HIROSHIMA UNIVERSITY
The Frontier Development Program for Genome Editing

Meta-analysis of heat stressed transcriptomes using public gene expression database

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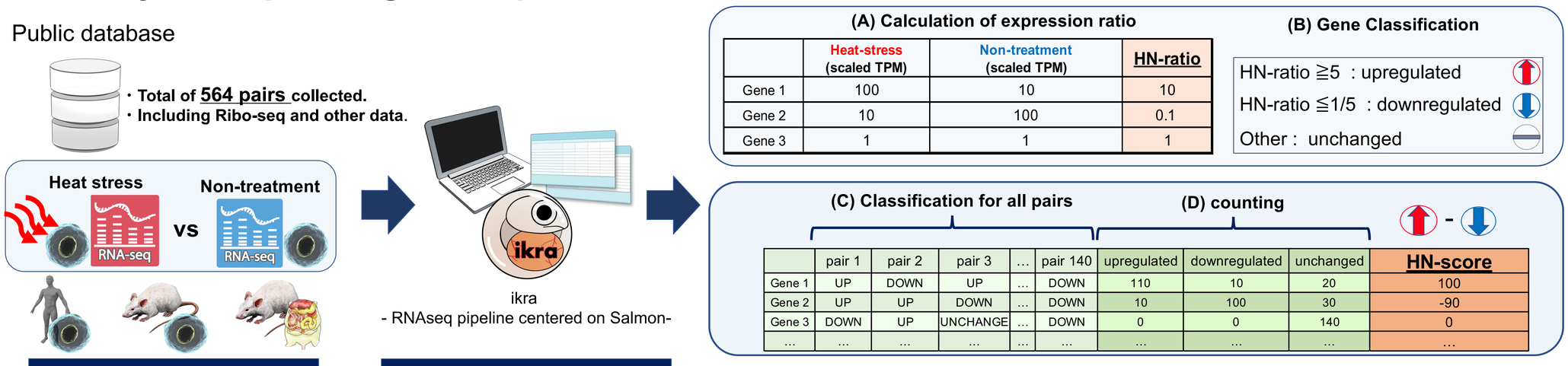
1. Background

Heat stress is an environmental stress defined as the exposure of organisms and cells to abnormally high temperatures. Heat-stress research has predominantly focused on response systems involving heat shock factors (HSFs) acting as transcription factors and heat shock proteins (HSPs) functioning as molecular chaperones. However, to comprehensively elucidate the mechanisms underlying an organism's response to heat stress, it is essential to investigate and analyze genes that have been underrepresented, less well-known, or overlooked in previous studies. In this study, we analyzed heat stress-responsive genes using a meta-analysis of numerous gene expression datasets.

2. Analysis of public gene expression data



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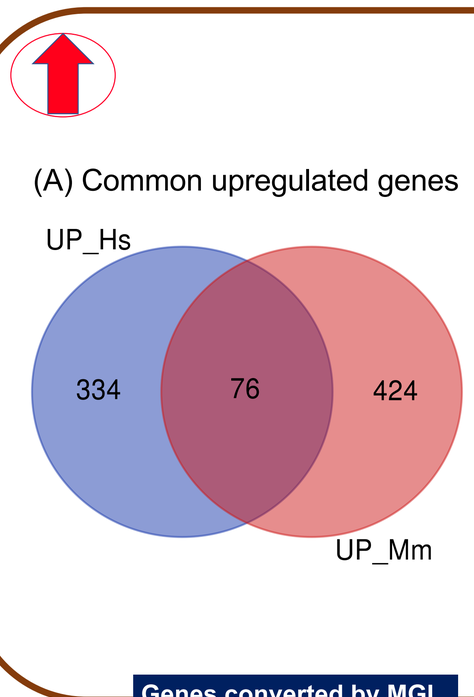
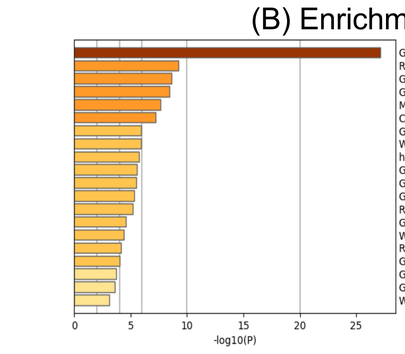
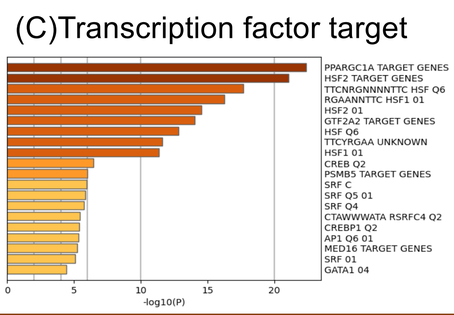
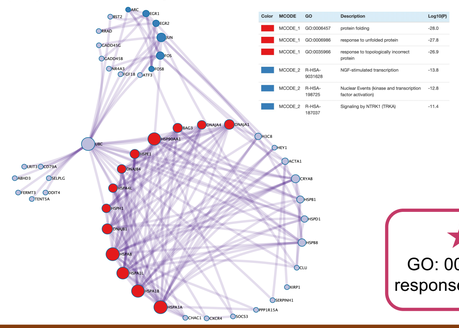
3. Common upregulated and downregulated genes in human and mouse

To identify common Heat stress response mechanisms, we narrowed down our results to the upregulated and downregulated genes common to both human and mouse and identified **76 upregulated genes** and **37 downregulated genes**, and performed enrichment analysis, etc.









(E) Upregulated gene lists (1)

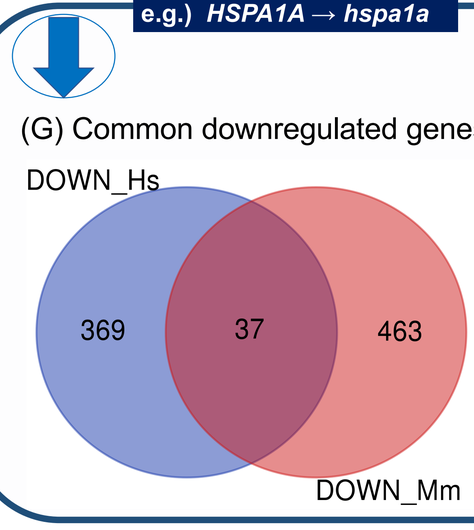
	Gene symbol	Gene name (HGNC)	HN-score human	HN-score mouse	HN-score Total
★	HSPA1B	heat shock protein family A (Hsp70) member 1B	231	149	380
★	HSPA1A	heat shock protein family A (Hsp70) member 1A	239	137	376
★	DNAJB1	DnaJ heat shock protein family (Hsp40) member B1	210	71	281
★	BAG3	BAG cochaperone 3	181	51	232
	HSPH1	heat shock protein family H (Hsp110) member 1	167	64	231
★	HSPB1	heat shock protein family B (small) member 1	112	111	223
	FOS	Fos proto-oncogene, AP-1 transcription factor subunit	165	51	216
★	CRYAB	crystallin alpha B	173	17	190
	HSPA1L	heat shock protein family A (Hsp70) member 1 like	150	32	182
	ZFAND2A	zinc finger, AN1-type domain 2A	165	12	177
	RRAD	RRAD, Ras related glycolysis inhibitor and calcium channel regulator	155	18	173
★	DNAJB4	DnaJ heat shock protein family (Hsp40) member B4	149	20	169
	ATF3	activating transcription factor 3	88	78	166
	DEDD2	death effector domain containing 2	143	22	165
★	DNAJA4	DnaJ heat shock protein family (Hsp40) member A4	106	35	141
	SERPINH1	serpin family H member 1	119	19	138
	TENT5A	terminal nucleotidyltransferase 5A	127	10	137
	HSPB8	heat shock protein family B (small) member 8	100	36	136
	TEX43	testis expressed 43	119	16	135
	EGR2	early growth response 2	104	28	132
	EGR1	early growth response 1	87	44	131
	FOSB	FosB proto-oncogene, AP-1 transcription factor subunit	118	13	131
	LY6G6C	lymphocyte antigen 6 family member G6C	89	26	115
	HSPA4L	heat shock protein family A (Hsp70) member 4 like	96	13	109
	CLU	clusterin	81	27	108
★	HSP90AA1	heat shock protein 90 alpha family class A member 1	68	37	105
	XIRP1	xin actin binding repeat containing 1	67	33	100
	USPL1	ubiquitin specific peptidase like 1	89	10	99
	ARC	activity regulated cytoskeletal-associated protein	71	23	94
★	DNAJA1	DnaJ heat shock protein family (Hsp40) member A1	67	26	93
	JUN	Jun proto-oncogene, AP-1 transcription factor subunit	63	28	91
	NR4A3	nuclear receptor subfamily 4 group A member 3	68	19	87
	CLDN6	Claudin 6	65	14	79
	BEST2	bestrophin 2	43	35	78
	ACTA1	actin alpha 1 , skeletal muscle	48	27	75
	PLA2G12B	phospholipase A2 group XIIB	62	13	75
	ADORA2A	adenosine A2a receptor	57	17	74
	LRIT3	leucine rich repeat, Ig-like and transmembrane domains 3	63	11	74

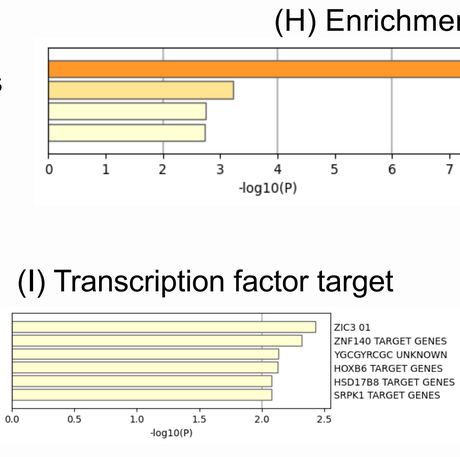
(F) Upregulated gene lists (2)

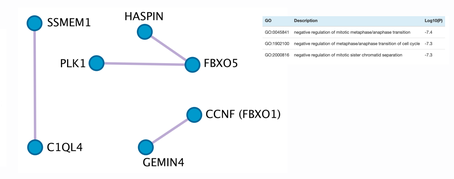
Gene symbol	Gene name (HGNC)	HN-score human	HN-score mouse	HN-score Total
DDIT4	DNA-damage-inducible transcript 4	46	26	72
NOXRED1	NADP dependent oxidoreductase domain containing 1	58	14	72
RASL11A	RAS like family 11 member A	58	14	72
SLC5A3	solute carrier family 5 member 3	58	11	69
FERMT3	FERM domain containing kindlin 3	53	15	68
PPP1R15A	protein phosphatase 1 regulatory subunit 15A	57	11	68
HSPD1	heat shock protein family D (Hsp60) member 1	55	12	67
OXT	oxytocin/neurophysin I prepropeptide	49	18	67
UBC	ubiquitin C	49	18	67
SELPLG	selectin P ligand	53	12	65
GADD45G	growth arrest and DNA damage inducible gamma	48	16	64
SOCS3	suppressor of cytokine signaling 3	47	17	64
CHAC1	ChaC glutathione specific gamma-glutamylcyclotransferase 1	33	30	63
ARL9	ADP ribosylation factor like GTPase 9	43	19	62
CCDC194	coiled-coil domain containing 194	47	15	62
TMC4	transmembrane channel like 4	52	10	62
HEY1	hes related family bHLH transcription factor with YRPW motif 1	51	10	61
HSPE1	heat shock protein family E (Hsp10) member 1	39	22	61
PRR18	proline rich 18	51	10	61
CD79A	CD79a molecule	40	18	58
HSPA8	heat shock protein family A (Hsp70) member 8	47	11	58
ABHD3	abhydrolase domain containing 3, phospholipase	47	10	57
LMAN1L	lectin, mannose binding 1 like	36	21	57
IQCF1	IQ motif containing F1	34	21	55
MYOCOS	myocilin opposite strand	37	16	53
IQCA1L	IQ motif containing with AAA domain 1 like	38	14	52
CARD9	caspase recruitment domain family member 9	39	12	51
RRH	retinal pigment epithelium-derived rhodopsin homolog	40	11	51
H3C8	H3 clustered histone 8	31	16	47
FGF18	fibroblast growth factor 18	34	12	46
GADD45B	growth arrest and DNA damage inducible beta	35	11	46
BST2	bone marrow stromal cell antigen 2	32	13	45
PDE6G	phosphodiesterase 6G	34	11	45
GUCA1B	guanylate cyclase activator 1B	33	11	44
CXCR4	C-X-C motif chemokine receptor 4	31	12	43
PIP5KL1	phosphatidylinositol-4-phosphate 5-kinase like 1	31	11	42
NRN1L	neuritin 1 like	31	10	41
TEX29	testis expressed 29	30	10	40

★ GO: 0009408 response to heat

Genes converted by MGI
e.g.) *HSPA1A* → *hspa1a*







(K) Downregulated gene lists (1)

Gene symbol	Gene Name(HGNC)	HN-score human	HN-score mouse	HN-score Total
TMEM89	transmembrane protein 89	-17	-31	-48
LIPT2	lipoyl(octanoyl) transferase 2	-29	-17	-46
EFNA4	ephrin A4	-20	-23	-43
PIF1	PIF1 5'-to-3' DNA helicase	-26	-17	-43
LFNG	LFNG O-fucosylpeptide 3-beta-N-acetylglucosaminyltransferase	-25	-14	-39
SSMEM1	serine rich single-pass membrane protein 1	-13	-26	-39
GLCE	glucuronic acid epimerase	-16	-22	-38
NANP	N-acetylneuraminic acid phosphatase	-19	-19	-38
ESPL1	extra spindle pole bodies like 1, separase	-15	-20	-35
HILPDA	hypoxia inducible lipid droplet associated	-22	-13	-35
H2AC21	H2A clustered histone 21	-20	-14	-34
NEIL3	nei like DNA glycosylase 3	-12	-22	-34
C1QL4	complement C1q like 4	-9	-24	-33
CCNF	cyclin F (FBXO1)	-17	-16	-33
GPR183	G protein-coupled receptor 183	-14	-19	-33
TEX38	testis expressed 38	-15	-18	-33
PET117	PET117 cytochrome c oxidase chaperone	-15	-17	-32
EVI2A	ecotropic viral integration site 2A	-12	-19	-31

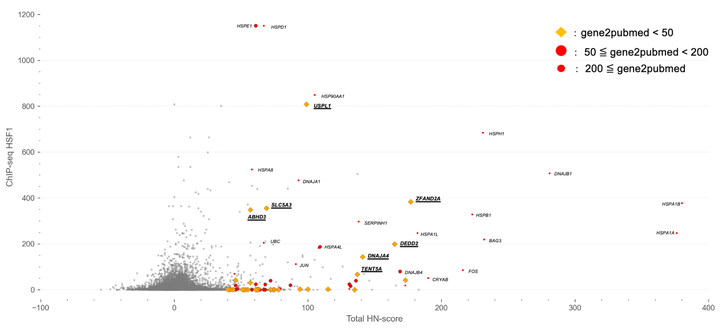
(L) Downregulated gene lists (2)

Gene symbol	Gene Name(HGNC)	HN-score human	HN-score mouse	HN-score Total
SPAG8	sperm associated antigen 8	-11	-20	-31
MAMSTR	MEF2 activating motif and SAP domain containing transcriptional regulator	-16	-14	-30
PRR22	proline rich 22	-13	-17	-30
IGSF10	immunoglobulin superfamily member 10	-12	-17	-29
PYM1	PYM homolog 1, exon junction complex associated factor	-14	-15	-29
TIGD5	tigger transposable element derived 5	-15	-13	-28
HASPIN	histone H3 associated protein kinase	-9	-18	-27
MFSD2A	MFSD2 lysolipid transporter A, lysophospholipid	-13	-14	-27
TRMT5	tRNA methyltransferase 5	-9	-18	-27
FBXO5	F-box protein 5 (EMI1)	-10	-16	-26
PHETA2	PH domain containing endocytic trafficking adaptor 2	-12	-14	-26
PLK1	polo like kinase 1	-9	-17	-26
IMMP2L	inner mitochondrial membrane peptidase subunit 2	-9	-16	-25
DNAJC27	DnaJ heat shock protein family (Hsp40) member C27	-11	-13	-24
GEMIN4	gem nuclear organelle associated protein 4	-10	-14	-24
PINLYP	phospholipase A2 inhibitor and LY6/PLAUR domain containing	-9	-15	-24
TSKU	tsukushi, small leucine rich proteoglycan	-10	-14	-24
PIGBOS1	PIGB opposite strand 1	-10	-13	-23
EMILIN1	elastin microfibril interfacer 1	-9	-13	-22

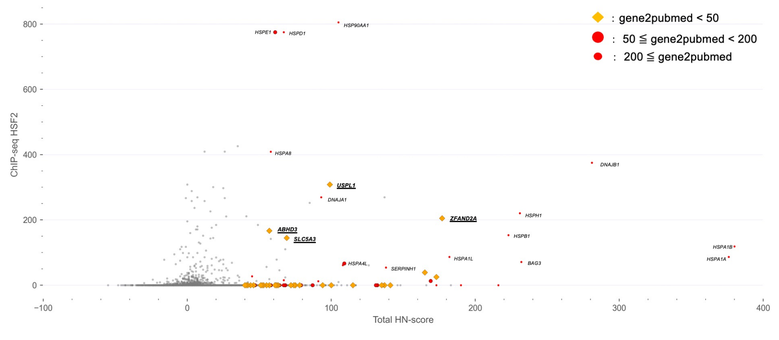
4. Integration of HN-score, transcription factor-binding information, and literature information

In addition to the HN-score data for each gene calculated, ChIP-seq data as transcription factor-binding information obtained from the ChIP-Atlas database and gene2pubmed data as literature information was integrated to visualize the characteristics of each gene and information on commonly upregulated genes in human and mouse were added.

HSF1



HSF2



PPARGC1A (PGC1-α)

5. Prospects

Based on the findings of this study, further functional analysis of the extracted genes using **genome editing** and other technologies can contribute to coping with climate change and potentially lead to new knowledge and technological advances.

Preprint **Code** **Supplementary figures**

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