

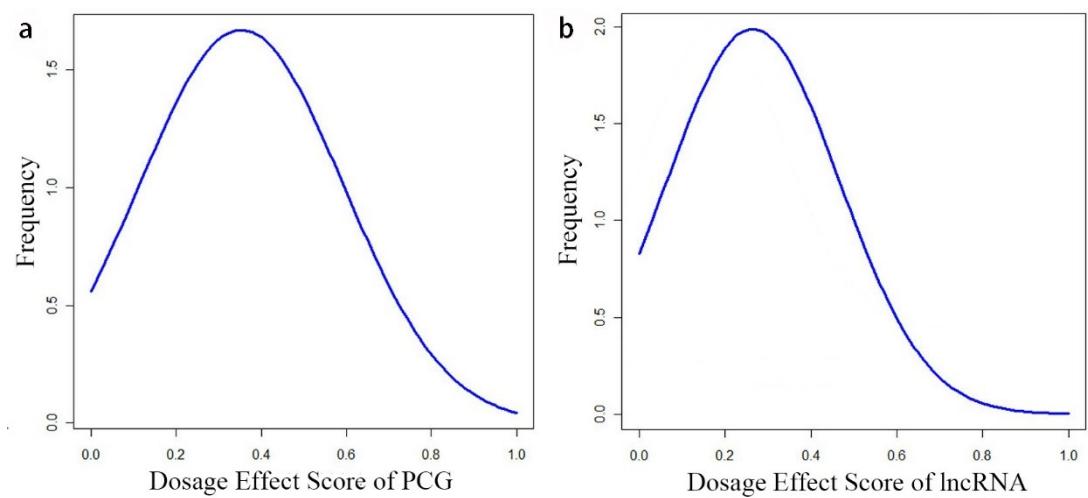
Comparative analysis revealed dosage sensitivity and regulatory patterns of lncRNA in prostate cancer

Yongjing Liu[§], Rui Zhang[§], Ning Zhao[§], Qiang Zhang, Zichuang Yan, Yuanshuai Zhou, Zhiqiang Chang and Yan Xu*

College of Bioinformatics Science and Technology, Harbin Medical University, Harbin 150081, China

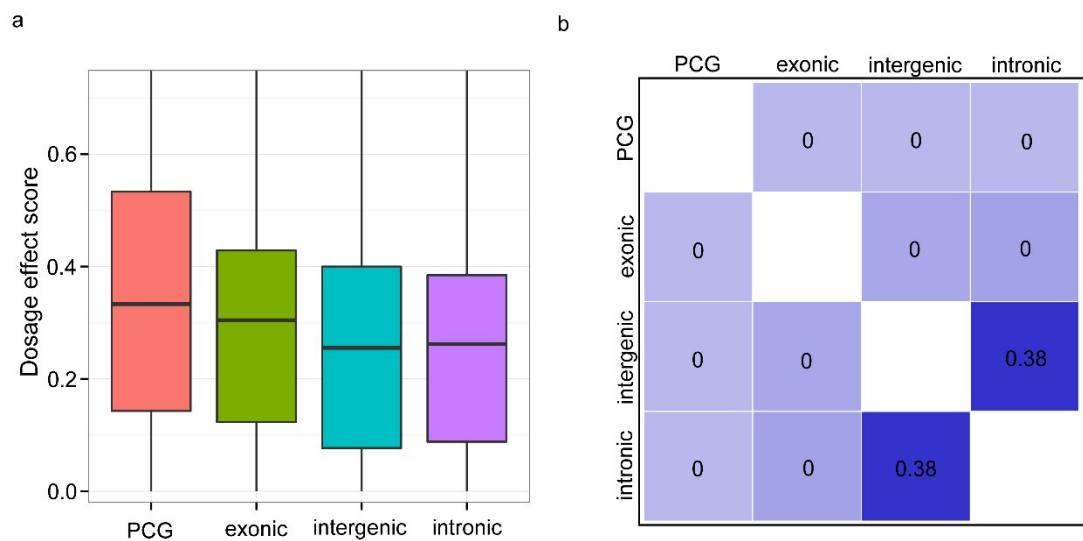
[§]These authors contributed equally to this work

*Corresponding author



Supplementary Figure 1 The dosage effect score distributions.

The two panels are the DES score distributions of PCGs and lncRNAs in prostate cancer. The distribution plot is consistent with Samur et al.'s study.



Supplementary Figure 2 The difference of DES between PCGs and lncRNAs at different genomic locations.

Supplementary Table S1 GO terms enriched by PCGs with high dosage sensitivity

Category	Term	Count	P-Value
BP	GO:0030163~protein catabolic process	43	1.52E-03
BP	GO:0009057~macromolecule catabolic process	51	1.75E-03
	GO:0051603~proteolysis involved in cellular protein catabolic		
BP	process	41	2.43E-03
BP	GO:0044257~cellular protein catabolic process	41	2.69E-03
BP	GO:0044265~cellular macromolecule catabolic process	47	3.21E-03
BP	GO:0007156~homophilic cell adhesion	14	3.33E-03
BP	GO:0008286~insulin receptor signaling pathway	7	4.02E-03
	GO:0007167~enzyme linked receptor protein signaling		
BP	pathway	26	4.88E-03
	GO:0019941~modification-dependent protein catabolic		
BP	process	38	5.98E-03
	GO:0043632~modification-dependent macromolecule		
BP	catabolic process	38	5.98E-03
BP	GO:0034329~cell junction assembly	7	6.75E-03
BP	GO:0008104~protein localization	53	7.54E-03
BP	GO:0033554~cellular response to stress	37	8.17E-03
BP	GO:0034330~cell junction organization	8	9.33E-03
BP	GO:0034644~cellular response to UV	3	9.91E-03
BP	GO:0048598~embryonic morphogenesis	23	1.00E-02
BP	GO:0001702~gastrulation with mouth forming second	5	1.03E-02
BP	GO:0007049~cell cycle	47	1.04E-02
BP	GO:0006939~smooth muscle contraction	6	1.13E-02
	GO:0007179~transforming growth factor beta receptor		
BP	signaling pathway	8	1.22E-02
BP	GO:0016265~death	44	1.25E-02
BP	GO:0006511~ubiquitin-dependent protein catabolic process	19	1.32E-02
BP	GO:0034613~cellular protein localization	28	1.42E-02
BP	GO:0010876~lipid localization	14	1.46E-02
BP	GO:0070727~cellular macromolecule localization	28	1.51E-02
BP	GO:0006607~NLS-bearing substrate import into nucleus	4	1.52E-02
BP	GO:0046907~intracellular transport	40	1.76E-02
BP	GO:0008219~cell death	43	1.78E-02
BP	GO:0016044~membrane organization	26	1.78E-02
BP	GO:0006869~lipid transport	13	1.86E-02
BP	GO:0048729~tissue morphogenesis	15	1.90E-02
BP	GO:0060562~epithelial tube morphogenesis	8	2.15E-02
BP	GO:0043966~histone H3 acetylation	5	2.18E-02
BP	GO:0035295~tube development	17	2.26E-02
BP	GO:0021955~central nervous system neuron axonogenesis	4	2.28E-02
BP	GO:0032869~cellular response to insulin stimulus	8	2.31E-02
BP	GO:0021915~neural tube development	8	2.31E-02

BP	GO:0043982~histone H4-K8 acetylation	3	2.34E-02
BP	GO:0043981~histone H4-K5 acetylation	3	2.34E-02
BP	GO:0043984~histone H4-K16 acetylation	3	2.34E-02
BP	GO:0070198~protein localization to telomere	3	2.34E-02
BP	GO:0043983~histone H4-K12 acetylation	3	2.34E-02
BP	GO:0001841~neural tube formation	6	2.48E-02
BP	GO:0021953~central nervous system neuron differentiation	6	2.48E-02
BP	GO:0002009~morphogenesis of an epithelium	10	2.55E-02
BP	GO:0007369~gastrulation	8	2.67E-02
	GO:0007178~transmembrane receptor protein		
BP	serine/threonine kinase signaling pathway	10	2.85E-02
BP	GO:0006644~phospholipid metabolic process	15	2.87E-02
BP	GO:0034502~protein localization to chromosome	3	3.19E-02
BP	GO:0034109~homotypic cell-cell adhesion	3	3.19E-02
BP	GO:0001838~embryonic epithelial tube formation	6	3.27E-02
BP	GO:0016331~morphogenesis of embryonic epithelium	7	3.36E-02
BP	GO:0001843~neural tube closure	5	3.51E-02
BP	GO:0060606~tube closure	5	3.51E-02
BP	GO:0035148~tube lumen formation	6	3.57E-02
BP	GO:0060541~respiratory system development	10	3.70E-02
BP	GO:0043543~protein amino acid acylation	7	3.88E-02
BP	GO:0008637~apoptotic mitochondrial changes	5	3.90E-02
BP	GO:0015031~protein transport	43	4.02E-02
BP	GO:0019637~organophosphate metabolic process	15	4.16E-02
BP	GO:0016337~cell-cell adhesion	19	4.19E-02
BP	GO:0000226~microtubule cytoskeleton organization	12	4.45E-02
BP	GO:0045184~establishment of protein localization	43	4.67E-02
BP	GO:0006468~protein amino acid phosphorylation	38	4.72E-02
BP	GO:0014020~primary neural tube formation	5	4.75E-02
BP	GO:0060284~regulation of cell development	15	4.93E-02
BP	GO:0034976~response to endoplasmic reticulum stress	5	5.22E-02
BP	GO:0046328~regulation of JNK cascade	7	5.39E-02
BP	GO:0030900~forebrain development	12	5.43E-02
BP	GO:0030324~lung development	9	5.54E-02
BP	GO:0016202~regulation of striated muscle tissue development	6	5.70E-02
BP	GO:0045216~cell-cell junction organization	5	5.70E-02
BP	GO:0042060~wound healing	14	5.80E-02
BP	GO:0032868~response to insulin stimulus	9	5.81E-02
BP	GO:0034660~ncRNA metabolic process	16	6.06E-02
BP	GO:0007281~germ cell development	9	6.09E-02
BP	GO:0048634~regulation of muscle development	6	6.11E-02
	GO:0030071~regulation of mitotic metaphase/anaphase		
BP	transition	4	6.22E-02
BP	GO:0016192~vesicle-mediated transport	33	6.23E-02

BP	GO:0051149~positive regulation of muscle cell differentiation	3	6.29E-02
BP	GO:0032925~regulation of activin receptor signaling pathway	3	6.29E-02
BP	GO:0008654~phospholipid biosynthetic process	9	6.38E-02
BP	GO:0030323~respiratory tube development	9	6.38E-02
BP	GO:0006473~protein amino acid acetylation	6	6.54E-02
	GO:0070302~regulation of stress-activated protein kinase		
BP	signaling pathway	7	6.82E-02
BP	GO:0006606~protein import into nucleus	8	6.83E-02
BP	GO:0007286~spermatid development	6	7.44E-02
BP	GO:0007004~telomere maintenance via telomerase	3	7.49E-02
BP	GO:0031623~receptor internalization	3	7.49E-02
BP	GO:0022402~cell cycle process	32	7.52E-02
BP	GO:0051170~nuclear import	8	7.52E-02
BP	GO:0016310~phosphorylation	43	7.55E-02
BP	GO:0006796~phosphate metabolic process	51	7.55E-02
BP	GO:0006793~phosphorus metabolic process	51	7.55E-02
BP	GO:0009260~ribonucleotide biosynthetic process	10	7.58E-02
BP	GO:0048610~reproductive cellular process	12	7.79E-02
BP	GO:0006461~protein complex assembly	29	7.88E-02
BP	GO:0070271~protein complex biogenesis	29	7.88E-02
BP	GO:0018209~peptidyl-serine modification	5	7.88E-02
BP	GO:0010033~response to organic substance	39	8.18E-02
BP	GO:0030397~membrane disassembly	2	8.19E-02
	GO:0031146~SCF-dependent proteasomal ubiquitin-		
BP	dependent protein catabolic process	2	8.19E-02
BP	GO:0051081~nuclear envelope disassembly	2	8.19E-02
BP	GO:0035239~tube morphogenesis	10	8.51E-02
BP	GO:0033365~protein localization in organelle	11	8.60E-02
BP	GO:0010833~telomere maintenance via telomere lengthening	3	8.74E-02
BP	GO:0032204~regulation of telomere maintenance	3	8.74E-02
	GO:0021952~central nervous system projection neuron		
BP	axonogenesis	3	8.74E-02
	GO:0007169~transmembrane receptor protein tyrosine kinase		
BP	signaling pathway	15	8.78E-02
BP	GO:0009259~ribonucleotide metabolic process	11	8.90E-02
BP	GO:0048515~spermatid differentiation	6	8.92E-02
BP	GO:0045926~negative regulation of growth	9	8.99E-02
BP	GO:0045766~positive regulation of angiogenesis	4	9.30E-02

Supplementary Table S2 GO terms enriched by PCGs with low dosage sensitivity

Category	Term	Count	P-Value
BP	GO:0031424~keratinization	6	2.69E-03
BP	GO:0030216~keratinocyte differentiation	7	3.65E-03
BP	GO:0009913~epidermal cell differentiation	7	5.62E-03
BP	GO:0045761~regulation of adenylate cyclase activity	8	5.96E-03
BP	GO:0031279~regulation of cyclase activity	8	7.03E-03
BP	GO:0030817~regulation of cAMP biosynthetic process	8	7.82E-03
BP	GO:0051339~regulation of lyase activity	8	7.82E-03
BP	GO:0030814~regulation of cAMP metabolic process	8	8.67E-03
BP	GO:0030802~regulation of cyclic nucleotide biosynthetic process	8	1.22E-02
BP	GO:0030808~regulation of nucleotide biosynthetic process	8	1.22E-02
BP	GO:0030799~regulation of cyclic nucleotide metabolic process	8	1.40E-02
BP	GO:0006140~regulation of nucleotide metabolic process	8	1.60E-02
BP	GO:0050731~positive regulation of peptidyl-tyrosine phosphorylation	5	2.11E-02
BP	GO:0006913~nucleocytoplasmic transport	9	2.51E-02
BP	GO:0051169~nuclear transport	9	2.68E-02
BP	GO:0007616~long-term memory	3	2.88E-02
BP	GO:0055085~transmembrane transport	21	3.31E-02
BP	GO:0051350~negative regulation of lyase activity	5	3.52E-02
BP	GO:0031280~negative regulation of cyclase activity	5	3.52E-02
BP	GO:0007190~activation of adenylate cyclase activity	5	3.52E-02
BP	GO:0007194~negative regulation of adenylate cyclase activity	5	3.52E-02
BP	GO:0045762~positive regulation of adenylate cyclase activity	5	3.72E-02
BP	GO:0031281~positive regulation of cyclase activity	5	3.94E-02
BP	GO:0007611~learning or memory	7	3.96E-02
BP	GO:0007188~G-protein signaling, coupled to cAMP nucleotide second messenger	6	4.29E-02
BP	GO:0051349~positive regulation of lyase activity	5	4.38E-02
BP	GO:0008272~sulfate transport	3	4.38E-02
BP	GO:0009953~dorsal/ventral pattern formation	5	4.61E-02
BP	GO:0051091~positive regulation of transcription factor activity	5	4.61E-02
BP	GO:0030282~bone mineralization	3	4.94E-02
BP	GO:0001934~positive regulation of protein amino acid phosphorylation	6	5.06E-02
BP	GO:0010817~regulation of hormone levels	8	5.50E-02
BP	GO:0050890~cognition	29	5.72E-02
BP	GO:0048754~branching morphogenesis of a tube	5	5.88E-02

BP	GO:0060348~bone development	7	5.98E-02
BP	GO:0010578~regulation of adenylate cyclase activity involved in G-protein signaling	4	6.08E-02
BP	GO:0007193~inhibition of adenylate cyclase activity by G-protein signaling	4	6.08E-02
BP	GO:0010579~positive regulation of adenylate cyclase activity by G-protein signaling pathway	4	6.08E-02
BP	GO:0007189~activation of adenylate cyclase activity by G-protein signaling pathway	4	6.08E-02
BP	GO:0009595~detection of biotic stimulus	3	6.11E-02
BP	GO:0019933~cAMP-mediated signaling	6	6.35E-02
BP	GO:0032497~detection of lipopolysaccharide	2	6.61E-02
BP	GO:0050730~regulation of peptidyl-tyrosine phosphorylation	5	6.72E-02
BP	GO:0032755~positive regulation of interleukin-6 production	3	6.73E-02
BP	GO:0042327~positive regulation of phosphorylation	6	6.82E-02
BP	GO:0035270~endocrine system development	5	7.01E-02
BP	GO:0060429~epithelium development	10	7.21E-02
BP	GO:0043388~positive regulation of DNA binding	5	7.31E-02
BP	GO:0019935~cyclic-nucleotide-mediated signaling	7	7.39E-02
BP	GO:0045597~positive regulation of cell differentiation	10	7.50E-02
BP	GO:0010562~positive regulation of phosphorus metabolic process	6	7.55E-02
BP	GO:0045937~positive regulation of phosphate metabolic process	6	7.55E-02
BP	GO:0046903~secretion	12	7.80E-02
BP	GO:0003002~regionalization	9	7.81E-02
BP	GO:0051090~regulation of transcription factor activity	6	8.33E-02
BP	GO:0001763~morphogenesis of a branching structure	5	8.58E-02
BP	GO:0060441~branching involved in lung morphogenesis	2	8.72E-02
BP	GO:0060438~trachea development	2	8.72E-02
BP	GO:0021569~rhombomere 3 development	2	8.72E-02
BP	GO:0030855~epithelial cell differentiation	7	8.98E-02
BP	GO:0043410~positive regulation of MAPKKK cascade	4	9.36E-02
BP	GO:0048706~embryonic skeletal system development	5	9.59E-02
BP	GO:0009952~anterior/posterior pattern formation	7	9.71E-02
BP	GO:0009914~hormone transport	4	9.81E-02
BP	GO:0051099~positive regulation of binding	5	9.94E-02
BP	GO:0051094~positive regulation of developmental process	11	9.97E-02

Supplementary table S3 GO terms enriched by lncRNA ENSG00000250303

Category	Term	Count	P-Value
BP	GO:0006631~fatty acid metabolic process	10	6.49E-12
BP	GO:0009062~fatty acid catabolic process	5	2.45E-07
BP	GO:0019395~fatty acid oxidation	5	3.41E-07
BP	GO:0034440~lipid oxidation	5	3.41E-07
BP	GO:0030258~lipid modification	5	3.47E-06
BP	GO:0044242~cellular lipid catabolic process	5	5.12E-06
BP	GO:0016054~organic acid catabolic process	5	2.31E-05
BP	GO:0046395~carboxylic acid catabolic process	5	2.31E-05
BP	GO:0016042~lipid catabolic process	5	1.30E-04
BP	GO:0006633~fatty acid biosynthetic process	4	2.36E-04
BP	GO:0055114~oxidation reduction	7	3.20E-04
BP	GO:0006635~fatty acid beta-oxidation	3	8.47E-04
BP	GO:0016053~organic acid biosynthetic process	4	1.69E-03
BP	GO:0046394~carboxylic acid biosynthetic process	4	1.69E-03
BP	GO:0001561~fatty acid alpha-oxidation	2	6.20E-03
BP	GO:0008610~lipid biosynthetic process	4	1.30E-02
BP	GO:0006637~acyl-CoA metabolic process	2	2.46E-02
BP	GO:0000038~very-long-chain fatty acid metabolic process	2	2.91E-02
	GO:0008543~fibroblast growth factor receptor signaling		
BP	pathway	2	4.41E-02
BP	GO:0051781~positive regulation of cell division	2	5.89E-02
BP	GO:0051302~regulation of cell division	2	7.05E-02