Supplementary Material

Genetic analysis of radiation-induced changes in human gene expression

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Genome-wide Linkage Scan (3,280 2-hr & 3,280 6-hr post-IR expression phenotype) t=5: 197 2-hr, 198 6-hr post-IR phenotypes t=4: 1,275 2-hr, 1,298 6-hr post-IR phenotypes Select candidates for further analysis 2-fold change in expression level post-IR, one marker with t≥4 in linkage scan 6 "cis" phentoypes -340 "trans" phentoypes -Four 2-hr, Two 6-hr post-IR phenotypes 178 2-hr, 162 6-hr post-IR phenotypes **Text-Mining** (co-occurrence of target genes and potential regulators in pubmed abstract) 5 phenotypes with P≤0.05 73 potential regulators for 32 **Allele-Specific Assay of CP-110** phenotypes (1 of 5 phenotypes) **QTDT** (tested 58 regulators for 29 phenotypes with informative markers) **Differential Allelic IR**induced changes of CP110 14 potential regulators for 13 phenotypes (P<0.05) expression.

Association with cell death

(tested SNPs in 19 regulators)

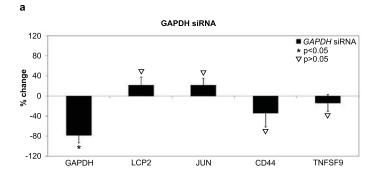
Significant allelic association between SNPs in 5 regulators and cell death (tested the 14 potential regulators identified by QTDT)

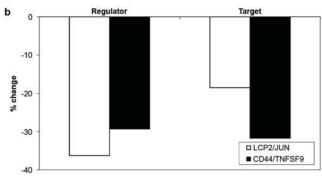
knocked-down 11 regulators

Measure expression of 11 target genes whose "regulators" were knocked down.

Expression levels of 5 target genes changed correspondingly

Supplementary Figure 2





Supplementary figure legend

Supplementary Figure 1. A flow chart of the manuscript. A brief summary of experimental approaches and results is presented.

Supplementary Figure 2. Knockdown experiments. (a) Effect of GAPDH siRNA transfection on expression of GAPDH and selected regulator and target genes. The changes in expression levels are represented as mean \pm s.e.m of 4 or more independent transfections. (b) Regulators of expression levels of IR-responsive genes were knocked down by indicated shRNAs. The changes in expression levels of the regulators and their corresponding target genes after knockdown of the regulators are shown. Data are represented as mean of 2 independent transfections.

Supplementary Table 1. SNPs in trans-acting regulators are significantly associated with expression levels of their target genes.

Regulator	SNP	Major allele	Target (time-point post IR)	Average Fold Change of Target Gene AA*	Average Fold Change of Target Gene AB*	Average Fold Change of Target Gene BB*	\mathbb{R}^2	P-value
CD44	rs2553809 TC	Т	TNFSF9 (2 hr)	2.8	2.3	1.9	0.25	0.005
SERPINE2	rs1377609 GA	G	ARHGDIA (2 hr)	1.1	0.7	NA	0.16	0.03
FAS	rs10509561 TA	Т	TRAF4 (6 hr)	1.8	1.5	1.3	0.16	0.03

^{*} A represents the major allele, and B is the minor allele.

Supplementary Table 2. PCR primers for RT-PCR analysis

Primer Name	Sequence (5' to 3')				
ACTB FOR	AAGATCATTGCTCCTCCTGAGC				
ACTB REV	CATACTCCTGCTTGCTGATCCA				
ARHGDIA FOR	ACAAACAAGGGACCAAGTGC				
ARHGDIA REV	CTGGCAGACACACACGAAG				
CD44 FOR	AGTCCCTGGATCACCGACAG				
CD44 REV	TTGGTCTCTGGTAGCAGGGATT				
<i>FAS</i> FOR	CCTGCTACAAATGGCAGCTT				
FAS REV	CTTGGGGGTATGACAAGAGC				
<i>GAPDH</i> FOR	CGTGGAAGGACTCATGACCA				
<i>GAPDH</i> REV	CACAGTCTTCTGGGTGGCAGT				
JUN FOR	CCACGTTAACAGTGGGTGCC				
JUN REV	AATGTTTGCAACTGCTGCGT				
LCP2 FOR	TGATTTGTTTTTTACAGCCAAACCT				
LCP2 REV	AACTAATGAATGCCTCTGACTGACAG				
SERPINE2 FOR	CAAAGCTTCAGCAGCAACAACT				
SERPINE2 REV	GGAGGCGATGATCTTGCAAT				
<i>SSB</i> FOR	CCTGCATCCAAACAACAGAA				
SSB REV	CCGCAAACAAAGTCGTTTA				
<i>TNFSF9</i> FOR	CTGGTGGCCCAAAATGTTCT				
TNFSF9 REV	GGTCACTGTACCAGCTCAGGG				
<i>TRAF4</i> FOR	CTTCTTGGGTAGGGCAGACA				
TRAF4 REV	ATGGCTCTTGGGACATAGCA				

Supplementary Table 3. siRNA oligonucleotides used in knockdown experiments

Gene Symbol	ene Symbol Genebank ID		Location	Sequence	
LCP2	NM_005565	A-012120-13	ORF	GUGGUACGUUUCUUAUAUU	
LCP2	NM_005565	A-012120-14	3'-UTR	GCAAUAAUUUAAGAGGCUU	
LCP2	NM_005565	A-012120-15	3'-UTR	UUAUUCUUCAAUGUUU	
LCP2	NM_005565	A-012120-16	3'-UTR	GUUUUAUACAUGUAAUUUG	
CD44	NM_001001392	A-009999-14	ORF	CUCUGAGCAUCGGAUUUGA	
CD44	NM_001001392	A-009999-15	3'-UTR	CCAUUCACCUUUAUGUUAU	
CD44	NM_001001392	A-009999-16	3'-UTR	CCUUUGAUCAGUAUAAUUU	
CD44	NM_001001392	A-009999-17	3'-UTR	CYGUUAUAUCAGAGGAGUA	
SERPINE2	NM_006216	A-012737-13	ORF	CCCCAAUGAUUUAUGGUAC	
SERPINE2	NM_006216	A-012737-14	ORF	CUGACAUGUUUGAUUCAUC	
SERPINE2	NM_006216	A-012737-15	ORF	CCAAGAAGAAUAAAGACAU	
SERPINE2	NM_006216	A-012737-16	ORF	CCAUGUUUCUCAUAUCUUG	
FAS	NM_152876	A-003776-14	3'-UTR	GGAUGAAAGAUUAAGAUUA	
FAS	NM_152876	A-003776-15	3'-UTR	CGAAAAUGUUCAAUAAUGU	
FAS	NM_152876	A-003776-16	3'-UTR	UUUCUAAGAUUUAAGAUUC	
FAS	NM_152876	A-003776-17	3'-UTR	GUUUGGAAUUAUAAAAUAU	
SSB	NM_003142	A-006877-13	ORF	UUGUUGUGUUUGAUAGCAU	
SSB	NM_003142	A-006877-14	ORF	GUCGUAGAUUUAAAGGAAA	
SSB	NM_003142	A-006877-15	ORF	UGGUGAAAUAAAAUGGAUA	
SSB	NM_003142	A-006877-16	3'-UTR	GAGAUUUCUUUGAAUGUAU	

Supplementary Table 4. shRNA constructs used in knockdown experiments

LCP2

$TRCN0000029811 \ \textbf{CCGGGATCGTTCATTAGCTCCGTTTCTCGAGAAACGGAGCTAATGAACGATCTTTTT}$

Clone ID: NM_005565.2-937s1c1 Accession Number(s): NM_005565.3

Region: CDS

CD44

$TRCN0000057566 \ \textbf{CCGGCCAACTCTAATGTCAATCGTTCTCGAGAACGATTGACATTAGAGTTGGTTTTTG}$

Clone ID: NM_000610.3-2215s1c1

Accession Number(s): NM_001001390.1, NM_001001389.1, NM_000610.3

Region: CDS