

1 **Analyzing the mechanism by which oyster peptides target IL-2 in**  
2 **melanoma cell apoptosis based on RNA-seq and m6A-seq**

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4 Jiaojiao Han<sup>a,b</sup>, Lingxin Geng<sup>a,b</sup>, Chenyang Lu<sup>a,b</sup>, Jun Zhou<sup>a,b</sup>, Ye Lijia<sup>a,b</sup>,  
5 Tinghong Ming<sup>a,b</sup>, Zhen Zhang<sup>a,b</sup>, Xiurong Su<sup>\*a,b</sup>

6 <sup>a</sup> State Key Laboratory for Managing Biotic and Chemical Threats to the Quality  
7 and Safety of Agro-products, Ningbo University, Ningbo, China

8 <sup>b</sup> School of Marine Science, Ningbo University, Ningbo, China

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10 \* Corresponding author

11 Dr. Xiurong Su

12 School of Marine Science, Ningbo University, 818 Fenghua Road, Ningbo,  
13 China

14 Tel/Fax: +86 574 87608368

15 E-mail address: [suxiurong\\_pub1ic@163.com](mailto:suxiurong_pub1ic@163.com)

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## Table Legend

**Table S1.** Sequences of the primers used for qRT-PCR analysis.

Gene	Forward primer	Reverse primer
<i>Bak</i>	GGTGAGTATCCAAGGACTGCAA	GATGGGACCATTGCCCAAGT
<i>Bad</i>	AGAGTTTGAGCCGAGTGAGC	ATGATGGCTGCTGCTGGTT
<i>Cct6</i>	AGACCCGGATAGTTCCTCCC	TCTAGGATGAAGGCCCATTTTCG
<i>Pak4</i>	CACTTCTGTCCCACCAGCAT	CCCATCTTTGGCACCTTTGC
<i>Rasa2</i>	TACCACAAACAGCCAGAGTTCA	CTCCTGACAGCAGAGCCAAT
<i>Gbp2</i>	GCTGGCTGGGAAGAAAAACG	ATGGCCAAGGCAAAGATCCA
<i>Cdk2</i>	GACACGCTGCTGGATGTCA	CAGAAAGCTAGGCCCTGGAG
<i>Tlr4</i>	TGCCGTTTTATCACGGAGGT	AAAGGCTCCCAGGGCTAAAC
<i>Pcna</i>	GTAGCAGAGTGGTCGTTGTCTT	CCAAAGAGACGTGGGACGAG
<i>Ncbp2</i>	GAAATCCGCAAACGCCAAGT	TTCATTGTCACCCTCTCGGC
<i>Pkm</i>	GTACCATTGTACCATGCGGAGA	GTAGGCGTTATCCAGCGTGA
<i>Hsp90ab1</i>	GGGTATCGGAAAGCAAGCCT	AGCGAATCTTGTCCAAGGCA
<i>Myh9</i>	GTGAAACTCCCACCCTACCC	CCAATCTGGTTCCCGACGAT

**Table S2.** Peptide sequences identified by MALDI-TOF/TOF-MS.

Peptide sequence	Peptide expected Mr	Peptide calculated Mr	Peptide score	Relative abundance (%)	Protein description
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RGITG	502.2599	502.2863	12.93	23.73	collagen alpha-1(IX) chain-like isoform X1
PSGCAP	531.2629	530.2159	17.97	20.29	transferrin, partial
PGVGMS	546.2948	546.2472	32.53	33.01	endothelial PAS domain-containing protein 1
GPVGAPG	553.2948	553.286	26.89	25.12	collagen alpha-1(XXVII) chain B-like
GPGVPK	554.3011	553.3224	20.06	33.27	titin isoform b, partial
KVGPLG	569.2999	569.3537	26.53	18.48	ankyrin repeat and SAM domain-containing protein 1A-like isoform X2
GGVPLQ	570.2982	569.3173	18.72	17.22	G-protein-coupled receptor GPR34 type 2a
PSPGNPG	624.3092	624.2867	30.6	25.72	transcription factor SOX-21
GLIWR	644.3278	643.3806	27.83	26.61	estrogen receptor alpha
GLLVLLPA	795.3912	794.5266	31.55	24.14	MHC class Ia antigen
VNPELPR	824.8842	823.8907	25.13	36.97	uncharacterized protein LOC105334086
RGPPKGIL	836.4139	836.5232	43.13	23.22	fidgetin-like protein 1
ILADSAPR	842.6676	841.6603	30.74	45.84	uncharacterized protein LOC105336797
NCPAVPTVR	957.6548	956.6621	23.06	35.46	uncharacterized protein LOC105325428
ADRNNLPVLEA	1211.5573	1210.6306	12.72	14.86	CYP1A
VSQGQPTLVIME	1301.5593	1300.6697	19.49	27.66	insulin-like growth factor I receptor 1a

PPTGITTLDPFEVP	1483.6652	1482.7606	19.56	28.46	putative cytochrome oxidase subunit 3
LGAGHILQNDLLPIIS	1673.7651	1672.9512	20.6	23.08	timeless

**Table S3.** The results of potential targets screening with high fit values by Discovery Studio 2018.

Peptide	PDB ID	Pharmacophore	Fit Value	Biological function
	1tqf	Beta-secretase 1	3.0449	Responsible for the proteolytic processing of the amyloid precursor protein
	1t5c	Centromeric protein E	3.0486	Plays an important role in chromosome congression, microtubule-kinetochore conjugation and spindle assembly checkpoint activation.
	1srg	Streptavidin	3.0659	Forms a strong non-covalent specific complex with biotin
	1jj7	Peptide transporter TAP1	3.0747	ABC transporter associated with antigen processing
	1f5v	Oxygen insensitive NADPH nitroreductase	3.0850	Catalyzes the reduction of nitroaromatic compounds using NADPH
ILADSAPR	1coy	Cholesterol Oxidase	3.1515	Catalyzes the oxidation and isomerization of cholesterol to cholestenone

	1amw	Heat Shock Protein 90	3.2056	Promotes the maturation, structural maintenance and proper regulation of specific target proteins involved in cell cycle control and signal transduction.
	1a4h	Heat Shock Protein 90	3.2556	Promotes the maturation, structural maintenance and proper regulation of specific target proteins involved in cell cycle control and signal transduction.
	1M48	Interleukin-2	3.4923	Play pivotal roles in the immune response and tolerance
□	1a0i	DNA ligase	3.5186	Seals nicks in double-stranded DNA during DNA replication, DNA recombination and DNA repair in an ATP-dependent reaction
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	3cyq	Chemotaxis protein motB	3.0483	MotA and MotB comprise the stator element of the flagellar motor complex
	2iyI	Cell division protein ftsy	3.0867	Involved in targeting and insertion of nascent membrane proteins into the cytoplasmic membrane
	1uk4	3C-like proteinase	3.1484	Contains the proteinases responsible for the cleavages of the polyprotein.

	3beg	Serine/threonine-protein kinase SRPK1	3.1521	Plays a central role in the regulatory network for splicing
VNPFLPR	2aio	Metallo-beta-lactamase L1	3.1762	Antibiotic resistance
	2orj	Pulmonary surfactant- associated protein D	3.1842	Contributes to the lung's defense against inhaled microorganisms, organic antigens and toxins
	3d9m	RNA-binding protein 16	3.4769	Anti-terminator protein required to prevent early mRNA termination during transcription
	2gz7	Replicase polyprotein 1ab	3.4800	Multifunctional protein involved in the transcription and replication of viral RNAs
	1w51	Beta-secretase 1	3.6149	Responsible for the proteolytic processing of the amyloid precursor protein
□	1M48	Interleukin-2	3.6568	Play pivotal roles in the immune response and tolerance
	1tyr	Transthyretin	3.0356	Thyroid hormone-binding protein
	1tqf	Beta-secretase 1	3.0431	Responsible for the proteolytic processing of the amyloid precursor protein
	1uk4	3C-like proteinase	3.1096	Contains the proteinases responsible for the cleavages

				of the polyprotein.
				Promotes the maturation, structural maintenance and proper regulation of specific target proteins involved in cell cycle control and signal transduction.
	1a4h	Heat Shock Protein 90	3.1253	
	1jj7	Peptide transporter TAP1	3.1923	ABC transporter associated with antigen processing
NCPAVPTVR	1f5v	Oxygen insensitive NADPH nitroreductase	3.4303	Catalyzes the reduction of nitroaromatic compounds using NADPH
	1t5c	Centromeric protein E	3.4844	Plays an important role in chromosome congression, microtubule-kinetochore conjugation and spindle assembly checkpoint activation
	1M48	Interleukin-2	3.5568	Play pivotal roles in the immune response and tolerance
	3iay	DNA polymerase delta catalytic subunit	3.5656	Participates in chromosomal DNA replication
□	3lbi	GTPase HRas	3.6358	Involved in the activation of Ras protein signal transduction

**Table S4.** The reversing docking results of other peptides.

Peptide	PDB ID	Pharmacophore	Fit Value	Biological function
RGITG	1uk4	3C-like proteinase	3.0524	Contains the proteinases responsible for the cleavages of the polyprotein
	2gz7	Replicase polyprotein 1ab	3.1611	Multifunctional protein involved in the transcription and replication of viral RNAs
	2orj	Pulmonary surfactant-associated protein D	2.9683	Contributes to the lung's defense against inhaled microorganisms, organic antigens and toxins
	2of4	Proto-oncogene tyrosine-protein kinase LCK	3.0181	Non-receptor tyrosine-protein kinase that plays an essential role in the selection and maturation of developing T-cells in the thymus and in the function of mature T-cells
	3i81	Insulin-like growth factor 1 recepto	2.9472	Receptor tyrosine kinase which mediates actions of insulin-like growth factor 1 (IGF1)
PSGCAP	3nw6	Insulin-like growth factor	3.1479	Receptor tyrosine



		1 receptor		kinase which mediates actions of insulin-like growth factor 1 (IGF1)
	3o95	Dipeptidyl peptidase 4	2.8874	Its interaction with ADA also regulates lymphocyte-epithelial cell adhesion
	1y6a	Vascular endothelial growth factor receptor 2	2.9063	Plays an essential role in the regulation of angiogenesis, vascular development, vascular permeability, and embryonic hematopoiesis
	1mmp	Matrilysin	3.0432	Activates procollagenase
	1fkh	Peptidyl-prolyl cis-trans isomerase FKBP1A	3.0785	It catalyzes the cis-trans isomerization of proline imidic peptide bonds in oligopeptides
PGVGMS	4drq	Peptidyl-prolyl cis-trans isomerase FKBP5	2.8958	Immunophilin protein with PPIase and co-chaperone activities
	2wxq	Phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit delta	3.1234	Uses ATP and PtdIns(4,5)P2 (phosphatidylinositol

		isoform		4,5-bisphosphate) to generate phosphatidylinositol 3,4,5-trisphosphate (PIP3)
	1yw2	Mitogen-activated protein kinase 14	2.9688	Serine/threonine kinase which acts as an essential component of the MAP kinase signal transduction pathway.
	2c5x	Cyclin-dependent kinase 2	3.0448	Serine/threonine-protein kinase involved in the control of the cell cycle
	3rwp	3-phosphoinositide-dependent protein kinase 1	2.9018	Isoform 3 is catalytically inactive
	4erk	Mitogen-activated protein kinase 1	3.02	Transcriptional activity is independent of kinase activity
GPVGAPG	4dfn	Tyrosine-protein kinase SYK	3.0718	Regulates neutrophil degranulation and phagocytosis through activation of the MAPK signaling cascade
	4djh	Kappa-type opioid receptor, Lysozyme	3.1424	Play a role in arousal and regulation of

				autonomic and neuroendocrine functions
	1ypl	thrombin light chain	2.9817	Functions in blood homeostasis, inflammation and wound healing
	2ab2	Mineralocorticoid receptor	3.0649	The effect of MC is to increase ion and water transport and thus raise extracellular fluid volume and blood pressure and lower potassium levels
GPGVPK	1pe5	Thermolysin	2.9676	Extracellular zinc metalloprotease
	1rq9	protease	3.0357	Showing features for domain
	3oqk	Renin	3.0608	Renin is a highly specific endopeptidase
	3uqf	Proto-oncogene tyrosine-protein kinase Src	3.1464	Non-receptor protein tyrosine kinase
	1gbn	Ornithine aminotransferase, mitochondrial	2.9322	Catalyzes the reversible interconversion of L-ornithine and 2-

				oxoglutarate to L-glutamate semialdehyde and L-glutamate
KVGPLG	1qpd	LCK Kinase	3.094 2.92	Interacts with FYB2 Plays a key role in T-cell antigen receptor (TCR)-linked signal transduction pathways
	3mpm	Tyrosine-protein kinase Lck		Confers resistance to the different beta-lactams antibiotics
	2aio	Metallo-beta-lactamase L1	3.002	A receptor for fibronectin and fibrinogen
	3vi4	Integrin alpha-5	3.1025	Activates several signaling pathways in response to ligand binding, including the ERK1/2 and the JNK pathway
	2i0v	cFMS tyrosine kinase	3.0284	
GGVPLQ	2i1m	Macrophage colony-stimulating factor 1 receptor	3.0743	Promotes the release of pro-inflammatory chemokines in response to IL34 and CSF1
	3dpk	Fibroblast growth factor receptor 1	3.0377	Tyrosine-protein kinase

	3g0e	Mast/stem cell growth factor receptor	3.079	In response to KITLG/SCF binding, KIT can activate several signaling pathways Integrin ITGAL/ITGB2 is a receptor for F11R Play a role in the contractions of the heart, gut and testes, and in spermatid differentiation
	1cqp	Integrin alpha-L	2.8869	
	2xhm	Angiotensin-converting enzyme	3.0432	
PSPGNPG	2wqb	Angiopoietin-1 receptor	3.0622	Required for normal angiogenesis and heart development during embryogenesis
	2xba	ALK tyrosine kinase receptor	2.8975	Plays an important role in the genesis and differentiation of the nervous system
	2hha	Hypothetical protein DPP4	3.0769	Cell surface glycoprotein receptor involved in the costimulatory signal essential for T-cell receptor (TCR)-mediated T-cell

	2ogz	Dipeptidyl peptidase	3.2137	activation Cell surface glycoprotein receptor involved in the costimulatory signal essential for T-cell receptor (TCR)- mediated T-cell activation
	2vdm	Integrin alpha-IIb	3.1919	Integrin alpha-IIb/beta-3 is a receptor for fibronectin, fibrinogen, plasminogen, prothrombin, thrombospondin and vitronectin
GLIWR	1r0p	Hepatocyte growth factor receptor	3.1734	Receptor tyrosine kinase that transduces signals from the extracellular matrix into the cytoplasm by binding to hepatocyte growth factor/HGF ligand
	1u59	Tyrosine-protein kinase ZAP-70	3.1027	Tyrosine kinase that plays an essential role

	1sx3	groEL protein	3.0813	in regulation of the adaptive immune response Together with its co-chaperonin GroES, plays an essential role in assisting protein folding
	1qy8	Endoplasmin	3.1016	Molecular chaperone that functions in the processing and transport of secreted proteins
	1tu6	Cathepsin K	2.9528	Thiol protease involved in osteoclastic bone resorption and may participate partially in the disorder of bone remodeling
GLLVLLPA	1zxn	DNA topoisomerase II, alpha isozyme	3.04	Key decatenating enzyme that alters DNA topology by binding to two double-stranded DNA molecules
	3svh	CREB-binding protein	2.9566	Acetylates histones, giving a specific tag for

	2w5y	Histone-lysine N-methyltransferase 2A	2.9299	transcriptional activation Histone methyltransferase that plays an essential role in early development and hematopoiesis
	3smr	WD repeat-containing protein 5	3.004	Contributes to histone modification
	3ooi	Histone-lysine N-methyltransferase, H3 lysine-36 specific	3.0954	Histone methyltransferase that dimethylates Lys-36 of histone H3
	3oxf	SET and MYND domain-containing protein 3	3.0501	Histone methyltransferase
	3tg4	N-lysine methyltransferase SMYD2	2.9279	The activity requires interaction with HSP90alpha
RGPPKGIL	2itx	Epidermal growth factor receptor	3.0129	Receptor tyrosine kinase binding ligands of the EGF family and activating several signaling cascades to convert extracellular cues into appropriate cellular responses



	3bpr	Proto-oncogene tyrosine-protein kinase MER	3.0024	Regulates many physiological processes including cell survival, migration
	3hng	Vascular endothelial growth factor receptor 1	3.024	Acts as a positive regulator of postnatal retinal hyaloid vessel regression
	4aoj	High affinity nerve growth factor receptor	3.1059	High affinity receptor for NGF which is its primary ligand
	2ivv	Proto-oncogene tyrosine-protein kinase receptor Ret	3.1074	Involved in the development of enteric nervous system and renal organogenesis during embryonic life
ADRNNLPVLEA	3oom	Activin receptor type-1	2.858	Bone morphogenetic protein (BMP) type I receptor
	1py5	TGF-beta receptor type I	3.1671	Transmembrane serine/threonine kinase forming with the TGF-beta type II serine/threonine kinase receptor
	3iod	Pantothenate	3.0875	Catalyzes the

		synthetase		condensation of pantoate with beta-alanine in an ATP-dependent reaction via a pantoyl-adenylate intermediate
VSQGQPTLVIME	2wgs	Glutamine synthetase	3.07	Involved in nitrogen metabolism via ammonium assimilation
	1hon	Adenylosuccinate synthetase	3.0185	Plays an important role in the de novo pathway of purine nucleotide biosynthesis
	3gid	Acetyl-CoA carboxylase 2	3.0844	Mitochondrial enzyme that catalyzes the carboxylation of acetyl-CoA to malonyl-CoA and plays a central role in fatty acid metabolism
	1tkg	Threonyl-tRNA synthetase	2.8855	Catalyzes the attachment of threonine to tRNA(Thr) in a two-step reaction
	3qtc	Pyrrolysyl-tRNA synthetase	2.9573	Catalyzes the attachment of pyrrolysine to tRNA(Pyl)

PPTGITTLDPFVEVP	1pg4	acetyl-CoA synthetase	2.9104	Catalyzes the conversion of acetate into acetyl-CoA
	2b69	UDP-glucuronate decarboxylase 1	2.993	Catalyzes the NAD-dependent decarboxylation of UDP-glucuronic acid to UDP-xylose
	3h0w	S-adenosylmethionine decarboxylase proenzyme	3.1292	Essential for biosynthesis of the polyamines spermidine and spermine
	1bn1	Carbonic anhydrase 2	3.1362	Catalyzes the reversible hydration of carbon dioxide
	2orj	Pulmonary surfactant-associated protein D	2.9472	Contributes to the lung's defense against inhaled microorganisms, organic antigens and toxins
LGAGHILQNDLLPIIS	3lbj	Protein Mdm4	3.0879	Along with MDM2, contributes to TP53 regulation
	2dq7	Proto-oncogene tyrosine-protein kinase Fyn	3.0032	Non-receptor tyrosine-protein kinase
	1tyr	Transthyretin	3.0489	Thyroid hormone-

	2gz7	Replicase polyprotein 1ab	2.862	binding protein Contains the proteinases responsible for the cleavages of the polyprotein
	1uk4	3C-like proteinase	3.0015	Multifunctional protein involved in the transcription and replication of viral RNAs

**Table S5.** The results of molecular docking.

Name	_CHARMm Energy	Bond Energy	Angle Energy	_CDOCKER ENERGY	_CDOCKER INTERACTION ENERGY	Electrostatic Energy	Van der Waals Energy	POSE NUMBER	RMS Gradient
ILADSAPR	-305.27	1.7578	25.9001	86.6552	74.9643	-341.453	- 20.1163	1	0.00974
NCPAVPTVR	-351.667	2.55349	35.3908	73.0932	67.1465	-402.267	-	1	0.00943

							23.0214		
VNPFLPR	-290.361	2.36685	32.7481	68.1828	71.7682	-337.482	-	1	0.00995
							22.9434		

**Table S6.** Abundance of differentially expressed gene in each group.

Gene Name	Log2(FC) value			Gene description
	control	ILADSAPR	IL-2	
<i>Cct6</i>	-1.35	0.86	0.39	chaperonin containing Tcp1, subunit 6
<i>Bad</i>	-1.02	0.71	0.27	BCL2-associated agonist of cell death
<i>Rasa2</i>	-1.17	0.69	0.21	RAS p21 protein activator 2
<i>Gm10260</i>	-1.24	0.73	0.23	predicted gene 10260
<i>Pcna</i>	1.21	0.55	0.43	proliferating cell nuclear antigen
<i>Gm28037</i>	-1.3	0.57	0.35	predicted gene, 28037
<i>Zfp708</i>	-1.27	0.42	0.59	zinc finger protein 708
<i>Pak4</i>	-1.23	0.47	0.51	p21 protein -activated kinase 4
<i>Gbp2</i>	-1.31	0.48	0.49	guanylate binding protein 2
<i>Cdk2</i>	1.26	0.48	0.47	cyclin-dependent kinase 2

<i>Gm20521</i>	-0.72	0.5	0.46	predicted gene 20521
<i>Ncbp2</i>	0.79	-0.12	-1.03	nuclear cap binding protein subunit 2
<i>Tlr4</i>	0.74	-0.17	-1.09	toll-like receptor 4
<i>Zfp955B</i>	-0.38	-0.14	1.11	zinc finger protein 955B
<i>Gm15850</i>	-0.36	-0.16	1.28	predicted gene 15850
<i>Gan</i>	-0.34	-0.43	1.26	Gigaxonin
<i>Cdc14B</i>	-0.21	-0.39	1.26	CDC14 cell division cycle 14B
<i>Zfp157</i>	-0.26	-0.41	1.27	zinc finger protein 157
<i>Ppp1R26</i>	-0.27	-0.47	1.24	protein regulatory subunit 26
<i>Gm42878</i>	-0.36	-0.43	1.25	predicted gene 42878
<i>Pou2F1</i>	-0.31	-0.44	1.31	POU domain 2, transcription factor 1
<i>Uhmk1</i>	-0.32	-0.46	1.3	U2AF homology motif (UHM) kinase 1
<i>Zfp966</i>	-0.35	-0.23	1.33	zinc finger protein 966
<i>Zfp82</i>	-0.38	-0.31	1.29	zinc finger protein 82
<i>Cpeb4</i>	-0.33	-0.39	1.24	cytoplasmic polyadenylation element 4
<i>Ddias</i>	-0.34	-0.36	1.24	damage induced apoptosis suppressor
<i>Em15</i>	-0.34	-0.36	1.3	embrane protein 154

<i>Chm</i>	-0.27	-0.32	1.34	choroideremia
<i>Gm37034</i>	-0.26	-0.33	1.36	predicted gene, 37034
<i>Bicd1</i>	-0.27	-0.31	1.31	bicaudal D homolog 1
<i>Gm9958</i>	-0.25	-0.33	1.33	predicted gene 9958
<i>Clock</i>	-0.3	-0.29	1.34	circadian locomotor output cycles kaput
<i>Zbed6</i>	-0.28	-0.37	1.29	zinc finger, BED type containing 6
<i>Gm43980</i>	-0.31	-0.29	1.29	predicted gene, 43980
<i>Pds5A</i>	-0.29	-0.27	1.4	PDS5 cohesin associated factor A
<i>Cep290</i>	-0.4	-0.3	1.35	centrosomal protein 290
<i>Ankrd12</i>	-0.43	-0.34	1.37	ankyrin repeat domain 12
<i>Rictor</i>	-0.44	-0.36	1.41	independent companion of MTOR
<i>Nbeal1</i>	-0.4	-0.35	1.37	neurobeachin like 1
<i>Kcnq1Ot1</i>	-0.42	-0.33	1.25	KCNQ1 overlapping transcript 1
<i>Zc3H7A</i>	-0.51	-0.29	1.29	zinc finger CCCH type containing 7 A
<i>Myo9A</i>	-0.47	-0.3	1.26	myosin IXa
<i>Polq</i>	-0.49	-0.33	1.31	polymerase (DNA directed), theta
<i>Cd2Ap</i>	-0.52	-0.33	1.33	CD2-associated protein

<i>Thoc2</i>	-0.43	-0.35	1.34	THO complex 2
<i>Atrx</i>	-0.44	-0.37	1.3	ATRX, chromatin remodeler
<i>Prpf39</i>	-0.43	-0.38	1.26	pre-mRNA processing factor 39
<i>Tet2</i>	-0.41	-0.29	1.32	tet methylcytosine dioxygenase 2
<i>Rock2</i>	-0.42	-0.27	1.4	Rho coiled containing protein kinase 2
<i>Cenpe</i>	-0.46	-0.29	1.29	centromere protein E
<i>Gm37494</i>	-0.55	-0.3	1.24	predicted gene, 37494
<i>Malat1</i>	-0.55	-0.33	1.25	metastasis associated lung transcript 1
<i>Ugg2</i>	-0.46	-0.31	1.23	UDP glycoprotein glucosyl transferase 2
<i>Upf2</i>	-0.44	-0.31	1.43	UPF2 regulator
<i>Ap3M1</i>	-0.47	-0.35	1.41	adaptor-related protein complex 3
<i>Cenpf</i>	-0.48	-0.33	1.41	centromere protein F
<i>Ino80D</i>	-0.47	-0.34	1.33	INO80 complex subunit D
<i>Paxbp1</i>	-0.48	-0.26	1.35	PAX3 and PAX7 binding protein 1
<i>Smg1</i>	-0.47	-0.28	1.39	SMG1 homolog
<i>Ago3</i>	-0.52	-0.3	1.38	argonaute RISC catalytic subunit 3
<i>Zfp329</i>	-0.53	-0.34	1.38	zinc finger protein 329



<i>Sacs</i>	-0.55	-0.33	1.4	sacsin
<i>Ccdc88A</i>	-0.51	-0.25	1.44	coiled coil domain containing 88A
<i>Vps13A</i>	-0.5	-0.29	1.39	vacuolar protein sorting 13A
<i>Rasa12</i>	-0.49	-0.27	1.25	RAS protein activator like 2
<i>Firre</i>	-0.44	-0.31	1.29	functional intergenic repeating element
<i>Trpm7</i>	-0.46	-0.32	1.3	transient receptor potential , member 7
<i>Mdm4</i>	-0.48	-0.35	1.34	mouse 3T3 cell double minute 4
<i>Zfx2Os</i>	-0.47	-0.3	1.33	zinc finger homeobox 2, opposite strand
<i>Casp82P2</i>	-0.47	-0.35	1.41	caspase 8 associated protein 2
<i>Tmem170B</i>	-0.51	-0.29	1.44	transmembrane protein 170B
<i>Zfp445</i>	-0.53	-0.37	1.35	zinc finger protein 445
<i>Tmtc3</i>	-0.47	-0.28	1.36	transmembrane tetratricopeptide containing 3
<i>Bod1L</i>	-0.49	-0.3	1.4	biorientation of chromosomes in cell division 1-like
<i>Taok1</i>	-0.53	-0.33	1.29	TAO kinase 1
<i>Ccdc18</i>	-0.56	-0.34	1.27	coiled-coil domain containing 18
<i>Rif</i>	-0.51	-0.31	1.46	replication timing regulatory factor
<i>Med13</i>	-0.51	-0.35	1.37	mediator complex subunit 13

<i>Pet117</i>	-0.48	-0.33	1.33	PET117 homolog
<i>Gm14633</i>	-0.44	-0.24	1.39	predicted gene 14633
<i>Gdf1</i>	-0.5	-0.27	1.38	growth differentiation factor 1
<i>Rnf26</i>	-0.51	-0.26	1.28	ring finger protein 26
<i>Gm20708</i>	-0.53	-0.31	1.35	predicted gene 20708
<i>Gm21982</i>	0.69	-1.16	0.66	predicted gene 21982
<i>Adat3</i>	0.72	-1.22	0.69	adenosine deaminase, tRNA-specific 3
<i>Gm15107</i>	0.73	-1.21	0.71	predicted gene 15107
<i>Pcdhgb1</i>	0.68	-1.19	0.69	protocadherin gamma subfamily B, 1
<i>Gm17028</i>	1.13	0.34	0.31	predicted gene 17028
<i>Gm21969</i>	1.25	-0.72	0.28	predicted gene 21969
<i>Gm7293</i>	1.18	-0.74	-0.5	predicted gene 7293
<i>Cd63</i>	-0.44	1.25	-0.41	CD63 antigen
<i>Gm3174</i>	-0.46	1.22	-0.43	predicted gene, 31748
<i>Gm15093</i>	-0.43	1.23	-0.41	predicted gene 15093
<i>Gm4613</i>	-0.47	1.19	-0.44	predicted gene 4613
<i>A13Rik</i>	0.33	1.3	-1.17	RIKEN cDNA gene

<i>Usf2</i>	0.47	0.89	-1.14	upstream transcription factor 2
<i>D9300</i>	0.62	0.64	-1.21	RIKEN cDNA 9300 gene
<i>Ac138284</i>	0.67	0.61	-1.23	RIKEN cDNA 138284 gene
<i>Bak</i>	-0.72	0.58	1.17	BCL2-antagonist/killer
<i>Nfat5</i>	0.36	0.34	-1.03	nuclear factor of activated T cells 5
<i>Rin1</i>	-0.47	0.25	-0.43	Ras and Rab interactor-like
<i>Hkdc1</i>	-0.43	-0.28	1.41	hexokinase domain containing 1

**Table S7.** Summary of m6A peaks in B16 cells and distribution.

Samples ID	m6A peaks	m6A related gene	% peaks in 5'UTR	% peaks in 3'UTR	% peaks in 1st Exon	% peaks in other Exon
control	21271	9001	14.2	51.35	4.66	29.79
ILADSAPR	23416	9593	13.74	49.55	4.99	31.72
IL-2	24140	9910	15.13	49.77	4.9	30.21

**Table S8.** The differential genes detected in the comparison between the control and ILADSAPR group analyzed jointly by RNA-

seq and M6A seq.

Gene ID	Gene Name	Diff.log2.fc	m6A regulation	log2(fc)	pval	qval	Gene regulation	Description
ENSMUSG00000033								
364	<i>Usp37</i>	-0.59	down	-1.41	0.04	1	down	ubiquitin specific peptidase 37
ENSMUSG00000006								translocated promoter region, nuclear
005	<i>Tpr</i>	-1.26	down	-1.50	0.03	1	down	basket protein
ENSMUSG00000057								
335	<i>Cep170</i>	-1.79	down	-1.46	0.03	1	down	centrosomal protein 170
ENSMUSG00000043						0.8		UPF2 regulator of nonsense transcripts
241	<i>Upf2</i>	-2.70	down	-1.90	0.01	0	down	homolog (yeast)
ENSMUSG00000026								c-abl oncogene 1, non-receptor tyrosine
842	<i>Abl1</i>	0.31	up	-1.39	0.04	1	down	kinase
ENSMUSG00000036								
202	<i>Rif1</i>	-2.93	down	-1.48	0.03	1	down	replication timing regulatory factor 1
ENSMUSG00000074	<i>Qser1</i>	-1.48	down	-1.34	0.05	1	down	glutamine and serine rich 1

994									
ENSMUSG000000035						0.8			SHC (Src homology 2 domain containing)
109	<i>Shc4</i>	-0.25	down	-1.85	0.01	0	down		family, member 4
ENSMUSG000000035									
093	<i>Secisbp2l</i>	-1.63	down	-1.50	0.03	1	down		SECIS binding protein 2-like
ENSMUSG000000045									ESF1 nucleolar pre-rRNA processing
624	<i>Esf1</i>	-2.01	down	-1.45	0.03	1	down		protein homolog
ENSMUSG000000028									zinc finger, RAN-binding domain containing
180	<i>Zranb2</i>	-2.03	down	-1.65	0.02	1	down	2	
ENSMUSG000000041						0.8			
734	<i>Kirrel</i>	0.32	up	1.83	0.01	0	up		kin of IRRE like (Drosophila)
ENSMUSG000000039						0.6			
967	<i>Zfp292</i>	-3.81	down	-2.00	0.00	1	down		zinc finger protein 292
ENSMUSG000000028						0.9			family with sequence similarity 219,
439	<i>Fam219a</i>	0.95	up	-1.71	0.01	8	down		member A
ENSMUSG000000045						0.2			
973	<i>Slc25a51</i>	-0.40	down	2.35	0.00	4	up		solute carrier family 25, member 51

ENSMUSG00000053						0.9		
841	<i>Txlna</i>	-0.46	down	1.71	0.01	7	up	taxilin alpha
ENSMUSG00000039								
410	<i>Prdm16</i>	-0.16	down	1.58	0.02	1	up	PR domain containing 16
ENSMUSG00000029								ski sarcoma viral oncogene homolog
050	<i>Ski</i>	0.15	up	1.46	0.03	1	up	(avian)
ENSMUSG00000014								YES proto-oncogene 1, Src family tyrosine
932	<i>Yes1</i>	-2.45	down	-1.56	0.02	1	down	kinase
ENSMUSG00000061						0.4		biorientation of chromosomes in cell
755	<i>Bod1l</i>	-3.03	down	-2.18	0.00	2	down	division 1-like
ENSMUSG00000038								
538	<i>Ubn2</i>	-1.30	down	-1.40	0.04	1	down	ubinuclein 2
ENSMUSG00000030								
016	<i>Zfp638</i>	-2.27	down	-1.48	0.03	1	down	zinc finger protein 638
ENSMUSG00000060								
477	<i>Irak2</i>	-0.40	down	1.37	0.04	1	up	interleukin-1 receptor-associated kinase 2
ENSMUSG00000007	<i>Ankrd26</i>	-3.43	down	-1.37	0.04	1	down	ankyrin repeat domain 26

827

ENSMUSG000000003

153

*Slc2a3*

-0.46 down

1.47 0.03

1 up

solute carrier family 2 (facilitated glucose transporter), member 3

ENSMUSG000000068

566

*Myadm*

-0.21 down

1.33 0.04

1 up

myeloid-associated differentiation marker

ENSMUSG000000054 *1600014C10*

676

*Rik*

0.46 up

1.35 0.04

1 up

RIKEN cDNA 1600014C10 gene

ENSMUSG000000033

904

*Ccp110*

-3.90 down

-1.70 0.01

1 down

centriolar coiled coil protein 110

ENSMUSG000000031

0.9

antigen identified by monoclonal antibody

004

*Mki67*

-0.83 down

-1.71 0.01

7 down

Ki 67

ENSMUSG000000036

990

*Otud4*

-1.80 down

-1.43 0.03

1 down

OTU domain containing 4

ENSMUSG000000049

305

*Ccdc71*

0.25 up

-1.62 0.02

1 down

coiled-coil domain containing 71

ENSMUSG000000041

268

*Dmxl2*

-1.52 down

-1.63 0.02

1 down

Dmx-like 2

ENSMUSG00000019						0.7		
817	<i>Plagl1</i>	0.58	up	-1.89	0.01	7	down	pleiomorphic adenoma gene-like 1
ENSMUSG00000003						0.6		
226	<i>Ranbp2</i>	-1.64	down	-1.99	0.00	1	down	RAN binding protein 2
ENSMUSG00000035						0.0		
370	<i>Adat3</i>	0.11	up	-6.18	0.00	0	down	adenosine deaminase, tRNA-specific 3
ENSMUSG00000046								
311	<i>Zfp62</i>	-1.42	down	-1.51	0.03	1	down	zinc finger protein 62
ENSMUSG00000049						0.9		
470	<i>Aff4</i>	-2.68	down	-1.74	0.01	7	down	AF4/FMR2 family, member 4
ENSMUSG00000069								
793	<i>Slfn9</i>	-1.29	down	-1.65	0.02	1	down	schlafen 9
ENSMUSG00000059						0.7		
995	<i>Atxn7l3</i>	-0.27	down	1.88	0.01	4	up	ataxin 7-like 3
ENSMUSG00000037								
669	<i>Ldah</i>	0.41	up	-1.38	0.04	1	down	lipid droplet associated hydrolase
ENSMUSG00000020	<i>Rock2</i>	-1.75	down	-1.81	0.01	0.8	down	Rho-associated coiled-coil containing



580						6		protein kinase 2
ENSMUSG00000039								
219	<i>Arid4b</i>	-4.32	down	-1.56	0.02	1	down	AT rich interactive domain 4B (RBP1-like)
ENSMUSG00000021								
413	<i>Prpf4b</i>	-0.95	down	-1.41	0.04	1	down	pre-mRNA processing factor 4B
ENSMUSG00000006								
740	<i>Kif5b</i>	-0.94	down	-1.48	0.03	1	down	kinesin family member 5B metastasis associated lung
ENSMUSG00000092						0.1		adenocarcinoma transcript 1 (non-coding RNA)
341	<i>Malat1</i>	-2.65	down	-2.65	0.00	0	down	
ENSMUSG00000024						0.5		
795	<i>Kif20b</i>	-2.56	down	-2.10	0.00	1	down	kinesin family member 20B
ENSMUSG00000040								
621	<i>Gemin8</i>	-0.71	down	1.46	0.03	1	up	gem nuclear organelle associated protein 8
ENSMUSG00000036						0.7		UPF3 regulator of nonsense transcripts homolog B (yeast)
572	<i>Upf3b</i>	-1.68	down	-1.91	0.01	9	down	
ENSMUSG00000056	<i>Rlim</i>	-1.39	down	-1.62	0.02	1	down	ring finger protein, LIM domain interacting

537

ENSMUSG00000031

0.3

229            *Atrx*                    -2 down            -2.25 0.00        4 down            ATRX, chromatin remodeler

ENSMUSG00000023

0.0441

944            *Hsp90ab1*                -0.134 down            4 0.01        1 down            heat shock protein 90 alpha (cytosolic)

ENSMUSG00000022

0.1349 0.02

443            *Myh9*                    -0.153 down            7 3            1 down            myosin, heavy polypeptide 9, non-muscle

ENSMUSG00000032

- 0.00

294            *Pkm*                    0.153 down            0.1148 9            1 down            pyruvate kinase, muscle

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