1] (47)	<i>AEN, ANKRA2, ANXA4, ARHGEF3, ASCC3, BAX, BBC3, BTG3, C11orf24, CCNG1, CD70, CDKN1A, DDB2, DRAM1, EI24, FBXO22, FDXR, GADD45A, GLS2, GNG7, IER5, IL21R, LIG1, LY9, MDM2, METTL7A, MGAT3, MYC, PCNA, PLK2, PLK3, POLH, PPM1D, PTP4A1, RPS27L, SESN1, TCF3, TM7SF3, TMEM30A, TNFRSF10B, TNFSF4, TRIAP1, TRIM22, UROD, XPC, ZMAT3, ZNF337</i>
Dressman <i>et al.</i> [2] (8)	<i>BAX, BBC3, CDKN1A, DDB2, PRKCH, TMEM30A, TP53I3, XPC</i>

Table S3. Canonical pathways enriched by the three sets of biomarkers associated with distinct radiation doses.

Source	Pathway name	$-\log(P)$ *	Gene No.
29 biomarkers in higher and lower doses	Mitotic Roles of Polo-Like Kinase	5.54	4
	Cell Cycle: G2/M DNA Damage Checkpoint Regulation	2.66	2
	Pyridoxal 5'-phosphate Salvage Pathway	2.33	2
	Salvage Pathways of Pyrimidine Ribonucleotides	2.02	2
35 biomarkers in higher dose	Role of CHK Proteins in Cell Cycle Checkpoint Control	3.81	3
	Role of BRCA1 in DNA Damage Response	3.70	3
	Mitotic Roles of Polo-Like Kinase	3.66	3
	p53 Signaling	3.07	3
	Cell Cycle: G2/M DNA Damage Checkpoint Regulation	2.52	2
51 biomarkers in lower dose	p53 Signaling	6.60	6
	Hereditary Breast Cancer Signaling	4.89	5
	Role of BRCA1 in DNA Damage Response	4.68	4
	Cell Cycle: G2/M DNA Damage Checkpoint Regulation	3.67	3
	ATM Signaling	3.26	3

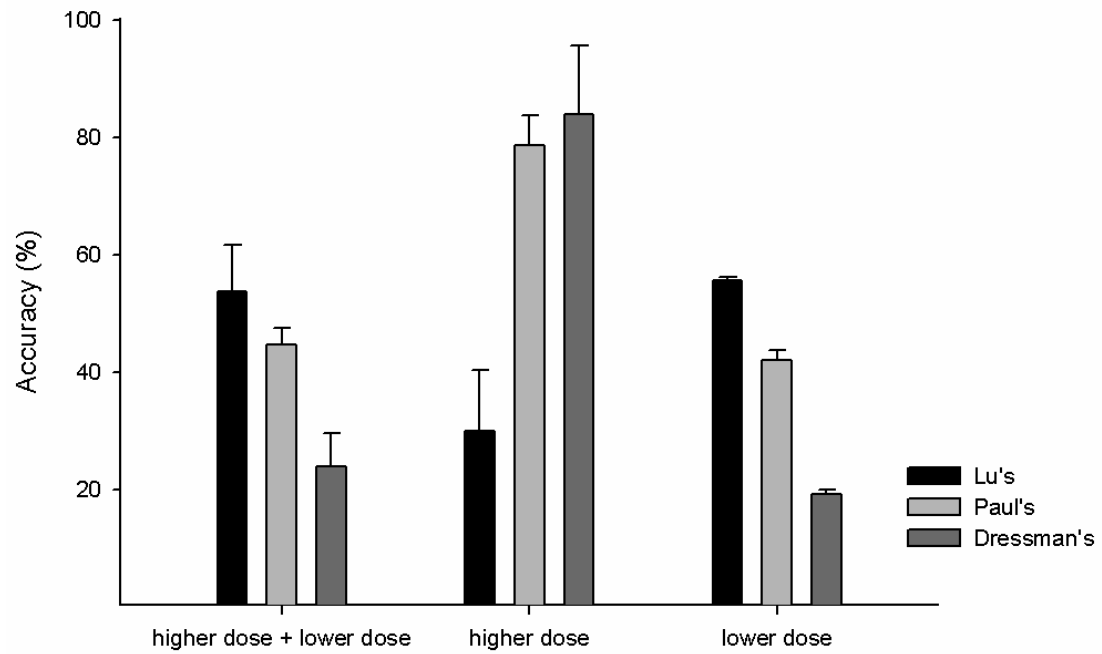
* Only pathways with $-\log(P) > 2$ were shown here

Table S4. Upstream regulators enriched by the three sets of biomarkers associated with distinct radiation doses.

Source	Regulator	$-\log(P)^*$	Gene No.
29 biomarkers in higher and lower doses	<i>FOXM1</i>	20.65	10
	<i>ERBB2</i>	13.97	10
	<i>TP53</i>	13.23	13
	<i>TGFB1</i>	11.28	10
35 biomarkers in higher dose	<i>FOXM1</i>	19.69	10
	<i>ERBB2</i>	13.02	10
	<i>CDK4</i>	11.99	9
	<i>TP53</i>	11.95	13
51 biomarkers in lower dose	<i>CCND1</i>	11.62	9
	<i>TP53</i>	16.05	18
	<i>SLC29A1</i>	14.15	7
	<i>ANXA2</i>	12.91	7

* Only regulators with $-\log(P) > 10$ were shown here

Figure S1. Prediction performances of the three sets of biomarkers in external datasets collected at 24 hours after irradiation. A 10-fold cross-validation was repeated 10,000 times and the prediction accuracies in the samples treated with high (N=5) and/or low (N=66) radiation doses were plotted.



References

1. Paul S, Amundson SA. Development of gene expression signatures for practical radiation biodosimetry. *Int J Radiat Oncol Biol Phys* 2008;71:1236-1244.
2. Dressman HK, Muramoto GG, Chao NJ, et al. Gene expression signatures that predict radiation exposure in mice and humans. *PLoS Med* 2007;4:e106.