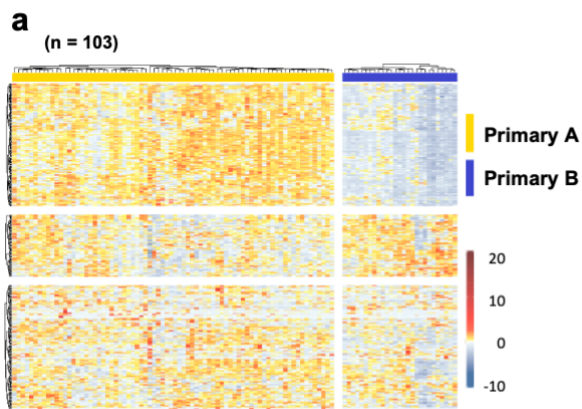


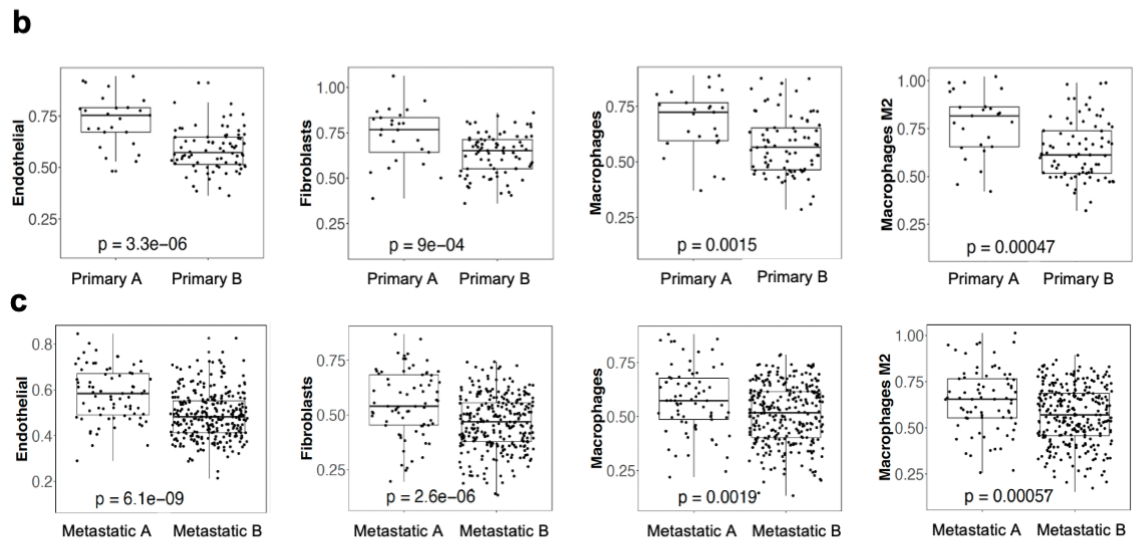
Distinct patterns of proteostasis network gene expression are associated with different prognoses in melanoma patients

Rachel Wellman, Daniel Jacobson, Maria Secrier and John Labbadia

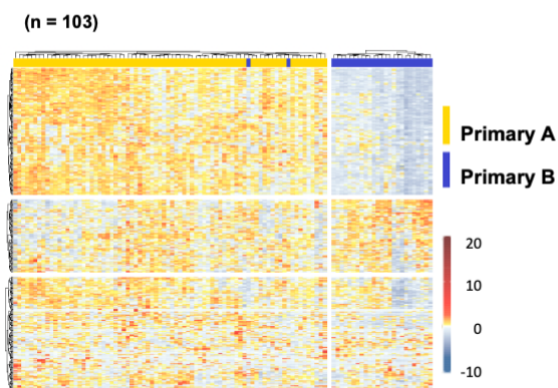
Supplementary figures and tables



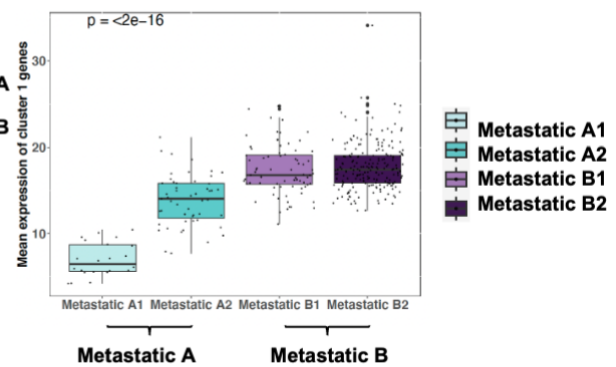
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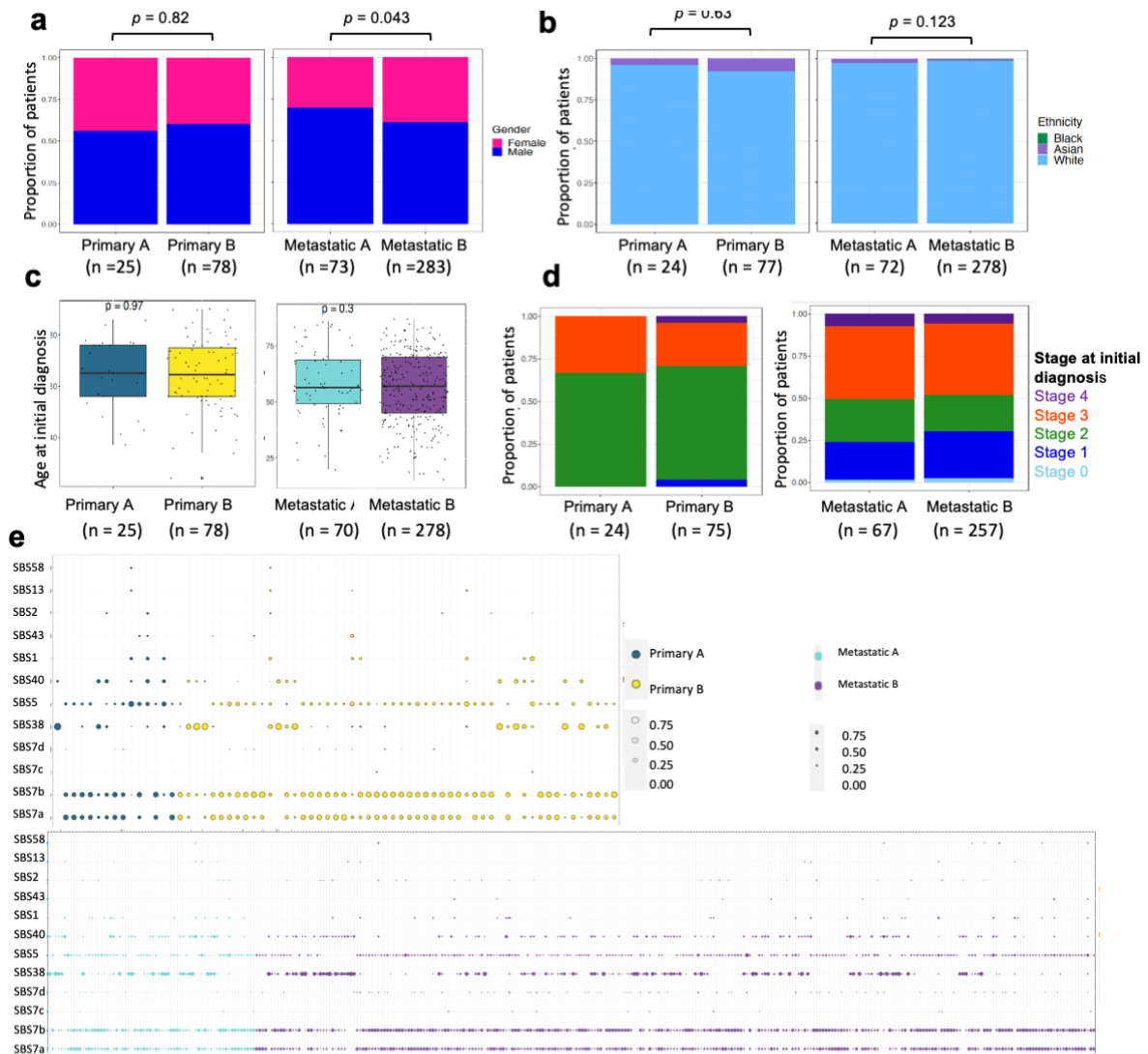


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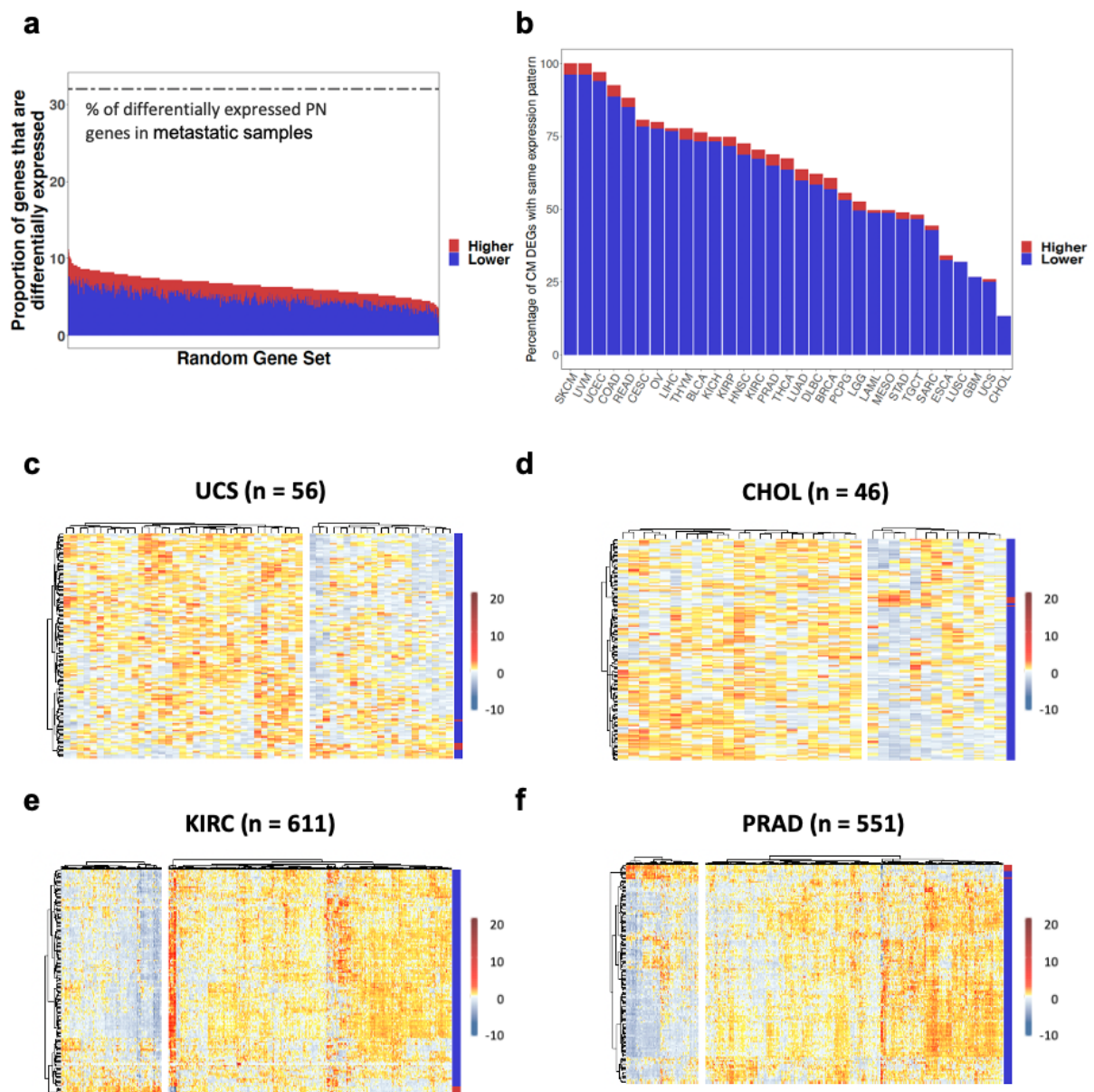
Supplementary Figure 1: CM samples exhibit distinct PN gene expression patterns following correction for tumour purity

(a) PN gene expression in cutaneous melanoma (CM) primary samples clustered using Ward's hierarchical agglomerative clustering method. (b-c) Relative prevalence of endothelial cells, fibroblasts, macrophages and M2 macrophages in (b) primary and (c) metastatic CM sample groups. Primary A (n = 25), primary B (n = 78), metastatic A (n = 73) and metastatic B (n = 283). (d) PN gene expression in cutaneous melanoma (CM) primary samples following correction for tumor purity and clustering using Ward's hierarchical agglomerative clustering method. (e) Mean expression of PN genes within cluster 1 of metastatic sample groups A1 (n = 22), A2 (n = 51), B1 (n = 75) and B2 (n = 208). In all cases, P-values were calculated using Student's t-test. Boxes indicate the interquartile range (IQR), the upper whisker extends to the largest value that is less than (third quartile + (1.5 * IQR)). The lower whisker extends to the smallest value that is greater than (first quartile - (1.5 * IQR)).



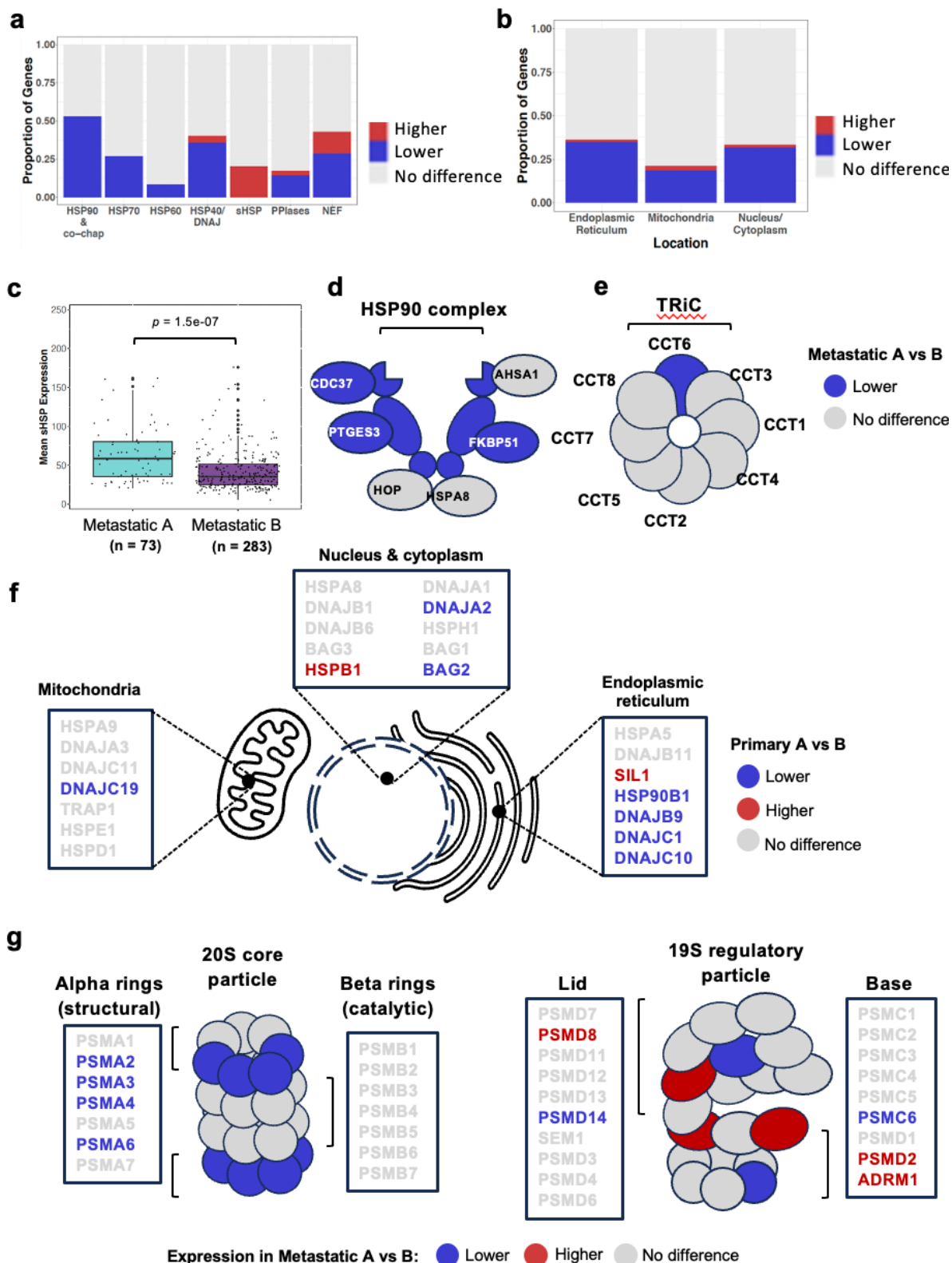
Supplementary Figure 2: Differences in PN gene expression are not associated with differences in demographic features or mutational signatures

(a-b) Proportion of cutaneous melanoma (CM) patients of (a) each gender or (b) different ethnicities within primary or metastatic groups A and B. (c) Mean age at diagnosis of patients in primary or metastatic groups A and B. Boxes indicate the interquartile range (IQR), the upper whisker extends to the largest value that is less than (third quartile + (1.5 * IQR)). The lower whisker extends to the smallest value that is greater than (first quartile - (1.5 * IQR)). (d) Proportion of CM patients at different stages of initial diagnosis in primary and metastatic groups A and B. (e) Balloon plots showing the relative contribution of different mutational signatures to tumours from primary and metastatic groups A and B. P-values were calculated using (a, b and d) Fisher's Exact Test or (c) Student's T-test.



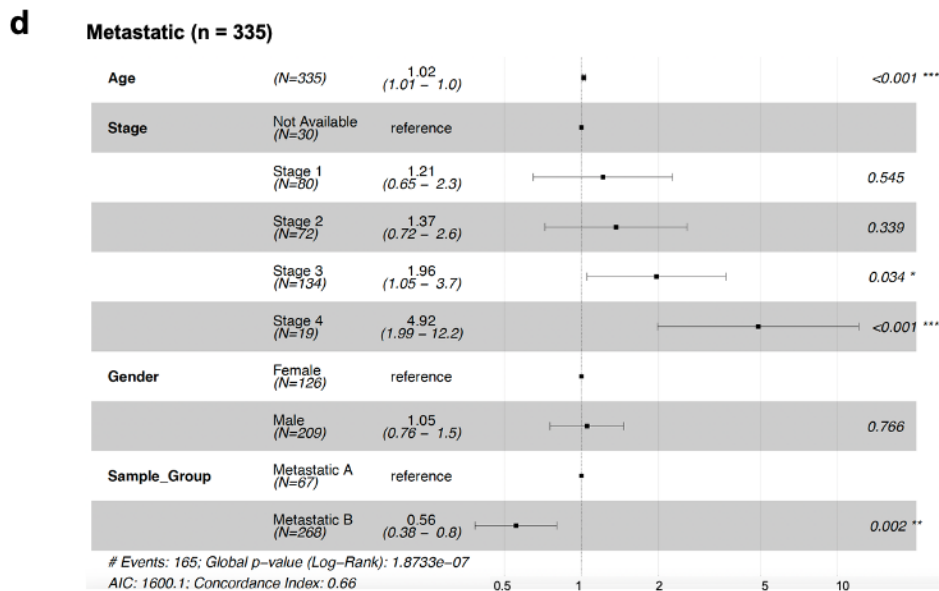
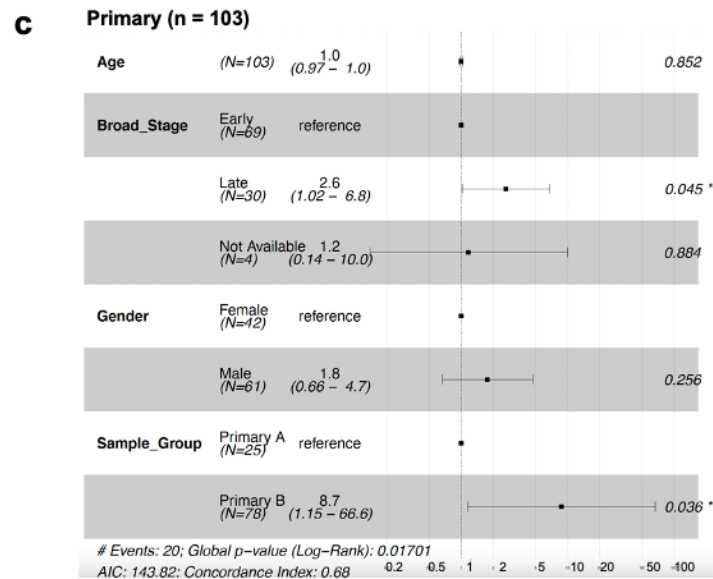
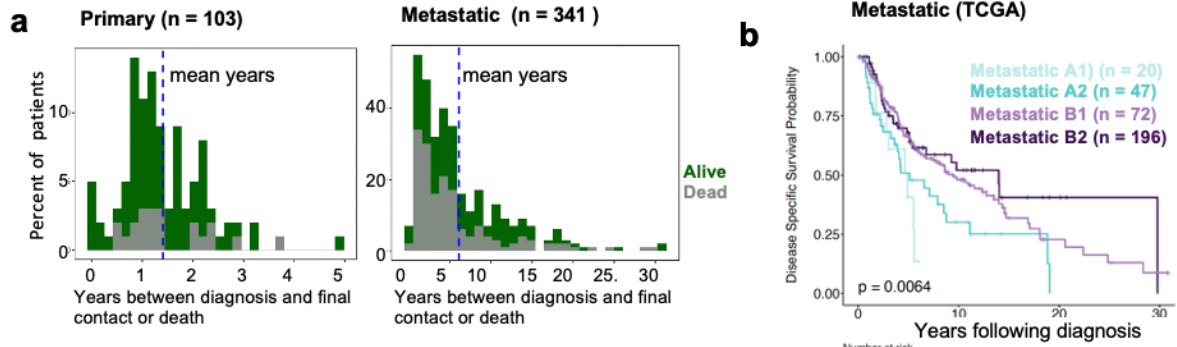
Supplementary Figure 3: Differential regulation of PN genes across CM samples shows low similarity with other cancers and is enriched changes compared to non-PN genes

(a) Proportion of random gene sets that were differentially expressed between cutaneous melanoma (CM) metastatic groups A and B (p-value < 0.05 calculated by Student's T-test and DESeq2, adjusted p-value < 0.1 calculated by Benjamini Hochberg correction). (b) Percentage of genes that are differentially regulated PN between primary CM groups that are also differentially expressed in other cancers (p < 0.05 calculated by Student's t-test adjusted p-value < 0.1 calculated by Benjamini Hochberg correction). (c-f) Heatmaps of PN genes differentially expressed in CM in (c) kidney renal clear cell carcinoma (KIRC) (d) prostate adenocarcinoma (PRAD), (e) uterine Carcinosarcoma (UCS) and (f) cholangiocarcinoma (CHOL).



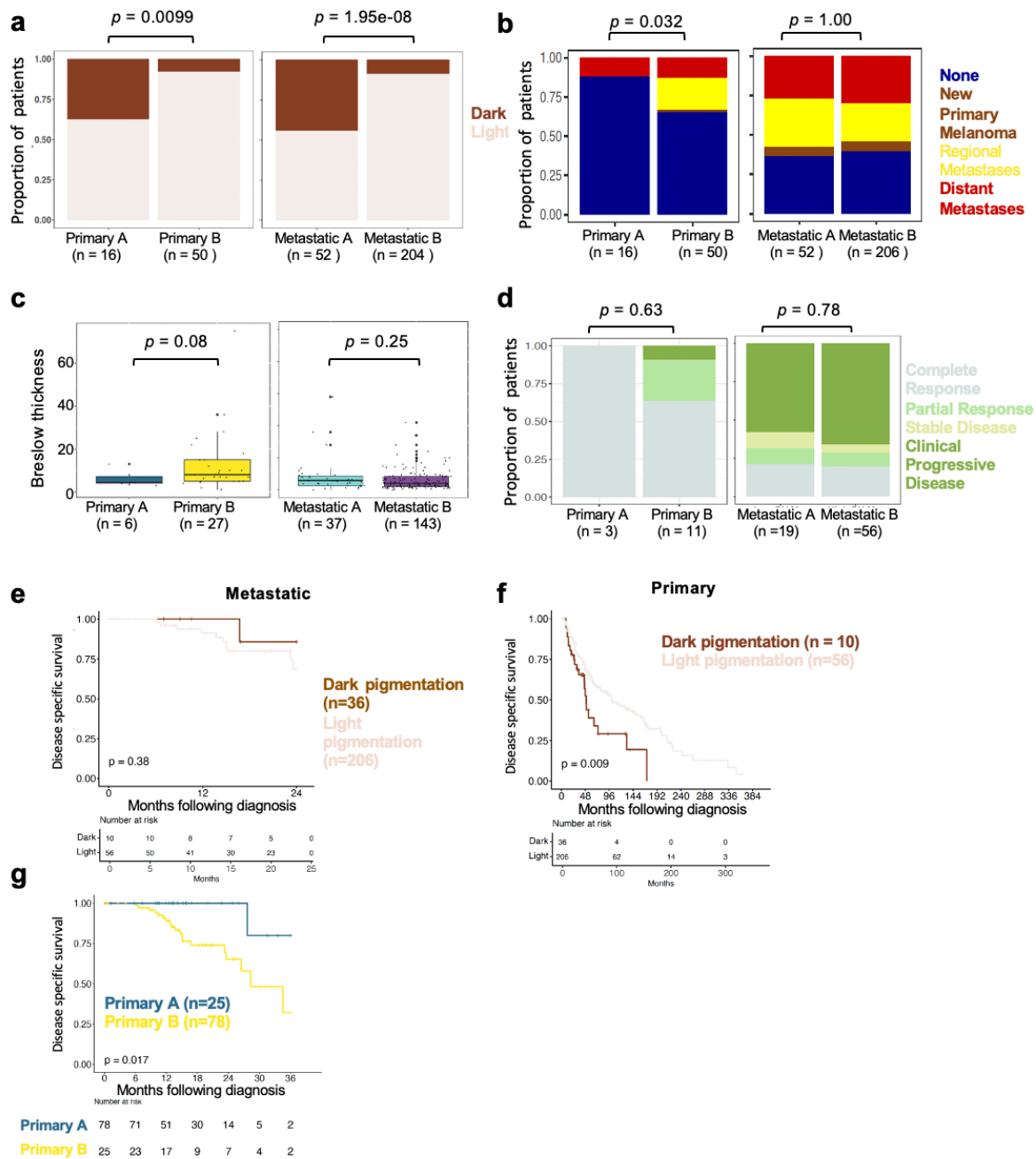
Supplementary Figure 4: Specific components of the sHSP, HSP90, HSP60, HSP70/DNAJ and proteasome systems are differentially expressed across metastatic CM samples

(a) Proportion of genes within each Proteostasis network (PN) sub-group showing significantly altered expression between metastatic groups A and B (p-value < 0.05 calculated by Student's T-test and DEseq2, adjusted p-value < 0.1 calculated by Benjamini Hochberg correction). (b) Proportion of PN genes within each sub-cellular compartment showing significantly altered expression between metastatic groups A and B (p-value < 0.05 calculated by Student's T-test and DEseq2, adjusted p-value < 0.1 calculated by Benjamini Hochberg correction). (c) Mean expression of sHSP genes in metastatic sample groups. P-values were calculated using Student's t-test. Boxes indicate the interquartile range (IQR), the upper whisker extends to the largest value that is less than (third quartile + (1.5 * IQR)). The lower whisker extends to the smallest value that is greater than (first quartile - (1.5 * IQR)). (d-g) Cartoons highlighting the PN components that exhibit differential expression between Primary A and B among (d) HSP90 and co-chaperones, (e) CCT/TRIC subunits (f) core chaperones and co-chaperones of sub-cellular compartments and (g) proteasome core and regulatory particle subunits.



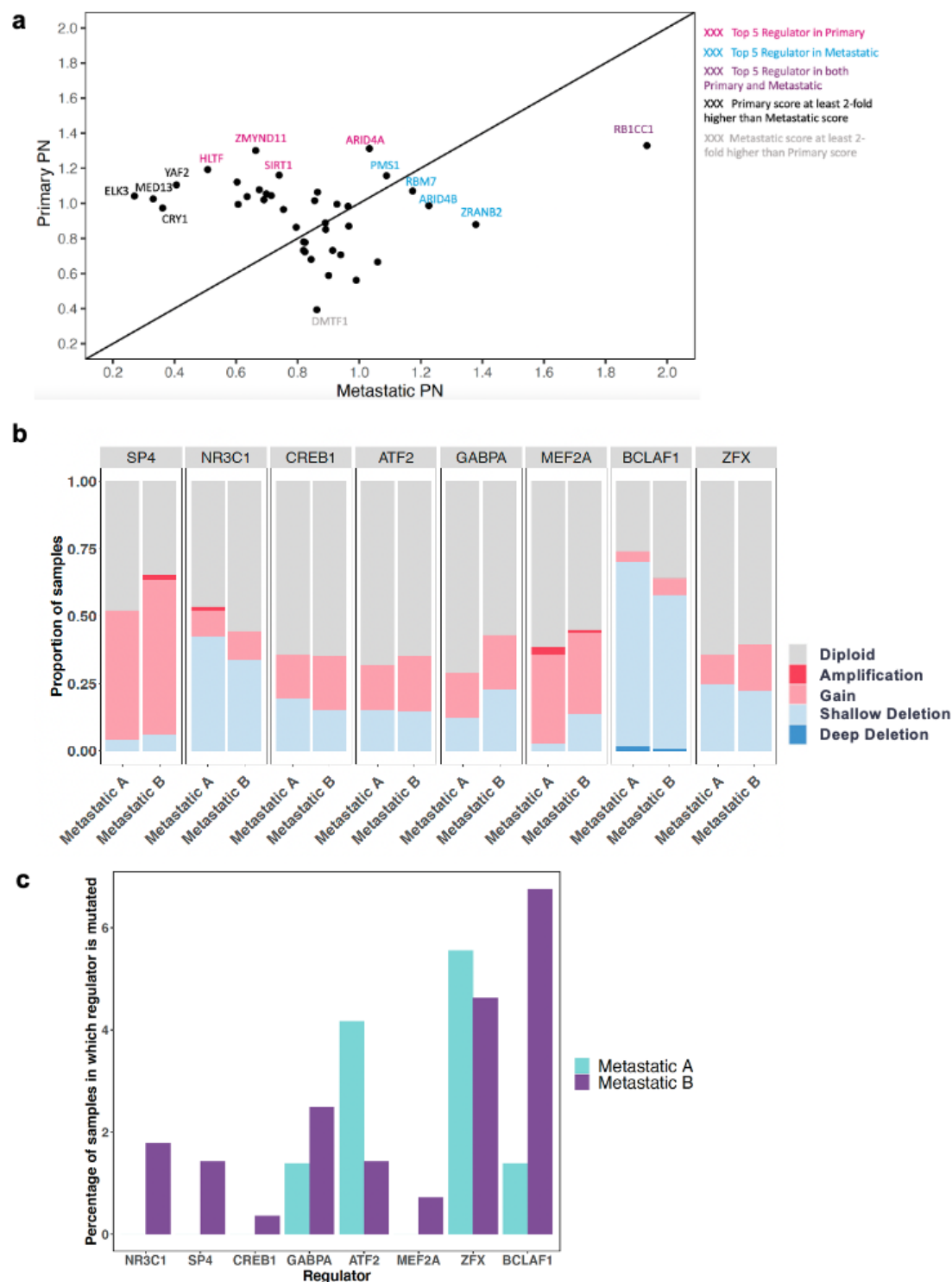
Supplementary Figure 5: Stage at diagnosis, gender and stage of diseases do not fully explain survival differences between CM PN groups

(a) Number of years between diagnosis and final contact or death, and mean number of years from diagnosis to final contact or death, in primary and metastatic cohorts. (b) Disease-specific survival curves for Metastatic A1, Metastatic A2, Metastatic B1 and Metastatic B2 patients. P values were calculated using log rank test. (c-d) Forrest plots showing the impact of age, clinical stage at diagnosis and gender on disease specific survival of individuals within (c) primary and (d) metastatic sample groups. P-values were calculated using Log-rank test.



Supplementary Figure 6: Survival differences between PN groups are associated with altered metastasis and tumour pigmentation

(a-d) (a) Levels of pigmentation, (b) incidence of further metastasis, (c) tumour thickness and (d) response to chemotherapy across melanomas in primary and metastatic groups A and B. In (c), boxes indicate the interquartile range (IQR), the upper whisker extends to the largest value that is less than (third quartile + (1.5 * IQR)) and the lower whisker extends to the smallest value that is greater than (first quartile - (1.5 * IQR)). (e-f) Disease-specific survival curves by level of pigmentation in (e) metastatic or (f) primary patients. (g) Disease-specific survival curves for patients in primary groups A and B for whom no subsequent metastasis was recorded. P values were calculated using Fisher's Exact Test (a, b and d), Student's t-test (c) and Log rank test (e-g).



Supplementary Figure 7: Specific transcriptional regulators are associated with differences in PN gene expression across CM samples but do not exhibit changes in copy number and exhibit low rates of mutation

(a) Scatterplot of Regenerich scores for transcriptional regulators associated with differences in Proteostasis network gene expression across primary and metastatic cohorts. (b) Incidence of copy number variation of key regulators in metastatic groups A and B. (c) Incidence of non-synonymous mutations within key regulators across metastatic groups A and B.

Supplementary Table 1: PN genes included in study

Folding	
Gene Symbol	Gene Name
AHSA1	Activator of 90 kDa heat shock protein ATPase homolog 1
AHSA2P	Putative activator of 90 kDa heat shock protein ATPase homolog 2 aka AHSA2
AHSP	Alpha-hemoglobin-stabilizing protein
AIPL1	Aryl-hydrocarbon-interacting protein-like 1
ANKRD13C	Ankyrin repeat domain-containing protein 13C
BAG1	BAG family molecular chaperone regulator 1
BAG2	BAG family molecular chaperone regulator 2
BAG3	BAG family molecular chaperone regulator 3
BAG4	BAG family molecular chaperone regulator 4
BAG5	BAG family molecular chaperone regulator 5
BAG6	Large proline-rich protein BAG6
BBS10	Bardet-Biedl syndrome 10 protein
BBS12	Bardet-Biedl syndrome 12 protein
BBS4	Bardet-Biedl syndrome 4 protein
BCAP31	B-cell receptor-associated protein 31
BCS1L	Mitochondrial chaperone BCS1
C1GALT1C1	C1GALT1-specific chaperone 1
C1GALT1C1L	C1GALT1-specific chaperone 1-like protein
CALR	Calreticulin
CANX	Calnexin
CCT2	T-complex protein 1 subunit beta
CCT3	T-complex protein 1 subunit gamma
CCT4	T-complex protein 1 subunit delta
CCT5	T-complex protein 1 subunit epsilon
CCT6A	T-complex protein 1 subunit zeta
CCT6B	T-complex protein 1 subunit zeta-2
CCT7	T-complex protein 1 subunit eta
CCT8	T-complex protein 1 subunit theta
CCT8L1P	Putative T-complex protein 1 subunit theta-like 1
CCT8L2	T-complex protein 1 subunit theta-like 2
CDC37	Hsp90 co-chaperone Cdc37
CDC37L1	Hsp90 co-chaperone Cdc37-like 1
CHCHD4	Mitochondrial intermembrane space import and assembly protein 40
CHORDC1	Cysteine and histidine-rich domain-containing protein 1
CLGN	Calmegin
CLNS1A	Methylosome subunit pICln
CLPX	ATP-dependent Clp protease ATP-binding subunit clpX-like, mitochondrial
CLU	Clusterin
CNPY3	Protein canopy homolog 3
CRYAA	Alpha-crystallin A chain
CRYAB	Alpha-crystallin B chain
CYBC1	Cytochrome b-245 chaperone 1
DNAAF4	Dynein assembly factor 4, axonemal
DNAJA1	DnaJ homolog subfamily A member 1

Folding (continued)

Gene Symbol	Gene Name
DNAJA2	DnaJ homolog subfamily A member 2
DNAJA3	DnaJ homolog subfamily A member 3, mitochondrial
DNAJA4	DnaJ homolog subfamily A member 4
DNAJB1	DnaJ homolog subfamily B member 1
DNAJB11	DnaJ homolog subfamily B member 11
DNAJB12	DnaJ homolog subfamily B member 12
DNAJB13	DnaJ homolog subfamily B member 13
DNAJB14	DnaJ homolog subfamily B member 14
DNAJB2	DnaJ homolog subfamily B member 2
DNAJB3	DnaJ homolog subfamily B member 3
DNAJB4	DnaJ homolog subfamily B member 4
DNAJB5	DnaJ homolog subfamily B member 5
DNAJB6	DnaJ homolog subfamily B member 6
DNAJB7	DnaJ homolog subfamily B member 7
DNAJB8	DnaJ homolog subfamily B member 8
DNAJB9	DnaJ homolog subfamily B member 9
DNAJC1	DnaJ homolog subfamily C member 1
DNAJC10	DnaJ homolog subfamily C member 10
DNAJC11	DnaJ homolog subfamily C member 11
DNAJC12	DnaJ homolog subfamily C member 12
DNAJC13	DnaJ homolog subfamily C member 13
DNAJC14	DnaJ homolog subfamily C member 14
DNAJC15	DnaJ homolog subfamily C member 15
DNAJC16	DnaJ homolog subfamily C member 16
DNAJC17	DnaJ homolog subfamily C member 17
DNAJC18	DnaJ homolog subfamily C member 18
DNAJC19	Mitochondrial import inner membrane translocase subunit TIM14
DNAJC2	DnaJ homolog subfamily C member 2
DNAJC21	DnaJ homolog subfamily C member 21
DNAJC22	DnaJ homolog subfamily C member 22
DNAJC24	DnaJ homolog subfamily C member 24
DNAJC25	DnaJ homolog subfamily C member 25
DNAJC27	DnaJ homolog subfamily C member 27
DNAJC28	DnaJ homolog subfamily C member 28
DNAJC3	DnaJ homolog subfamily C member 3
DNAJC30	DnaJ homolog subfamily C member 30
DNAJC4	DnaJ homolog subfamily C member 4
DNAJC5	DnaJ homolog subfamily C member 5
DNAJC5B	DnaJ homolog subfamily C member 5B
DNAJC5G	DnaJ homolog subfamily C member 5G
DNAJC6	DnaJ homolog subfamily C member 6
DNAJC7	DnaJ homolog subfamily C member 7 =TPR2
DNAJC8	DnaJ homolog subfamily C member 8
DNAJC9	DnaJ homolog subfamily C member 9
DNLZ	DNL-type zinc finger protein
ERP27	Endoplasmic reticulum resident protein 27
ERP29	Endoplasmic reticulum resident protein 29
ERP44	Endoplasmic reticulum resident protein 44
FKBP10	Peptidyl-prolyl cis-trans isomerase FKBP10
FKBP11	Peptidyl-prolyl cis-trans isomerase FKBP11

Folding (continued)

Gene Symbol	Gene Name
FKBP14	Peptidyl-prolyl cis-trans isomerase FKBP14
FKBP15	Peptidyl-prolyl cis-trans isomerase FKBP15
FKBP1A	Peptidyl-prolyl cis-trans isomerase FKBP1A
FKBP1B	Peptidyl-prolyl cis-trans isomerase FKBP1B
FKBP1C	Peptidylprolyl isomerase
FKBP2	Peptidyl-prolyl cis-trans isomerase FKBP2
FKBP3	Peptidyl-prolyl cis-trans isomerase FKBP3
FKBP4	Peptidyl-prolyl cis-trans isomerase FKBP4
FKBP5	Peptidyl-prolyl cis-trans isomerase FKBP5
FKBP6	Inactive peptidyl-prolyl cis-trans isomerase FKBP6
FKBP7	Peptidyl-prolyl cis-trans isomerase FKBP7
FKBP8	Peptidyl-prolyl cis-trans isomerase FKBP8
FKBP9	Peptidyl-prolyl cis-trans isomerase FKBP9
FKBP9P1	FKBP Prolyl Isomerase 9 Pseudogene 1
FKBPL	Folliculin-interacting protein 1
FNIP2	Folliculin-interacting protein 2
GAK	Cyclin-G-associated kinase
GRPEL1	GrpE protein homolog 1, mitochondrial
GRPEL2	GrpE protein homolog 2, mitochondrial
HOPX	Homeodomain-only protein
HSCB	Iron-sulfur cluster co-chaperone protein HscB
HSP90AA1	Heat shock protein HSP 90-alpha
HSP90AA2P	Heat shock protein HSP 90-alpha A2 aka HSP90AA2
HSP90AA4P	Putative heat shock protein HSP 90-alpha A4
HSP90AA5P	Putative heat shock protein HSP 90-alpha A5
HSP90AB1	Heat shock protein HSP 90-beta
HSP90AB2P	Putative heat shock protein HSP 90-beta 2
HSP90AB3P	Putative heat shock protein HSP 90-beta-3
HSP90B1	Endoplasmin
HSP90B2P	Putative endoplasmin-like protein
HSPA12A	Heat shock 70 kDa protein 12A
HSPA12B	Heat shock 70 kDa protein 12B
HSPA13	Heat shock 70 kDa protein 13
HSPA14	Heat shock 70 kDa protein 14
HSPA1A	Heat shock 70 kDa protein 1A
HSPA1B	Heat shock 70 kDa protein 1B
HSPA1L	Heat shock 70 kDa protein 1-like
HSPA2	Heat shock-related 70 kDa protein 2
HSPA4	Heat shock 70 kDa protein 4
HSPA4L	Heat shock 70 kDa protein 4L
HSPA5	Endoplasmic reticulum chaperone BiP
HSPA6	Heat shock 70 kDa protein 6
HSPA7	Putative heat shock 70 kDa protein 7
HSPA8	Heat shock cognate 71 kDa protein
HSPA9	Stress-70 protein, mitochondrial
HSPB1	Heat shock protein beta-1
HSPB2	Heat shock protein beta-2
HSPB3	Heat shock protein beta-3
HSPB6	Heat shock protein beta-6
HSPB7	Heat shock protein beta-7

Folding (continued)

Gene Symbol	Gene Name
HSPB8	Heat shock protein beta-8
HSPB9	Heat shock protein beta-9
HSPBP1	Hsp70-binding protein 1
HSPD1	60 kDa heat shock protein, mitochondrial
HSPE1	10 kDa heat shock protein, mitochondrial
HSPH1	Heat shock protein 105 kDa
HYOU1	Hypoxia up-regulated protein 1
LRP2BP	LRP2-binding protein
LRPAP1	Alpha-2-macroglobulin receptor-associated protein
MKKS	McKusick-Kaufman/Bardet-Biedl syndromes putative chaperonin
NAA10	N-Alpha-Acetyltransferase 10, NatA Catalytic Subunit
NPM1	Nucleophosmin
P4HB	Protein disulfide-isomerase
PDCL	Phosducin-like protein
PDCL3	Phosducin-like protein 3
PDIA2	Protein disulfide-isomerase A2
PDIA3	Protein disulfide-isomerase A3
PDIA4	Protein disulfide-isomerase A4
PDIA5	Protein disulfide-isomerase A5
PDIA6	Protein disulfide-isomerase A6
PDRG1	p53 and DNA damage-regulated protein 1
PEX19	Peroxisomal biogenesis factor 19
PFDN1	Prefoldin subunit 1
PFDN2	Prefoldin subunit 2
PFDN4	Prefoldin subunit 4
PFDN5	Prefoldin subunit 5
PFDN6	Prefoldin subunit 6
PPIA	Peptidyl-prolyl cis-trans isomerase A
PPIAL4A	Peptidyl-prolyl cis-trans isomerase A-like 4A
PPIAL4C	Peptidyl-prolyl cis-trans isomerase A-like 4C
PPIAL4D	Peptidyl-prolyl cis-trans isomerase A-like 4D
PPIAL4E	Peptidyl-prolyl cis-trans isomerase A-like 4E
PPIAL4F	Peptidyl-prolyl cis-trans isomerase A-like 4F
PPIAL4G	Peptidyl-prolyl cis-trans isomerase A-like 4G
PPIAL4H	Peptidyl-prolyl cis-trans isomerase A-like 4H
PPIB	Peptidyl-prolyl cis-trans isomerase B
PPIC	Peptidyl-prolyl cis-trans isomerase C
PPID	Peptidyl-prolyl cis-trans isomerase D
PPIE	Peptidyl-prolyl cis-trans isomerase E
PPIF	Peptidyl-prolyl cis-trans isomerase F, mitochondrial
PPIG	Peptidyl-prolyl cis-trans isomerase G
PPIH	Peptidyl-prolyl cis-trans isomerase H
PPIL1	Peptidyl-prolyl cis-trans isomerase-like 1
PPIL3	Peptidyl-prolyl cis-trans isomerase-like 3
PPIL4	Peptidyl-prolyl cis-trans isomerase-like 4
PPWD1	Peptidylprolyl isomerase domain and WD repeat-containing protein 1
PTGES3	Prostaglandin E synthase 3
RCN3	Reticulocalbin 3ulocalbin 3
SACS	Sacsin
SELENOF	Selenoprotein F

Folding (continued)

Gene Symbol	Gene Name
SERPINH1	Serpin H1
SGTA	Small glutamine-rich tetratricopeptide repeat-containing protein alpha
SGTB	Small glutamine-rich tetratricopeptide repeat-containing protein beta
SIL1	Nucleotide exchange factor SIL1
SNCA	Alpha-synuclein
SPATA5	ATPase family protein 2 homolog
ST13	Hsc70-interacting protein
STIP1	Stress-induced-phosphoprotein 1
TBCA	Tubulin-specific chaperone A
TBCC	Tubulin-specific chaperone C
TBCD	Tubulin-specific chaperone D
TCP1	T-complex protein 1 subunit alpha
TIMM10	Mitochondrial import inner membrane translocase subunit Tim10
TIMM13	Mitochondrial import inner membrane translocase subunit Tim13
TIMM44	Mitochondrial import inner membrane translocase subunit TIM44
TIMM8A	Mitochondrial import inner membrane translocase subunit Tim8 A
TIMM8B	Mitochondrial import inner membrane translocase subunit Tim8 B
TIMM9	Mitochondrial import inner membrane translocase subunit Tim9
TMEM126B	Complex I assembly factor TMEM126B, mitochondrial
TMX3	thioredoxin related transmembrane protein 3
TOMM34	Mitochondrial import receptor subunit TOM34
TOR1A	Torsin-1A
TOR1B	Torsin-1B
TRAP1	Heat shock protein 75 kDa, mitochondrial
TSACC	TSSK6-activating co-chaperone protein
TSC1	Hamartin
TTC4	Tetratricopeptide repeat protein 4
UNC45B	Protein unc-45 homolog B
VBP1	Prefoldin subunit 3 aka PFDN3

Ubiquitination

Gene Symbol	Gene Name
AMFR	E3 ubiquitin-protein ligase AMFR Autocrine motility factor receptor
CDC34	Ubiquitin-conjugating enzyme E2 R1
FBXO2	F-box only protein 2
FBXO6	F-box only protein 6
GET4	Golgi to ER traffic protein 4 homolog
HUWE1	E3 ubiquitin-protein ligase HUWE1 aka Tom1
LRR1	Leucine-rich repeat protein 1
LRRC29	Leucine-rich repeat-containing protein 29
LRRC41	Leucine-rich repeat-containing protein 41
LTN1	E3 ubiquitin-protein ligase listerin
MARCHF6	E3 ubiquitin-protein ligase MARCHF6
PRKN	E3 ubiquitin-protein ligase parkin
RBX1	E3 ubiquitin-protein ligase RBX1
RNF103	E3 ubiquitin-protein ligase RNF103
RNF126	E3 ubiquitin-protein ligase RNF126
RNF185	E3 ubiquitin-protein ligase RNF185
RNF5	E3 ubiquitin-protein ligase RNF5
RNFT1	E3 ubiquitin-protein ligase RNFT1
RPS27A	Ubiquitin-40S ribosomal protein S27a
SEL1L	Protein sel-1 homolog 1
SELENOS	Selenoprotein S
STT3B	Dolichyl-diphosphooligosaccharide-protein glycosyltransferase subunit STT3B
STUB1	E3 ubiquitin-protein ligase CHIP
SUGT1	Protein SGT1 homolog
SYVN1	E3 ubiquitin-protein ligase synoviolin
TRAF2	TNF receptor-associated factor 2
TRAF3	TNF receptor-associated factor 3
TRIM11	E3 ubiquitin-protein ligase TRIM11
TRIM13	E3 ubiquitin-protein ligase TRIM13
UBA1	Ubiquitin-like modifier-activating enzyme 1
UBA52	Ubiquitin-60S ribosomal protein L40
UBE2A	Ubiquitin-conjugating enzyme E2 A
UBE2B	Ubiquitin-conjugating enzyme E2 B
UBE2C	Ubiquitin-conjugating enzyme E2 C
UBE2D1	Ubiquitin-conjugating enzyme E2 D1
UBE2D2	Ubiquitin-conjugating enzyme E2 D2
UBE2D3	Ubiquitin-conjugating enzyme E2 D3
UBE2D4	Ubiquitin-conjugating enzyme E2 D4
UBE2E1	Ubiquitin-conjugating enzyme E2 E1
UBE2F	Ubiquitin-conjugating enzyme E2 F
UBE2G1	Ubiquitin-conjugating enzyme E2 G1
UBE2G2	Ubiquitin-conjugating enzyme E2 G2
UBE2H	Ubiquitin-conjugating enzyme E2 H
UBE2J1	Ubiquitin-conjugating enzyme E2 J1
UBE2J2	Ubiquitin-conjugating enzyme E2 J2
UBE2K	Ubiquitin-conjugating enzyme E2 K
UBE2L3	Ubiquitin-conjugating enzyme E2 L3
UBE2L5	Ubiquitin-conjugating enzyme E2 L5
UBE2L6	Ubiquitin/ISG15-conjugating enzyme E2 L6
UBE2M	NEDD8-conjugating enzyme Ubc12
UBE2N	Ubiquitin-conjugating enzyme E2 N
UBE2NL	Putative ubiquitin-conjugating enzyme E2 N-like
UBE2O	"(E3-independent) E2 ubiquitin-conjugating enzyme"
UBE2Q1	Ubiquitin-conjugating enzyme E2 Q1
UBE2Q2	Ubiquitin-conjugating enzyme E2 Q2

Ubiquitination (continued)

Gene Symbol	Gene Name
UBE2QL1	Ubiquitin-conjugating enzyme E2Q-like protein 1
UBE2R2	Ubiquitin-conjugating enzyme E2 R2
UBE2S	Ubiquitin-conjugating enzyme E2 S
UBE2U	Ubiquitin-conjugating enzyme E2 U
UBE2V1	Ubiquitin-conjugating enzyme E2 variant 1
UBE2V2	Ubiquitin-conjugating enzyme E2 variant 2
UBE2W	Ubiquitin-conjugating enzyme E2 W
UBE2Z	Ubiquitin-conjugating enzyme E2 Z
UBE3A	Ubiquitin-protein ligase E3A aka E6-AP
UBE3B	Ubiquitin-protein ligase E3B
UBE3C	Ubiquitin-protein ligase E3C aka Hul5
UBE3D	E3 ubiquitin-protein ligase E3D
UBE4A	Ubiquitin conjugation factor E4 A
UBE4B	Ubiquitin conjugation factor E4 B
UBR1	E3 ubiquitin-protein ligase UBR1
UBR2	E3 ubiquitin-protein ligase UBR2
UBR3	E3 ubiquitin-protein ligase UBR3
UBR4	E3 ubiquitin-protein ligase UBR4
UBR5	E3 ubiquitin-protein ligase UBR5
UBR7	Putative E3 ubiquitin-protein ligase UBR7

Deubiquitination

Gene Symbol	Gene Name
ATXN3	Ataxin-3
MINDY1	Ubiquitin carboxyl-terminal hydrolase MINDY-1
MINDY2	Ubiquitin carboxyl-terminal hydrolase MINDY-2
MINDY3	Ubiquitin carboxyl-terminal hydrolase MINDY-3
MINDY4	Probable ubiquitin carboxyl-terminal hydrolase MINDY-4
OTUB1	Ubiquitin thioesterase OTUB1
OTUB2	Ubiquitin thioesterase OTUB2
OTUD1	OTU domain-containing protein 1
OTUD3	OTU domain-containing protein 3
OTUD4	OTU domain-containing protein 4
OTUD5	OTU domain-containing protein 5
OTUD6A	OTU domain-containing protein 6A
OTUD6B	Deubiquitinase OTUD6B
OTUD7A	OTU domain-containing protein 7A
UHL1	Ubiquitin carboxyl-terminal hydrolase isozyme L1
UHL3	Ubiquitin carboxyl-terminal hydrolase isozyme L3
UHL5	Ubiquitin carboxyl-terminal hydrolase isozyme L5 aka CGI-70, INO80R, UCH37
USP14	Ubiquitin carboxyl-terminal hydrolase 14
USP19	Ubiquitin carboxyl-terminal hydrolase 19
USP25	Ubiquitin carboxyl-terminal hydrolase 25
USP26	Ubiquitin carboxyl-terminal hydrolase 26
USP4	Ubiquitin carboxyl-terminal hydrolase 4
USP9X	Probable ubiquitin carboxyl-terminal hydrolase FAF-X
YOD1	Ubiquitin thioesterase OTU1

Degradation

Gene Symbol	Gene Name
ADRM1	Proteasomal ubiquitin receptor ADRM1
ECPAS	Proteasome adapter and scaffold protein ECM29
NFE2L1	Endoplasmic reticulum membrane sensor NFE2L1
PAAF1	Proteasomal ATPase-associated factor 1
POMP	Proteasome maturation protein
PSMA1	Proteasome subunit alpha type-1
PSMA2	Proteasome subunit alpha type-2
PSMA3	Proteasome subunit alpha type-3
PSMA4	Proteasome subunit alpha type-4
PSMA5	Proteasome subunit alpha type-5
PSMA6	Proteasome subunit alpha type-6
PSMA7	Proteasome subunit alpha type-7
PSMA8	Proteasome subunit alpha-type 8
PSMB1	Proteasome subunit beta type-1
PSMB10	Proteasome subunit beta type-10
PSMB11	Proteasome subunit beta type-11
PSMB2	Proteasome subunit beta type-2
PSMB3	Proteasome subunit beta type-3
PSMB4	Proteasome subunit beta type-4
PSMB5	Proteasome subunit beta type-5
PSMB6	Proteasome subunit beta type-6
PSMB7	Proteasome subunit beta type-7
PSMB8	Proteasome subunit beta type-8
PSMB9	Proteasome subunit beta type-9
PSMC1	26S proteasome regulatory subunit 4
PSMC2	26S proteasome regulatory subunit 7
PSMC3	26S proteasome regulatory subunit 6A
PSMC4	26S proteasome regulatory subunit 6B
PSMC5	26S proteasome regulatory subunit 8
PSMC6	26S proteasome regulatory subunit 10B
PSMD1	26S proteasome non-ATPase regulatory subunit 1
PSMD10	26S proteasome non-ATPase regulatory subunit 10
PSMD11	26S proteasome non-ATPase regulatory subunit 11
PSMD12	26S proteasome non-ATPase regulatory subunit 12
PSMD13	26S proteasome non-ATPase regulatory subunit 13
PSMD14	26S proteasome non-ATPase regulatory subunit 14
PSMD2	26S proteasome non-ATPase regulatory subunit 2
PSMD3	26S proteasome non-ATPase regulatory subunit 3
PSMD4	26S proteasome non-ATPase regulatory subunit 4
PSMD5	26S proteasome non-ATPase regulatory subunit 5
PSMD6	26S proteasome non-ATPase regulatory subunit 6
PSMD7	26S proteasome non-ATPase regulatory subunit 7
PSMD8	26S proteasome non-ATPase regulatory subunit 8
PSMD9	26S proteasome non-ATPase regulatory subunit 9
PSME1	Proteasome activator complex subunit 1
PSME2	Proteasome activator complex subunit 2
PSME3	Proteasome activator complex subunit 3
PSME4	Proteasome activator complex subunit 4
PSMF1	Proteasome inhibitor PI31 subunit
PSMG1	Proteasome assembly chaperone 1
PSMG2	Proteasome assembly chaperone 2
PSMG3	Proteasome assembly chaperone 3
PSMG4	Proteasome assembly chaperone 4
RAD23A	UV excision repair protein RAD23 homolog A
RAD23B	UV excision repair protein RAD23 homolog B

Degradation (continued)	
Gene Symbol	Gene Name
SEM1	26S proteasome complex subunit SEM1
TPP2	Tripeptidyl-peptidase 2
UBQLN1	Ubiquilin-1
UBQLN2	Ubiquilin-2
UBQLN4	Ubiquilin-4
ZSWIM2	E3 ubiquitin-protein ligase ZSWIM2

Autophagy

Gene Symbol	Gene Name
ATG10	Ubiquitin-like-conjugating enzyme ATG10
ATG101	Autophagy-related protein 101
ATG12	Ubiquitin-like protein ATG12
ATG13	Autophagy-related protein 13
ATG14	Beclin 1-associated autophagy-related key regulator
ATG16L1	Autophagy-related protein 16-1
ATG16L2	Autophagy-related protein 16-2
ATG2A	Autophagy-related protein 2 homolog A
ATG2B	Autophagy-related protein 2 homolog B
ATG3	Ubiquitin-like-conjugating enzyme ATG3
ATG4A	Cysteine protease ATG4A
ATG4B	Cysteine protease ATG4B
ATG4C	Cysteine protease ATG4C
ATG4D	Cysteine protease ATG4D
ATG5	Autophagy protein 5
ATG7	Ubiquitin-like modifier-activating enzyme ATG7
ATG9A	Autophagy-related protein 9A
ATG9B	Autophagy-related protein 9B
ATXN3L	Ataxin-3-like protein
BECN1	Beclin-1 aka ATG6
BECN2	Beclin-2
GABARAP	Gamma-aminobutyric acid receptor-associated protein
GABARAPL1	Gamma-aminobutyric acid receptor-associated protein-like 1
GABARAPL2	Gamma-aminobutyric acid receptor-associated protein-like 2
HDAC6	Histone deacetylase 6
LAMP2	Lysosome-associated membrane glycoprotein 2
MAP1LC3A	Microtubule-associated proteins 1A/1B light chain 3A
MAP1LC3B	Microtubule-associated proteins 1A/1B light chain 3B
MAP1LC3B2	Microtubule-associated proteins 1A/1B light chain 3 beta 2
MAP1LC3C	Microtubule-associated proteins 1A/1B light chain 3C
PIK3C2B	Phosphatidylinositol 4-phosphate 3-kinase C2 domain-containing subunit beta
PIK3C3	Phosphatidylinositol 3-kinase catalytic subunit type 3
PIK3CA	Phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit alpha isoform
PIK3CB	Phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit beta isoform
PIK3R2	Phosphatidylinositol 3-kinase regulatory subunit beta
PIK3R4	Phosphoinositide 3-kinase regulatory subunit 4
SQSTM1	Sequestosome-1
ULK1	Serine/threonine-protein kinase ULK1 aka ATG1
VMP1	Vacuole membrane protein 1
WDFY3	WD repeat and FYVE domain-containing protein 3
WDR45	WD repeat domain phosphoinositide-interacting protein 4
WDR45B	WD repeat domain phosphoinositide-interacting protein 3

Supplementary Table 2: PN gene expression changes between groups

Genes with lower expression in Group A than Group B in both metastatic and primary

AHSA2P	MKKS
ANKRD13C	OTUD3
ATG12	OTUD4
ATG14	OTUD6B
ATG2B	PFDN4
ATG3	PIK3C3
ATG4C	PIK3CA
ATG5	PPIG
ATXN3	PPIL3
BAG2	PPIL4
BAG4	PPWD1
BBS10	PSMA2
BBS12	PSMA3
C1GALT1C1	PSMA4
C1GALT1C1	PSMA6
CCT6B	PSMC6
CDC37L1	PSMD14
CHORDC1	PSME4
CLPX	RNFT1
DNAJA2	SACS
DNAJB14	SEL1L
DNAJB4	SELENOF
DNAJB9	SGTB
DNAJC1	SPATA5
DNAJC10	SUGT1
DNAJC2	TMEM126B
DNAJC21	TMX3
DNAJC24	TPP2
DNAJC25	UBE2B
DNAJC27	UBE2D1
DNAJC28	UBE2J1
DNAJC3	UBE2V2
DNAJC7	UBE2W
FKBP14	UBE3A
FKBP5	UBR1
FNIP2	UBR2
GRPEL2	UBR3
HSP90AA1	UCHL5
HSP90AA2P	USP14
HSP90AA4P	USP25
HSP90B1	USP9X
HSP90B2P	VBP1
HSPA13	WDFY3
HSPA14	YOD1
HSPA4L	
LTN1	
MINDY2	
MINDY3	

Genes with lower expression in Group A than Group B in primary and no difference in metastatic

BBS4
CANX
CCT2
CCT4
DNAJA1
DNAJC13
DNAJC6
DNAJC9
ECPAS
HSPA12A
HSPD1
HSPH1
LAMP2
MARCHF6
NPM1
OTUD1
PDCL
PDIA6
PIK3CB
PPID
PSMD10
PSMD12
PSMD5
PSMD7
PTGES3
RAD23B
RNF103
STT3B
UBE2D3
UBE2E1
UBE2E3
UBE2K
UBE2Q2
UBE3C
UBE4A
UBQLN1
UBQLN2
UBR5
VMP1

Genes with higher expression in Group A than Group B in both metastatic and primary

FKBP8
HSPB1
HSPBP1
SGTA
UBA52

Genes with higher expression in Group A than Group B in metastatic and no difference in primary

ADRM1
ATG2A
ATG4D
ATG9A
BAG6
BCAP31
CNPY3
DNAJC30
DNAJC4
ERP29
GAK
OTUB1
P4HB
PSMD2
PSMD8
RAD23A
SIL1
SQSTM1
STIP1
STUB1
TBCD
TIMM13
TRAF2
TRAP1
TRIM11
UBE2L5
UBE2M
UBE2O
UBE2S

Genes with lower expression in Group A than Group B in metastatic and no difference in primary

ATG16L2
ATG4A
DNAAF4
DNAJB7
DNAJC19
HSPA7
LRP2BP
PFDN5
PRKN
PSMA8
UBE3D

Genes with no difference in expression between Group A and B in primary or metastatic

AHSA1	DNAJC14	HSPA6	PPIAL4F	RNF5	UNC45B
AHSP	DNAJC15	HSPA8	PPIAL4G	SYVN1	USP19
AIPL1	DNAJC16	HSPA9	PPIAL4H	TBCA	USP26
AMFR	DNAJC17	HSPB2	PPIB	TBCC	USP4
ATG10	DNAJC18	HSPB3	PPIC	TCP1	WDR45
ATG101	DNAJC22	HSPB6	PPIE	TIMM10	WDR45B
ATG13	DNAJC5	HSPB7	PPIF	TIMM44	ZSWIM2
ATG16L1	DNAJC5B	HSPB8	PPIH	TIMM8A	
ATG4B	DNAJC5G	HSPB9	PPIL1	TIMM8B	
ATG7	DNAJC8	HSPE1	PSMA1	TIMM9	
ATG9B	DNLZ	HUWE1	PSMA5	TOMM34	
ATXN3L	ERP27	HYOU1	PSMA7	TOR1A	
BAG1	ERP44	LRPAP1	PSMB1	TOR1B	
BAG3	FBXO2	LRR1	PSMB10	TRAF3	
BAG5	FBXO6	LRRC29	PSMB11	TRIM13	
BCS1L	FKBP10	LRRC41	PSMB2	TSACC	
BECN1	FKBP11	MAP1LC3A	PSMB3	TSC1	
BECN2	FKBP15	MAP1LC3B	PSMB4	TTC4	
CALR	FKBP1A	MAP1LC3B2	PSMB5	UBA1	
CCT3	FKBP1B	MAP1LC3C	PSMB6	UBE2A	
CCT5	FKBP1C	MINDY1	PSMB7	UBE2C	
CCT6A	FKBP2	MINDY4	PSMB8	UBE2D2	
CCT7	FKBP3	NAA10	PSMB9	UBE2D4	
CCT8	FKBP4	NFE2L1	PSMC1	UBE2E2	
CCT8L1P	FKBP6	OTUB2	PSMC2	UBE2F	
CCT8L2	FKBP7	OTUD5	PSMC3	UBE2G1	
CDC34	FKBP9	OTUD6A	PSMC4	UBE2G2	
CDC37	FKBP9P1	OTUD7A	PSMC5	UBE2H	
CHCHD4	FKBPL	PAAF1	PSMD1	UBE2J2	
CLGN	GABARAP	PDCL3	PSMD11	UBE2L3	
CLNS1A	GABARAPL1	PDIA2	PSMD13	UBE2L6	
CLU	GABARAPL2	PDIA3	PSMD3	UBE2N	
CRYAA	GET4	PDIA4	PSMD4	UBE2NL	
CRYAB	GRPEL1	PDIA5	PSMD6	UBE2Q1	
CYBC1	HDAC6	PDRG1	PSMD9	UBE2QL1	
DNAJA3	HOPX	PEX19	PSME1	UBE2R2	
DNAJA4	HSCB	PFDN1	PSME2	UBE2T	
DNAJB1	HSP90AA5P	PFDN2	PSME3	UBE2U	
DNAJB11	HSP90AB1	PFDN6	PSMF1	UBE2V1	
DNAJB12	HSP90AB2P	PIK3C2B	PSMG1	UBE2Z	
DNAJB13	HSP90AB3P	PIK3R2	PSMG2	UBE3B	
DNAJB2	HSPA12B	PIK3R4	PSMG3	UBE4B	
DNAJB3	HSPA1A	POMP	PSMG4	UBQLN4	
DNAJB5	HSPA1B	PPIA	RBX1	UBR4	
DNAJB6	HSPA1L	PPIAL4A	RCN3	UBR7	
DNAJB8	HSPA2	PPIAL4C	RNF126	UCHL1	
DNAJC11	HSPA4	PPIAL4D	RNF185	UCHL3	
DNAJC12	HSPA5	PPIAL4E	RPS27A	ULK1	

Supplementary Table 3: Numbers of genes that are differentially expressed in CM that are differentially expressed in other cancers

Study Abbreviation	Study Name	Number of Samples	Number of CM lower expressed genes with lower expression in one sample group than the other	Number of CM higher expressed genes with higher expression in one sample group than the other	Percentage of CM differentially expressed PN genes differentially expressed between groups
CM	Skin Cutaneous Melanoma	103	130	5	100.0
UVM	Uveal Melanoma	80	130	5	100.0
UCEC	Uterine Corpus Endometrial Carcinoma	587	127	4	97.0
COAD	Colon adenocarcinoma	521	120	5	92.6
READ	Rectum adenocarcinoma	177	115	4	88.1
CESC	Cervical squamous cell carcinoma and endocervical adenocarcinoma	309	106	3	80.7
OV	Ovarian serous cystadenocarcinoma	379	105	3	80.0
LIHC	Liver hepatocellular carcinoma	424	104	1	77.8
THYM	Thymoma	121	100	5	77.8
BLCA	Bladder urothelial carcinoma	433	99	4	76.3
KICH	Kidney chromophobe	89	99	2	74.8
KIRP	Kidney renal papillary cell carcinoma	321	97	4	74.8
HNSC	Head and neck squamous cell carcinoma	546	93	5	72.6
KIRC	Kidney renal clear cell carcinoma	611	91	4	70.4
PRAD	Prostate adenocarcinoma	551	88	5	68.9
THCA	Thyroid carcinoma	568	86	5	67.4
LUAD	Lung adenocarcinoma	594	81	5	63.7
DLBC	Lymphoid Neoplasm Diffuse Large B-cell Lymphoma	48	79	5	62.2
BRCA	Breast invasive carcinoma	1102	77	5	60.7
PCPG	Pheochromocytoma and Paraganglioma	186	72	3	55.6
LGG	Brain Lower Grade Glioma	529	67	4	52.6
LAML	Acute Myeloid Leukemia	151	66	1	49.6
MESO	Mesothelioma	86	66	1	49.6
STAD	Stomach adenocarcinoma	407	63	3	48.9
TGCT	Testicular Germ Cell Tumors	156	63	2	48.1
SARC	Sarcoma	265	58	2	44.4
ESCA	Oesophageal carcinoma	173	44	2	34.1
LUSC	Lung squamous cell carcinoma	551	43	0	31.9
GBM	Glioblastoma multiforme	174	36	0	26.7
UCS	Uterine Carcinosarcoma	56	34	1	25.9
CHOL	Cholangiocarcinoma	46	18	0	13.3

Supplementary Table 4: Significance of difference in levels of immune cell infiltration

Immune Cell Type	Primary p.value	Primary Significance	Metastatic p.value	Metastatic Significance
Endothelial	0.0000033	****	6.1E-09	****
Fibroblasts	0.0009	***	0.0000026	****
Macrophages M2	0.00047	***	0.00057	***
Macrophages	0.0015	**	0.0019	**
Neutrophils	0.0064	**	0.0093	**
Eosinophils	0.008	**	0.008	**
Monocytes	0.0041	**	0.012	*
Plasma cells	0.019	*	0.012	*
B cells	0.0048	**	0.029	*
T regulatory cells	0.01	**	0.026	*
T cells CD4	0.033	*	0.086	ns
Dendritic cells	0.035	*	0.11	ns
T cells CD8	0.035	*	0.12	ns
Cytotoxic cells	0.024	*	0.14	ns
T cells gamma delta	0.048	*	0.13	ns
Macrophages M1	0.077	ns	0.24	ns
NK cells	0.13	ns	0.35	ns
Mast cells	0.51	ns	0.6	ns

Supplementary Table 5: classes of regulatory function executed by key regulators

Regulators	DNA Binding	DNA Methylation	RNA Binding	Protein Binding	Histone Acetylation and Methylation	Chromatin Remodelling And Organisation	DNA Damage Response and Repair
RB1CC1				Yes			
ARID4A	Yes	Yes	Yes		Yes	Yes	
ZRANB2	Yes		Yes		Yes		
ARID4B	Yes	Yes	Yes		Yes	Yes	
ZMYND11	Yes	Yes		Yes		Yes	
HLTF	Yes	Yes	Yes	Yes		Yes	Yes
RBM7		Yes	Yes	Yes	Yes		
PMS1	Yes			Yes			Yes
SIRT1	Yes	Yes		Yes	Yes	Yes	Yes
TMF1	Yes						
GCFC2	Yes						
YAF2	Yes				Yes		
ZNF451		Yes			Yes	Yes	
NR3C1	Yes	Yes	Yes	Yes	Yes	Yes	
RNF19A				Yes			
SP4	Yes						
DDX5	Yes		Yes	Yes	Yes		Yes
ZBTB11	Yes						
CREB1	Yes			Yes	Yes		Yes
SP3	Yes				Yes		
SNAPC1	Yes						
ZNF148	Yes				Yes		
ELK3	Yes						
GABPA	Yes			Yes			
CEBPZ	Yes		Yes		Yes		
TRIP11					Yes		
ATF2	Yes			Yes	Yes	Yes	Yes
MED13	Yes			Yes			
FMR1		Yes	Yes	Yes	Yes	Yes	Yes
DMTF1	Yes						
MEF2A	Yes			Yes	Yes		
SKIL	Yes			Yes			Yes
BTA1	Yes				Yes		
ZNF638	Yes	Yes	Yes			Yes	
ATRX	Yes	Yes		Yes	Yes	Yes	Yes
DEK	Yes		Yes	Yes	Yes	Yes	Yes
CRY1	Yes			Yes	Yes		Yes
ERCC8				Yes			Yes
NAB1				Yes			
PNN	Yes	Yes	Yes		Yes		
SMARCE1	Yes	Yes	Yes	Yes	Yes	Yes	
ZMYM2	Yes			Yes			
CNOT3							Yes
ZNF510	Yes						
ZFX	Yes						
MATR3			Yes	Yes	Yes		
RLF	Yes	Yes			Yes	Yes	
NFYB	Yes			Yes			
MLLT10	Yes		Yes	Yes			

Supplementary Table 6: Allocation of GO terms to functional categories

DNA Binding

ARID DNA-binding domain
ARID DNA-binding domain superfamily
Cis-regulatory region sequence-specific DNA binding
Core promoter sequence-specific DNA binding
DNA binding
DNA-binding
DNA-binding transcription activator activity
DNA-binding transcription activator activity, RNA polymerase II-specific
DNA-binding transcription factor activity
DNA-binding transcription factor activity, RNA polymerase II-specific
DNA-binding transcription factor binding
DNA-binding transcription repressor activity
DNA-binding transcription repressor activity, RNA polymerase II-specific
Double-stranded DNA binding
Lambda repressor-like, DNA-binding domain superfamily
Myb-like DNA-binding domain
p53-like transcription factor, DNA-binding
Positive regulation of transcription regulatory region DNA binding
Regulation of transcription regulatory region DNA binding
RNA polymerase II cis-regulatory region sequence-specific DNA binding
RNA polymerase II core promoter sequence-specific DNA binding
RNA polymerase II transcription regulatory region sequence-specific DNA binding
RNA polymerase II-specific DNA-binding transcription factor binding
SANT SWI3, ADA2, N-CoR and TFIIB DNA-binding domains
Sequence-specific DNA binding
Sequence-specific double-stranded DNA binding
Single-stranded DNA binding
Transcription regulatory region sequence-specific DNA binding

DNA Methylation

DNA methylation
DNA methylation or demethylation
methyl-CpG binding
Methyl-CpG binding domain
Methylation
Methyltransferase
Methyltransferase activity
Methyltransferase complex

DNA Damage Response and Repair

Cellular response to DNA damage stimulus

Damaged DNA binding

DNA damage

DNA damage checkpoint

DNA Damage Recognition in GG-NER

DNA damage response

DNA damage response (only ATM dependent)

DNA damage response, signal transduction by p53 class mediator

DNA damage response, signal transduction by p53 class mediator resulting in cell cycle arrest

DNA damage response, signal transduction by p53 class mediator resulting in transcription of p21 class mediator

DNA damage response, signal transduction resulting in transcription

DNA Damage/Telomere Stress Induced Senescence

DNA Double Strand Break Response

DNA double-strand break processing

DNA Double-Strand Break Repair

DNA integrity checkpoint

DNA IR-damage and cellular response via ATR

DNA IR-double strand breaks and cellular response via ATM

DNA repair

DNA Repair

DNA repair complex

DNA repair complex, and DNA N-glycosylase activity

DNA repair pathways, full network

DNA replication, and interstrand cross-link repair

Double-strand break repair

Double-strand break repair via break-induced replication

Double-strand break repair via nonhomologous end joining

G1 DNA damage checkpoint

G2 DNA damage checkpoint

G2/M DNA damage checkpoint

Gap-filling DNA repair synthesis and ligation in TC-NER

Homologous DNA Pairing and Strand Exchange

Intracellular signal transduction involved in G1 DNA damage checkpoint

Intrinsic apoptotic signaling pathway in response to DNA damage

Intrinsic apoptotic signaling pathway in response to DNA damage by p53 class mediator

miRNA regulation of DNA damage response

Mitotic DNA damage checkpoint

Mitotic G1 DNA damage checkpoint

Nucleotide-excision repair, DNA duplex unwinding

Nucleotide-excision repair, DNA incision

Nucleotide-excision repair, DNA incision, 5-to lesion

Positive regulation of DNA repair

Positive regulation of response to DNA damage stimulus

Processing of DNA double-strand break ends

Regulation of DNA repair

Regulation of intrinsic apoptotic signaling pathway in response to DNA damage

Regulation of response to DNA damage stimulus

Signal transduction in response to DNA damage

Signal transduction involved in DNA damage checkpoint

Signal transduction involved in mitotic DNA damage checkpoint

Signal transduction involved in mitotic DNA integrity checkpoint

Signal transduction involved in mitotic G1 DNA damage checkpoint

SUMOylation of DNA damage response and repair proteins

TP53 Regulates Transcription of DNA Repair Genes

Histone acetylation and methylation

Acetylation

Acetylation-dependent protein binding

Acetylation-dependent protein binding

Acetyltransferase activity

Acetyltransferase complex

H3 histone acetyltransferase complex

H3 histone acetyltransferase complex, and histone H4-K12 acetylation

H4 histone acetyltransferase complex

H4 histone acetyltransferase complex, and INO80-type complex

H4 histone acetyltransferase complex, and Swr1 complex

H4/H2A histone acetyltransferase complex

HDACs deacetylate histones

HDACs deacetylate histones, and Methyl-CpG binding domain

HDACs deacetylate histones, and NoRC negatively regulates rRNA expression

HDACs deacetylate histones, and Sin3-type complex

Histone acetylation

Histone acetyltransferase activity

Histone acetyltransferase binding

Histone acetyltransferase complex

Histone deacetylase binding

Histone deacetylase complex

Histone deacetylation

Histone demethylase activity

Histone demethylase activity (H3-K9 specific), and histone methyltransferase activity (H4-K20 specific)

Histone demethylation

Histone H3 acetylation

Histone H3 deacetylation

Histone H3-K27 methylation

Histone H3-K4 methylation

Histone H3-K9 methylation

Histone H4 acetylation

Histone H4-K12 acetylation

Histone H4-K20 methylation

Histone lysine demethylation

Histone lysine methylation

Histone lysine methylation, and JmjC domain, hydroxylase

Regulation of histone H4 acetylation

Regulation of histone methylation

Regulation of peptidyl-lysine acetylation

Regulation of peptidyl-lysine acetylation

Regulation of protein acetylation

Regulation of protein acetylation

Regulation of protein deacetylation

Regulation of protein deacetylation

Regulation of TP53 Activity through Acetylation

RMTs methylate histone arginines

S-adenosylmethionine-dependent methyltransferase activity

Chromatin Remodelling and Organisation

ATP-dependent chromatin remodeling
CENP-A containing chromatin organization
Chromatin assembly
Chromatin assembly or disassembly
Chromatin disassembly
Chromatin modifying enzymes
Chromatin organization
Chromatin organization involved in negative regulation of transcription
Chromatin organization involved in regulation of transcription
Chromatin organization modifier domain
Chromatin regulator
Chromatin remodeling
Chromatin remodeling at centromere
Chromatin silencing
Chromatin-mediated maintenance of transcription
Chromatin-mediated maintenance of transcription
Covalent chromatin modification
Covalent chromatin modification
DNA methylation-dependent heterochromatin assembly
Heterochromatin assembly
Heterochromatin organization
Negative regulation of chromatin organization
Positive regulation of chromatin assembly or disassembly
Positive regulation of chromatin organization
Positive regulation of DNA methylation-dependent heterochromatin assembly
Positive regulation of heterochromatin assembly
rDNA heterochromatin assembly
Regulation of chromatin assembly or disassembly
Regulation of chromatin organization
Regulation of DNA methylation-dependent heterochromatin assembly
Regulation of heterochromatin assembly
SUMOylation of chromatin organization proteins
Regulation of histone H3-K4 methylation
Regulation of histone H3-K9 methylation

Protein Binding

Cytoskeletal protein binding
Enzyme binding
Heat shock protein binding
Identical protein binding
Kinase binding
Protein binding
Protein C-terminus binding
Protein kinase binding
Protein N-terminus binding
Protein phosphatase binding
Protein-containing complex binding
Ubiquitin protein ligase binding

RNA Binding

miRNA binding
Primary miRNA binding
Regulatory RNA binding
RNA binding
Single-stranded RNA binding