

## Supplemental Information Inventory

**Figure S1. Related to Figure 1.** Phenotype distribution in 493 (TRAMP x J:DO) F1 mice.

**Figure S2. Related to Figure 1.** Genome scans for other aggressive disease traits and modifier locus mapping for primary tumor burden as a binary trait in 493 (TRAMP x DO) F1 mice.

**Figure S3. Related to Table 1.** Coefficient plots for genes with statistically significant *cis*-eQTLs

**Figure S4. Related to Figure 3.** Candidate gene *cis*-eQTL analysis not reaching statistical significance in normal prostate tissue derived from 471 men

**Figure S5. Related to Figure 4.** Additional survival analyses in human gene expression cohorts

**Figure S6. Related to Figure 4.** Comparison of candidate gene expression in aggressive and indolent tumors, and matched normal tissue in mice and humans.

**Figure S7. Related to Figure 5.** Additional in vitro analysis of candidate gene over-expression in PC-3 and LNCaP cells.

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**Table S2. Related to Figure 1.** Association mapping for SNPs within the Chr. 8 distant metastasis free survival locus

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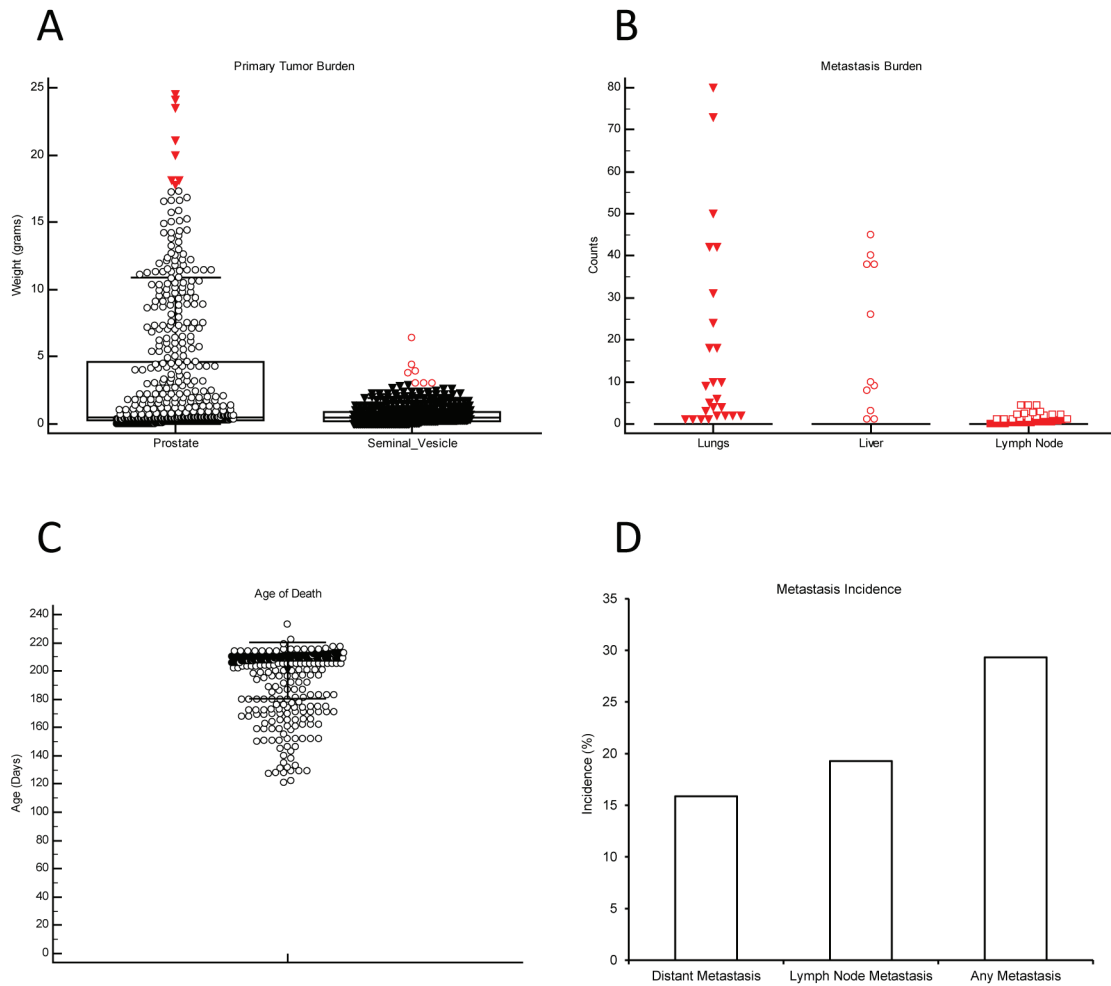
**Table S5. Related to Table 2.** GWAS analysis of the association between haplotypes in linkage disequilibrium with eleven candidate genes and aggressive prostate cancer

**Table S6. Related to Figure 3.** Analysis of candidate gene *cis*-eQTLs in normal prostate tissue derived from a cohort of 471 men

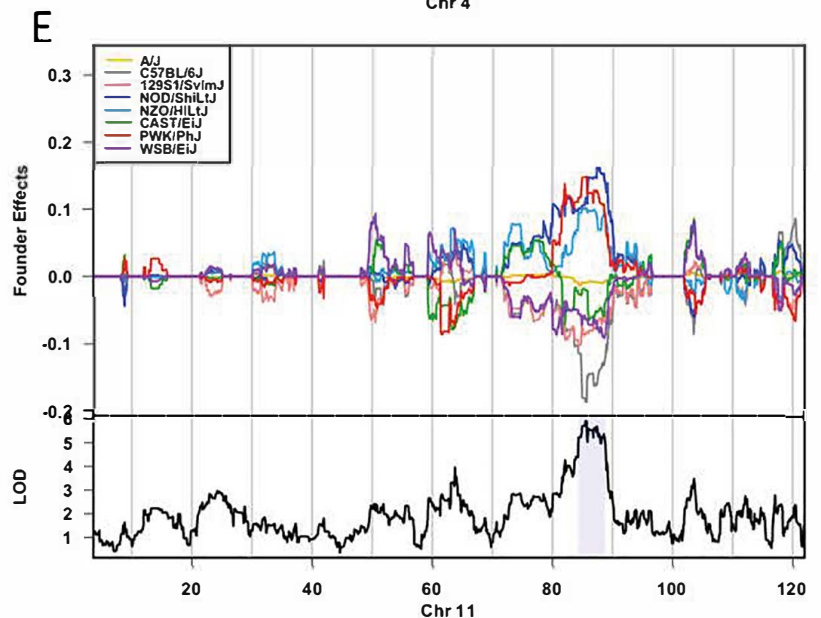
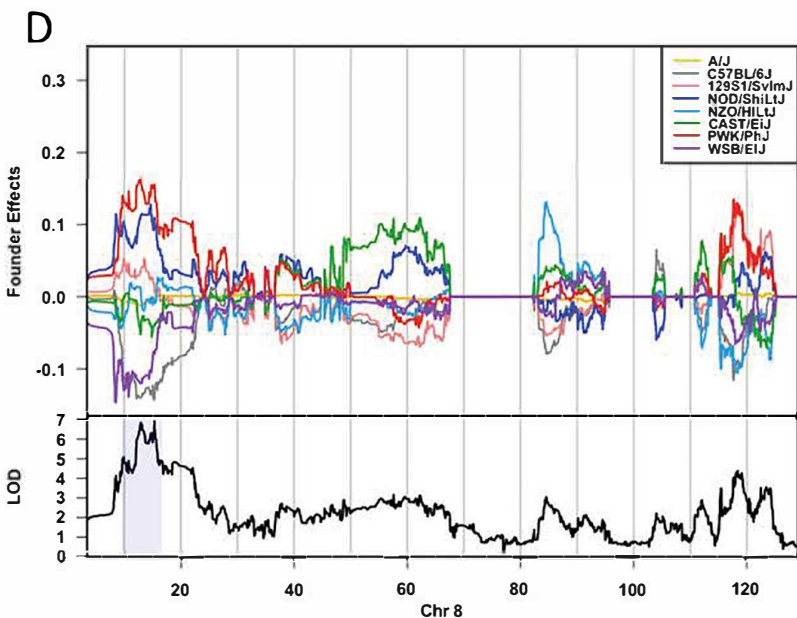
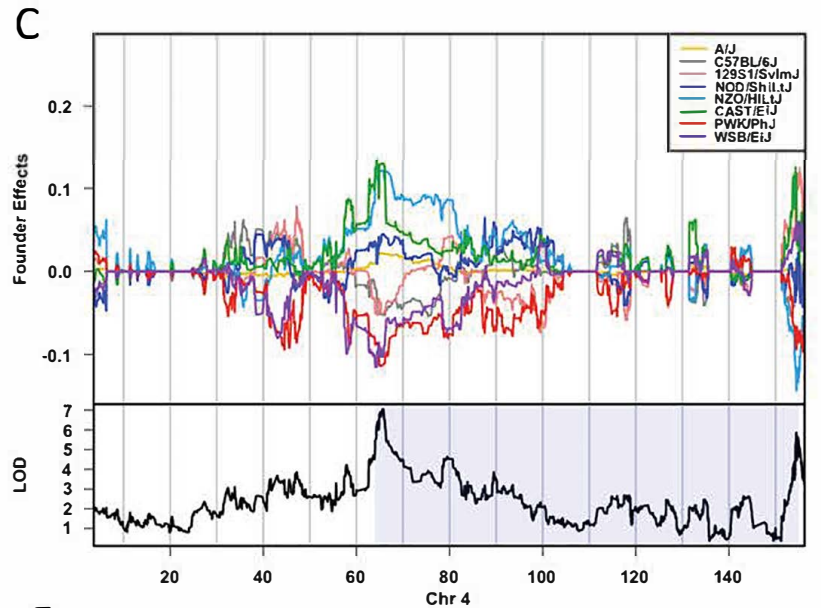
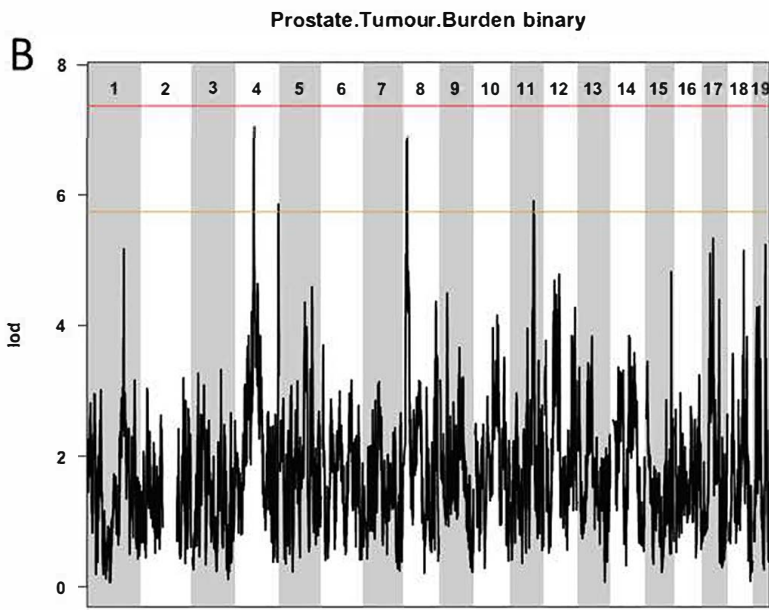
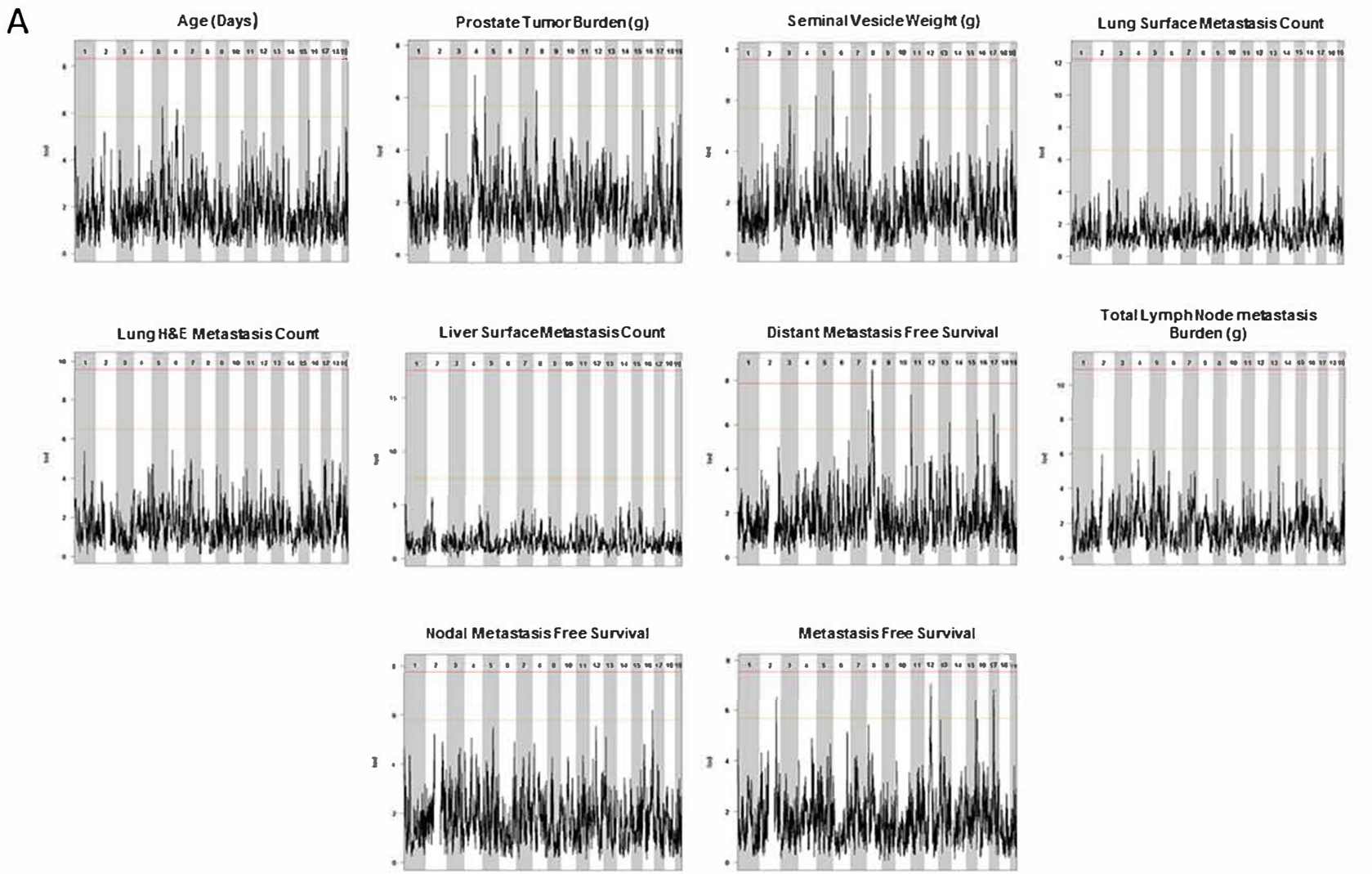
**Table S7. Related to Figure 4.** Logistic regression analyses for seven candidate genes in each of the three human prostate cancer gene expression cohorts

**Table S8. Related to Figure 5.** Microarray data analysis of dysregulated transcripts in four PC-3 clonal isolates over-expressing *RWDD4*

**Table S9. Related to Figure 5.** Microarray data analysis of dysregulated transcripts in four PC-3 clonal isolates over-expressing *CENPU*



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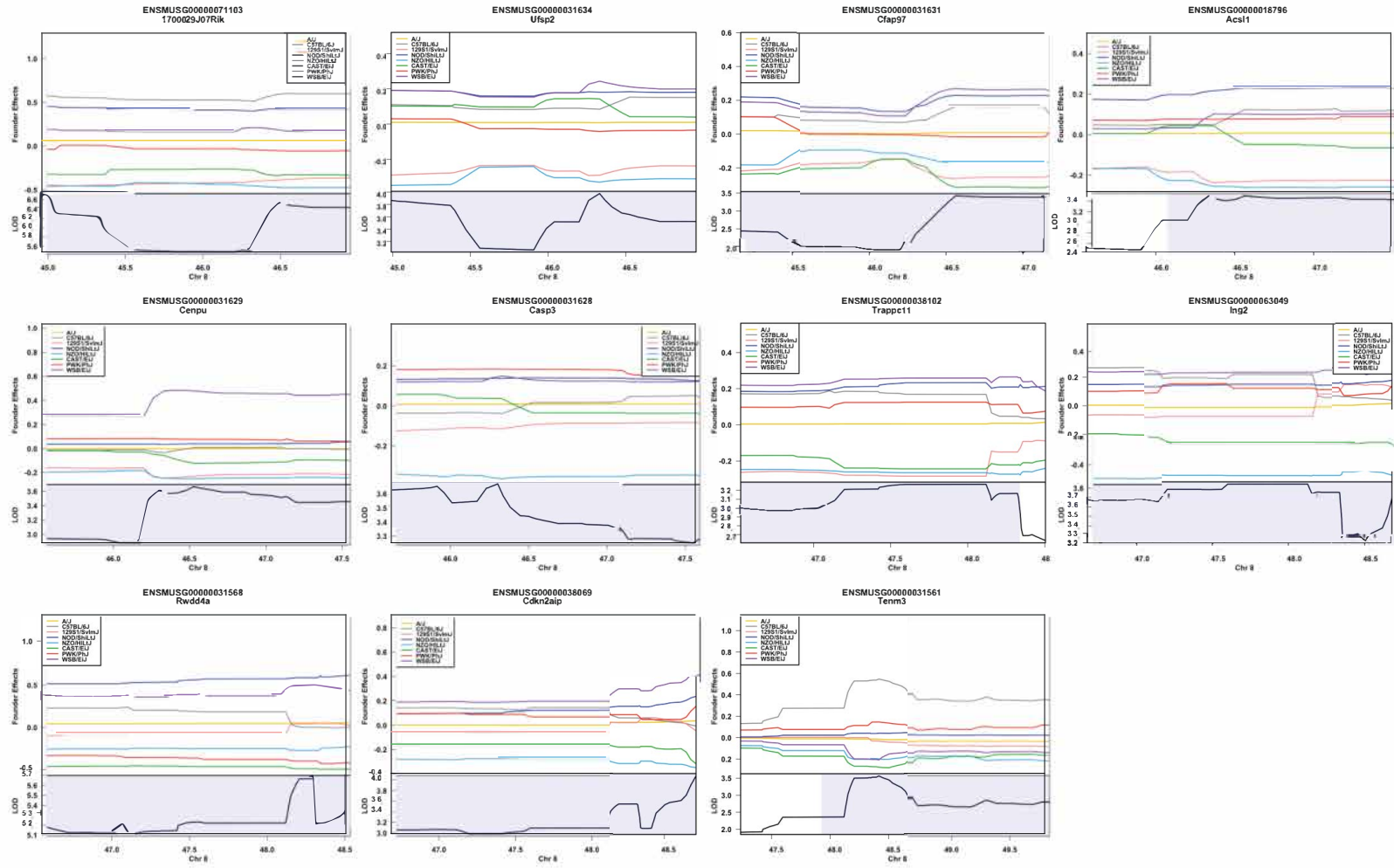
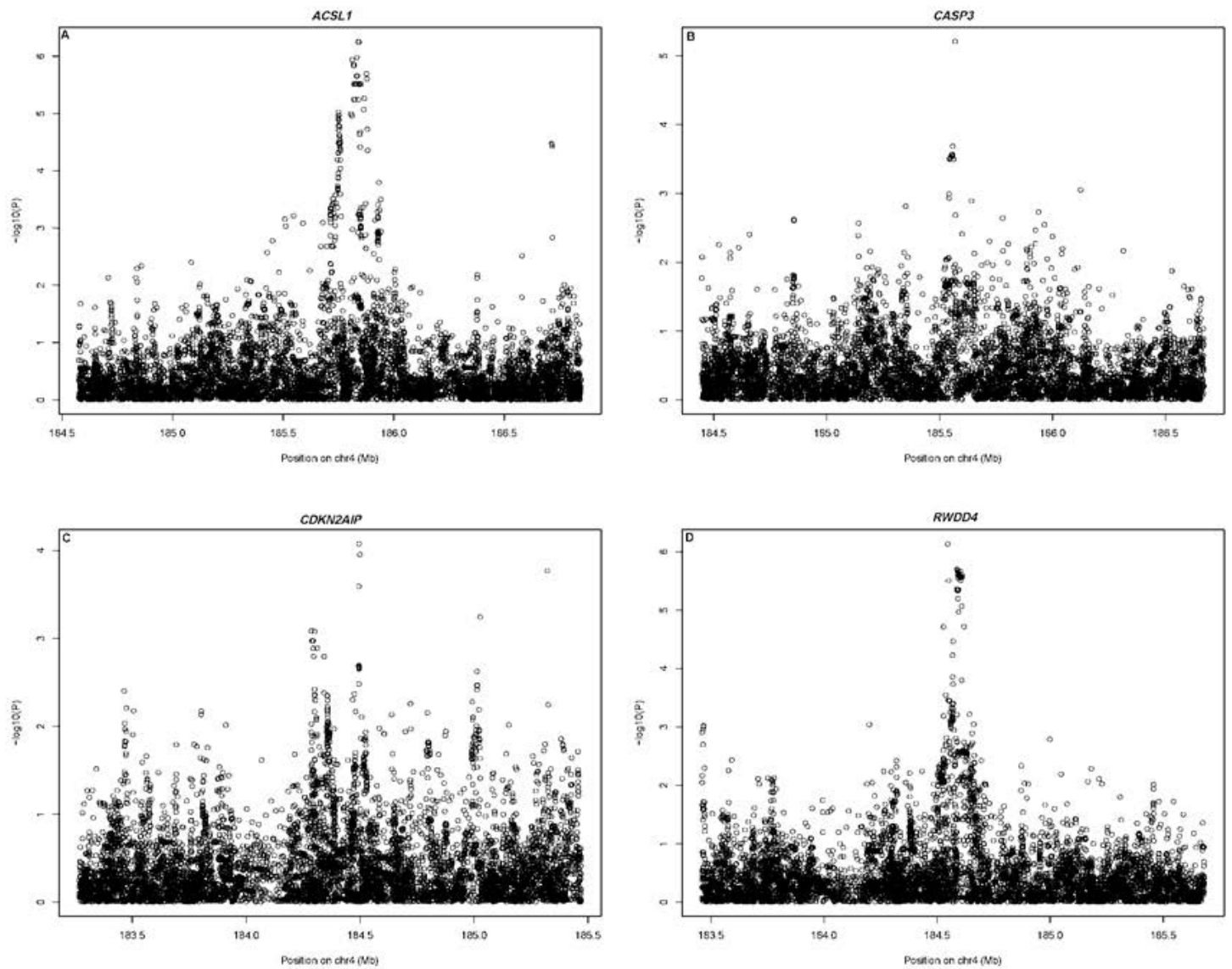


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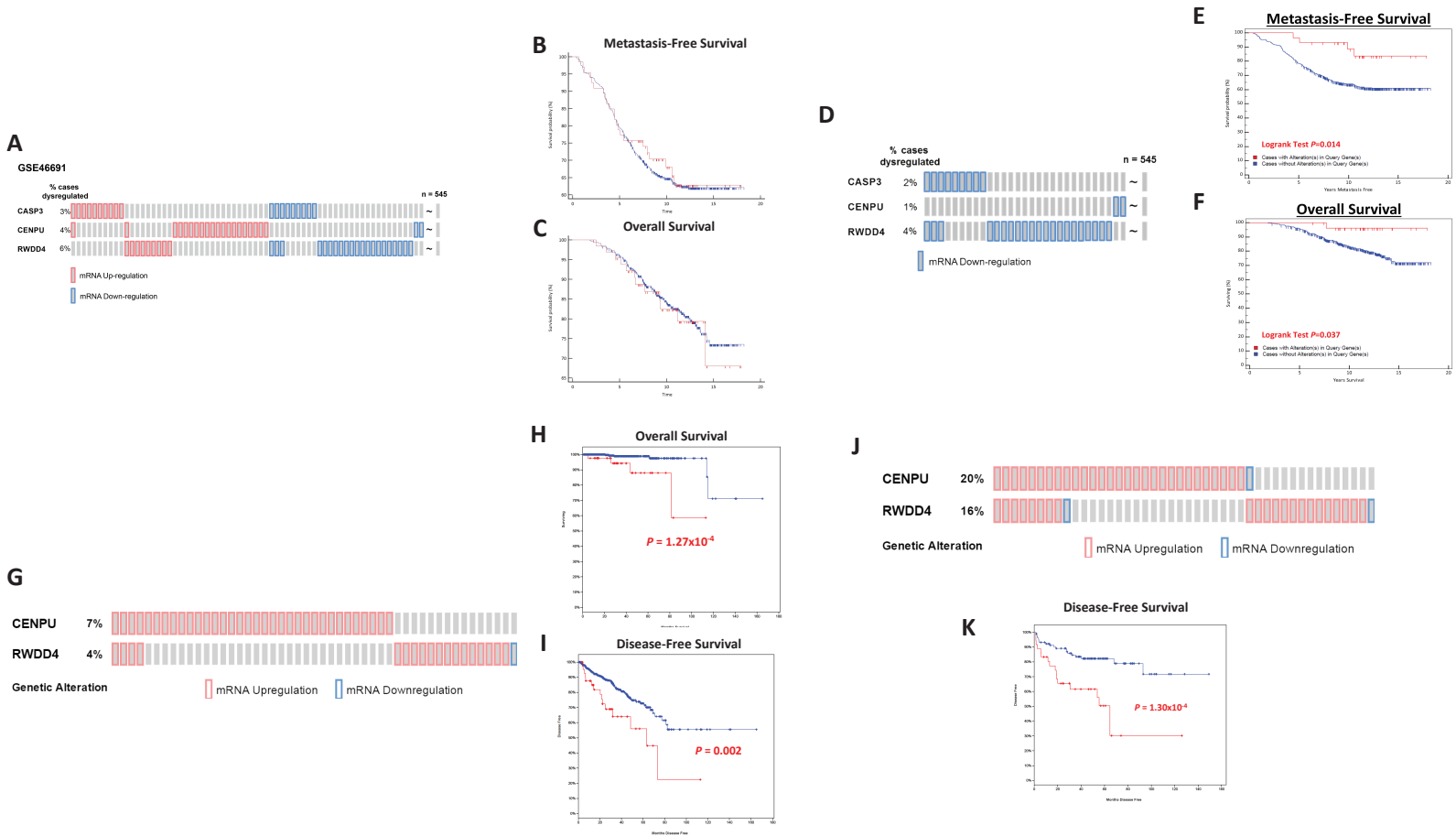
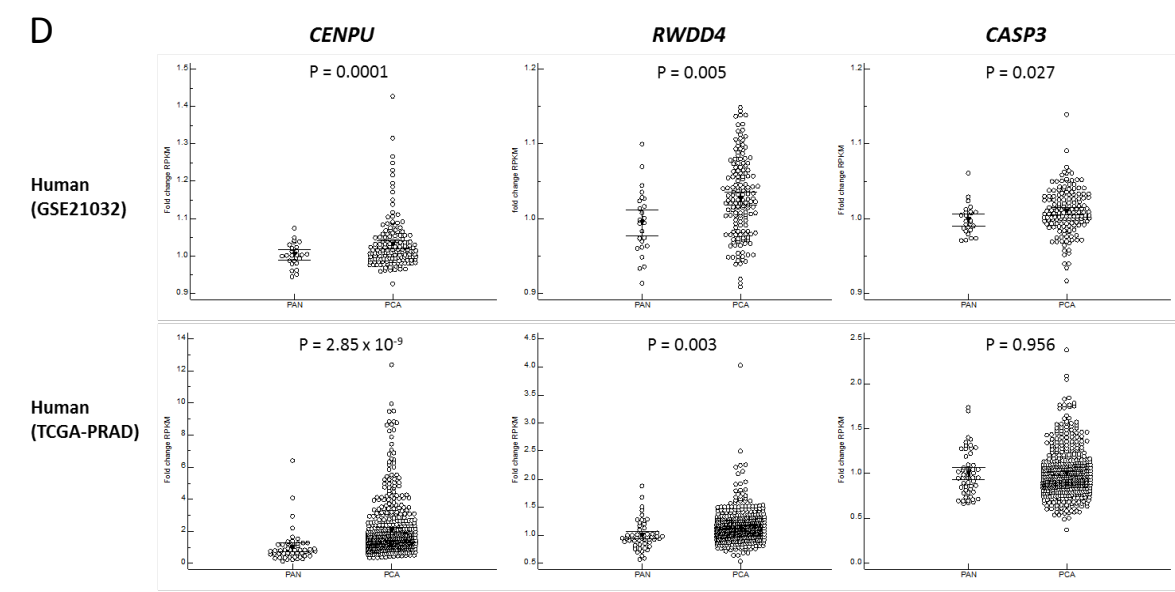
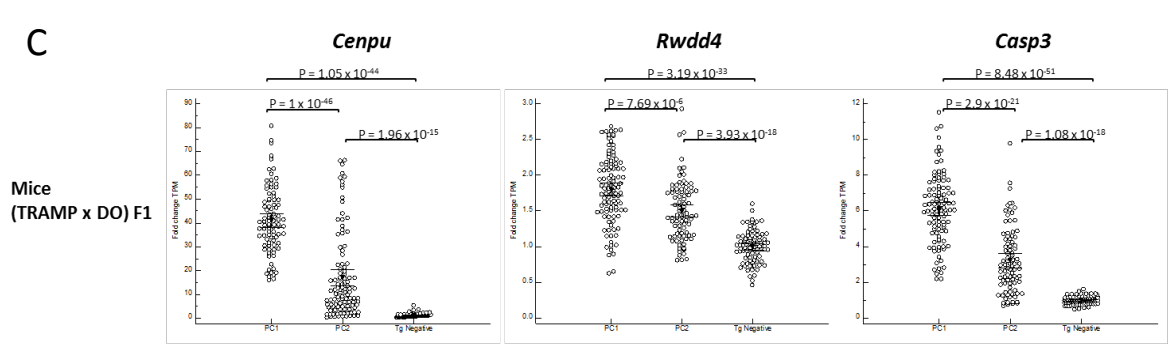
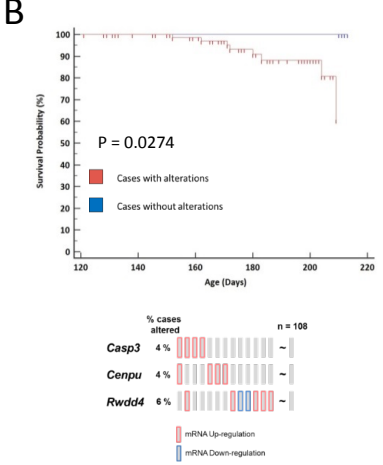
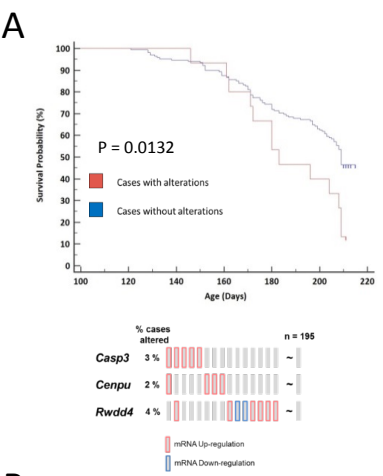
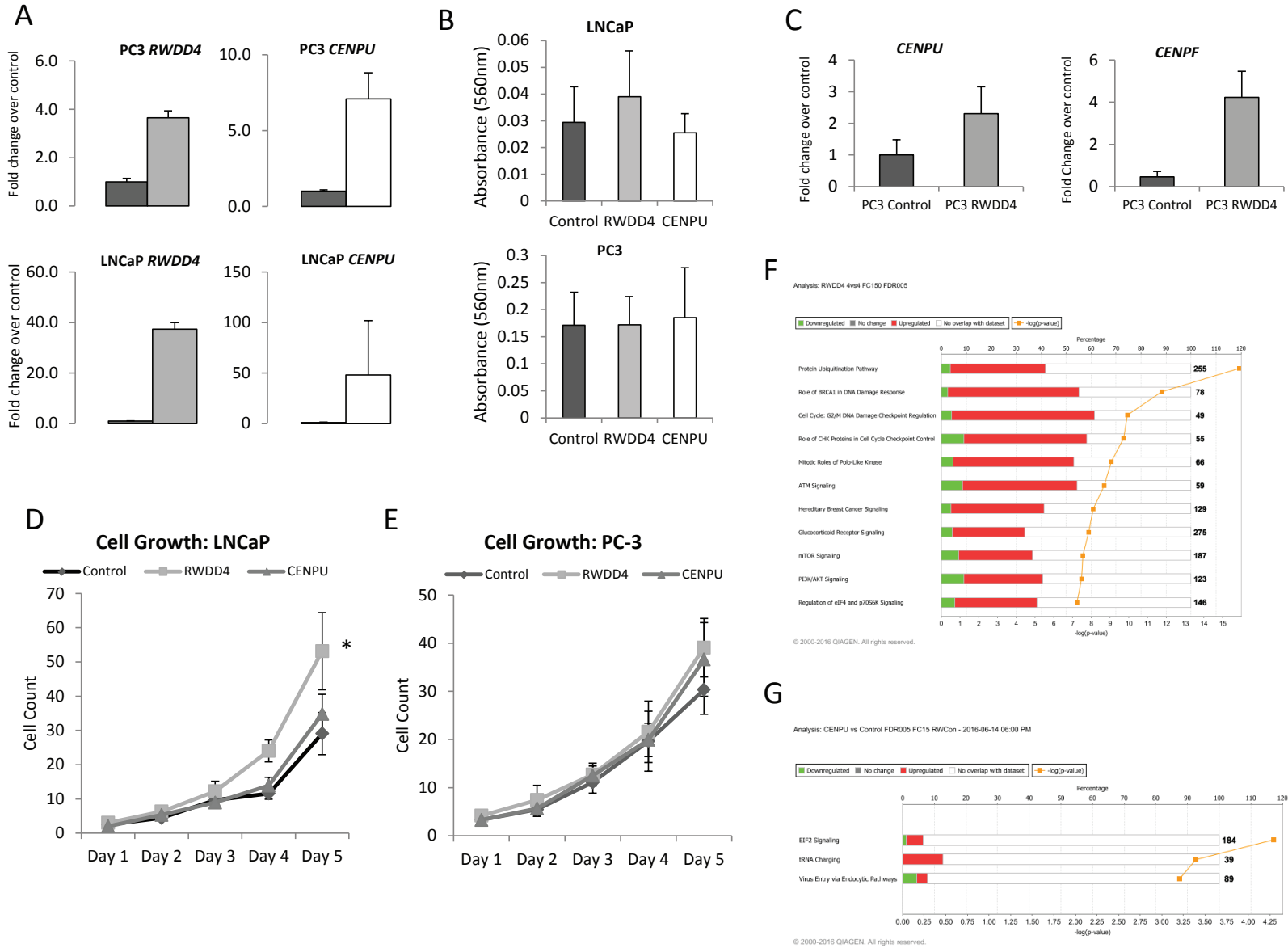


Figure S5. Related to Figure 4. Additional survival analyses in human gene expression cohorts



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**Table S1. Related to Figure 1.** Aggressive disease traits of 498 (TRAMP x J:DO) F1 mice displaying primary tumor burden in prostate and seminal vesicles, and metastases burden in the lung, liver and lymph nodes

	Age (Days)	Primary Tumor Burden		Metastases Burden			
		Prostate Tumor (g)	Seminal Vesicles (g)	Distant Metastases		Lymph Node Metastases	
				Lung Surface Counts	Liver Surface Counts	Lymph Node (g)	Lymph Node Counts
<b>Mean</b>	200.6	3.25	0.69	0.89	0.44	0.14	0.39
<b>St. Dev.</b>	19.9	4.85	0.73	6.34	3.85	0.48	0.91
<b>Distant Metastases Free Survival (%)</b>				15.9		19.3	
<b>Metastases Free Survival (%)</b>				29.3			

**Table S2. Related to Figure 1.** Association mapping for SNPs within the Chr. 8 distant metastasis free survival locus

**Table S3. Related to Figure 2 and Table 1. (TRAMP x J:DO) F1 primary tumor *cis*-eQTL analysis for expressed transcripts within the Chr. 8 distant metastasis free survival locus**

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**Table S5. Related to Table 2.** GWAS analysis of the association between haplotypes in linkage disequilibrium with eleven candidate genes and aggressive prostate cancer

Cohort	Candidate Gene	SNPs	SNP Distance	SNP position	Haplotype base	hap	Clinical trait	hap. frequency	t. value	P value	OR	OR.95%CI. low	OR.95%CI. high	Permutation P value
CGEMS	CDKN2AIP	rs11940756 rs1567597	68866 64768	184296922 184301020	G A	4.4295. G A	Gleason Score	0.12206	2.586056	0.009822	1.21152	1.047547	1.401159	0.0109
CGEMS	ING2	rs4862182 rs11725216 rs4415002	39661 92117 90913	184326127 184334102 184335306	G C T	4.4297. G C T	Gleason Score	0.210462	-3.17283	0.001547	0.691888	0.551084	0.868666	0.0028
CGEMS	TENM3	rs2726797 rs2726792 rs2675534	14249 8409 5375	183230887 183236727 183239761	A G C	4.4259. A G C	Pathological Stage	0.057583	2.81085	0.00502	1.139939	1.040443	1.248951	0.0062
CGEMS	TENM3	rs2168681 rs10050018 rs921961	0 0 0	183343563 183349618 183365667	G C T	4.4263. G C T	Distant Metastasis	0.073398	3.021017	0.002571	1.110862	1.037615	1.18928	0.0026
CGEMS	TENM3	rs2309764 rs6858496 rs12498650 rs6552597 rs6829893	0 0 0 0 0	183619206 183626332 183628872 183631266 183651765	C C G G G	4.4275. C C G G G	Distant Metastasis	0.134225	2.791587	0.005326	1.077528	1.022493	1.135526	0.0063
CGEMS	CDKN2AIP	rs6821104 rs955229	73260 68905	184292528 184296883	T C	4.4294. T C	Nodal Metastasis	0.120032	3.706497	0.00022	1.095923	1.044105	1.150312	1.00E-04
CGEMS	CDKN2AIP	rs11940756 rs1567597	68866 64768	184296922 184301020	A A	4.4295. A A	Nodal Metastasis	0.119627	3.382526	0.000741	1.087342	1.035843	1.141402	0.001
CGEMS	CDKN2AIP	rs6821104 rs955229	73260 68905	184292528 184296883	T T	4.4294. T T	Nodal Metastasis	0.485401	-2.82158	0.004856	0.956021	0.926615	0.98636	0.0061
CGEMS	ING2	rs4241767 rs13111484 rs4862197 rs6844630	73081 69645 64173 52408	184353138 184356574 184362046 184373811	C A C G	4.4299. C A C G	Nodal Metastasis	0.602595	2.653584	0.008067	1.045734	1.011757	1.080852	0.0077
CGEMS	TENM3	rs1350317 rs13106786 rs7670943 rs10520533 rs4862074	0 0 0 0 0	183412634 183423315 183424364 183428859 183440877	T G T A A	4.4266. T G T A A	Nodal Metastasis	0.351176	-2.90732	0.003711	0.952586	0.921896	0.984297	0.0034
CGEMS	TENM3	rs11132137 rs11726016 rs12499296	0 0 0	183525697 183531705 183536086	C G G	4.4270. C G	Nodal Metastasis	0.253852	2.647314	0.008217	1.0516	1.013148	1.091511	0.0071

						G										
		rs1516538	0	183321916	A	4.9366.										
		rs6838423	0	183322044	A	A										
		rs6823473	0	183323457	A	A										
		rs17253954	0	183324280	C	C										
		rs7666497	0	183326512	A	A										
		rs6830860	0	183327907	A	A										
		rs17073248	0	183328030	G	G										
		rs17073255	0	183330031	G	G	Aggressive									
ICPCG	TENM3	rs10520531	0	183335191	G	G	vs. Non- Aggressive	0.322069	2.936288	0.003322	1.160184	1.050641	1.281147	0.0033		
		rs10050018	0	183349618	A	4.9367.										
		rs11132125	0	183354559	A	A										
		rs6822105	0	183361857	G	G										
		rs17073286	0	183364714	G	G										
		rs12498833	0	183365002	G	G	Aggressive									
		rs921961	0	183365667	G	G	vs. Non- Aggressive									
ICPCG	TENM3	rs12505033	0	183367131	A	A	Aggressive	0.334485	2.814139	0.004891	1.150894	1.043579	1.269245	0.0049		
		rs13109717	0	183314359	A	4.9365.	Aggressive									
		rs10520529	0	183315919	G	A	vs. Non- Aggressive									
ICPCG	TENM3					G	Aggressive	0.325781	2.794193	0.005203	1.152297	1.043229	1.272768	0.0059		
		rs12186290	0	183579519	A	4.9385.										
		rs4386638	0	183581152	G	A										
		rs12498348	0	183582696	A	G										
		rs10428431	0	183583762	A	A										
		rs17073734	0	183584040	C	C										
		rs12648977	0	183589823	A	A										
		rs2309774	0	183590236	G	G										
		rs2309760	0	183591332	C	C										
		rs11132145	0	183591707	A	A										
		rs2309759	0	183593318	G	G	Aggressive									
ICPCG	TENM3	rs4535369	0	183594938	A	A	vs. Non- Aggressive	0.142089	2.718659	0.006555	1.207349	1.053989	1.383023	0.0053		

**Table S6. Related to Fig. 3.** Analysis of candidate gene cis-eQTLs in normal prostate tissue derived from a cohort of 471 men

**Table S7. Related to Fig. 4.** Logistic regression analyses for seven candidate genes in each of the three human prostate cancer gene expression cohorts

Gene	Clinical Trait	Cohort	Odds ratio	95% CI	Coefficient	Std. Error	Wald	P-Value	FDR
CASP3	Node Stage	TCGA	1.6309	1.2139 to 2.1912	0.48913	0.15066	10.5399	0.0012	0.021
CENPU	Recurrence	GSE21032	2.2838	1.4921 to 3.4955	0.82583	0.21717	14.4598	0.0001	0.0042
CENPU	Node Stage	GSE21032	2.1963	1.3517 to 3.5686	0.78677	0.24766	10.0923	0.0015	0.021
CENPU	Pathological Stage	GSE21032	1.7629	1.2629 to 2.4608	0.56694	0.17016	11.1005	0.0009	0.021
CENPU	Pathological Stage	TCGA	2.5823	1.7877 to 3.7302	0.94869	0.18764	25.5618	0.0001	0.0042
CENPU	Gleason	TCGA	3.5908	1.6060 to 8.0287	1.27838	0.41053	9.697	0.0018	0.0216
RWDD4	Node Stage	GSE21032	0.1187	0.0318 to 0.4428	-2.13087	0.67159	10.0673	0.0015	0.021
RWDD4	Gleason	GSE21032	2.3755	1.3401 to 4.2106	0.86519	0.29204	8.7765	0.0031	0.03255
ACSL1	Gleason	GSE21032	0.5189	0.3193 to 0.8434	-0.65607	0.24781	7.0092	0.0081	0.06804
ING2	Gleason	GSE21032	0.6129	0.4286 to 0.8765	-0.48959	0.18253	7.1945	0.0073	0.06804
CASP3	Pathological Stage	TCGA	1.4291	1.0862 to 1.8804	0.35707	0.14001	6.5044	0.0108	0.082473
TENM3	Node Stage	GSE21032	0.2292	0.0659 to 0.7971	-1.47302	0.63583	5.3669	0.0205	0.133754
ACSL1	Node Stage	TCGA	1.3111	1.0422 to 1.6493	0.27083	0.11709	5.3501	0.0207	0.133754
CENPU NM_024629	Metastasis	GSE46691	1.2351	1.0273 to 1.4851	0.21118	0.094024	5.0448	0.0247	0.1482
ACSL1	Node Stage	GSE21032	2.6479	1.1032 to 6.3556	0.97378	0.44671	4.7519	0.0293	0.152188
ING2	Recurrence	GSE21032	0.636	0.4236 to 0.9549	-0.45255	0.20736	4.7629	0.0291	0.152188
ING2	Pathological Stage	TCGA	0.8013	0.6553 to 0.9798	-0.22152	0.10259	4.6626	0.0308	0.152188
CENPU	Recurrence	TCGA	1.2767	1.0187 to 1.6001	0.24429	0.1152	4.497	0.034	0.158667
CDKN2AIP	Gleason	TCGA	1.5483	1.0218 to 2.3459	0.43714	0.21202	4.251	0.0392	0.173305
CASP3	Death	GSE46691	1.287	1.0086 to 1.6423	0.25233	0.12438	4.1153	0.0425	0.1744
RWDD4 NM_152682	Metastasis	GSE46691	1.3131	1.0078 to 1.7107	0.27237	0.13497	4.072	0.0436	0.1744
CASP3	Recurrence	TCGA	1.3119	1.0006 to 1.7201	0.27149	0.1382	3.8588	0.0495	0.180783
CASP3	Metastasis	GSE46691	1.2194	1.0007 to 1.4857	0.19832	0.10081	3.8704	0.0491	0.180783
ING2	Pathological Stage	GSE21032	0.7374	0.5342 to 1.0179	-0.30463	0.1645	3.4295	0.064	0.21504
CDKN2AIP	Recurrence	TCGA	0.7668	0.5793 to 1.0151	-0.2655	0.14311	3.4416	0.0636	0.21504
TENM3 NM_001080477	Recurrence	GSE46691	0.8347	0.6853 to 1.0166	-0.18073	0.10062	3.2261	0.0725	0.234231
CENPU NM_024629	Recurrence	GSE46691	1.1863	0.9765 to 1.4412	0.17083	0.09931	2.959	0.0854	0.265689
ING2	Recurrence	TCGA	0.8125	0.6345 to 1.0406	-0.20762	0.12621	2.7062	0.1	0.291393
RWDD4	Gleason	TCGA	0.7681	0.5605 to 1.0525	-0.26386	0.16071	2.6956	0.1006	0.291393
TENM3	Recurrence	GSE21032	1.4917	0.8890 to 2.5030	0.39993	0.26406	2.2938	0.1299	0.340988
CDKN2AIP	Death	GSE46691	0.8181	0.6327 to 1.0577	-0.20083	0.13109	2.3469	0.1255	0.340988
RWDD4 NM_152682	Death	GSE46691	1.2877	0.9284 to 1.7861	0.25288	0.16692	2.295	0.1298	0.340988
ING2	Node Stage	TCGA	0.8003	0.5971 to 1.0727	-0.22274	0.14946	2.221	0.1361	0.346436



CENPU	Gleason	GSE21032	1.2983	0.9079 to 1.8565	0.26102	0.18249	2.0458	0.1526	0.36624
TENM3	Gleason	TCGA	0.7921	0.5764 to 1.0886	-0.23302	0.16222	2.0633	0.1509	0.36624
ING2	Recurrence	GSE46691	1.143	0.9466 to 1.3801	0.13365	0.096185	1.9308	0.1647	0.3843
TENM3 NM_001080477	Metastasis	GSE46691	0.8749	0.7221 to 1.0601	-0.13363	0.097962	1.8608	0.1725	0.391622
CENPU	Node Stage	TCGA	1.1748	0.9278 to 1.4875	0.16109	0.12043	1.7893	0.181	0.400105
CDKN2AIP	Node Stage	GSE21032	0.6537	0.3410 to 1.2532	-0.42504	0.33202	1.6388	0.2005	0.431846
ACSL1	Death	TCGA	1.2903	0.8662 to 1.9222	0.25488	0.20335	1.5711	0.2101	0.440427
CASP3	Node Stage	GSE21032	1.4418	0.7973 to 2.6072	0.36588	0.30225	1.4654	0.2261	0.440427
TENM3 NM_001080477	Death	GSE46691	0.8653	0.6832 to 1.0961	-0.14462	0.1206	1.4381	0.2304	0.440427
CDKN2AIP	Metastasis	GSE46691	0.8765	0.7109 to 1.0808	-0.13177	0.10689	1.5196	0.2177	0.440427
ING2	Metastasis	GSE46691	1.1227	0.9291 to 1.3566	0.11574	0.096563	1.4367	0.2307	0.440427
RWDD4	Node Stage	TCGA	0.8432	0.6332 to 1.1228	-0.1706	0.14614	1.3628	0.2431	0.453787
RWDD4 NM_152682	Recurrence	GSE46691	1.1601	0.8948 to 1.5039	0.14846	0.13245	1.2563	0.2623	0.478983
TENM3	Gleason	GSE21032	0.7726	0.4818 to 1.2391	-0.25795	0.24098	1.1458	0.2844	0.489429
TENM3	Pathological Stage	GSE21032	1.2701	0.8228 to 1.9604	0.23908	0.22147	1.1653	0.2804	0.489429
ACSL1	Gleason	TCGA	0.8004	0.5319 to 1.2044	-0.22266	0.2085	1.1405	0.2855	0.489429
CENPU NM_024629	Death	GSE46691	1.1202	0.8999 to 1.3943	0.11347	0.1117	1.0319	0.3097	0.520296
CASP3	Pathological Stage	GSE21032	0.8663	0.6537 to 1.1481	-0.14352	0.1437	0.9974	0.3179	0.5236
TENM3	Pathological Stage	TCGA	1.1183	0.8942 to 1.3985	0.11178	0.11407	0.9602	0.3271	0.528392
CASP3	Gleason	GSE21032	1.1591	0.8543 to 1.5726	0.14762	0.15568	0.8992	0.343	0.533556
ACSL1	Recurrence	GSE46691	0.8859	0.6903 to 1.1369	-0.12114	0.12726	0.9062	0.3411	0.533556
CDKN2AIP	Pathological Stage	GSE21032	1.1735	0.8247 to 1.6698	0.16001	0.17995	0.7907	0.3739	0.56085
CDKN2AIP	Node Stage	TCGA	0.8698	0.6404 to 1.1813	-0.1395	0.15619	0.7977	0.3718	0.56085
CASP3	Gleason	TCGA	1.2244	0.7579 to 1.9782	0.20246	0.24475	0.6843	0.4081	0.601411
CDKN2AIP	Pathological Stage	TCGA	1.1082	0.8629 to 1.4230	0.10269	0.12761	0.6476	0.421	0.609724
CENPU	Death	TCGA	1.2219	0.7401 to 2.0172	0.20039	0.25578	0.6138	0.4334	0.617044
CASP3	Recurrence	GSE46691	0.9252	0.7568 to 1.1312	-0.077699	0.10255	0.5741	0.4486	0.62804
ING2	Death	TCGA	1.2218	0.7096 to 2.1036	0.20029	0.27723	0.522	0.47	0.647213
ING2	Gleason	TCGA	1.128	0.8043 to 1.5819	0.12041	0.17257	0.4869	0.4853	0.657503
TENM3	Node Stage	TCGA	0.9192	0.7106 to 1.1888	-0.084306	0.13127	0.4125	0.5207	0.694267
ING2	Death	GSE46691	1.0767	0.8514 to 1.3615	0.07388	0.11976	0.3805	0.5373	0.705206
CDKN2AIP	Death	TCGA	0.8052	0.3932 to 1.6490	-0.21663	0.36572	0.3509	0.5536	0.715422
CDKN2AIP	Gleason	GSE21032	0.8881	0.5923 to 1.3317	-0.11863	0.20669	0.3295	0.566	0.720364
CDKN2AIP	Recurrence	GSE21032	1.0905	0.7198 to 1.6520	0.086593	0.21195	0.1669	0.6829	0.856173
CASP3	Recurrence	GSE21032	1.0613	0.7678 to 1.4672	0.059529	0.16521	0.1298	0.7186	0.881148
TENM3	Recurrence	TCGA	0.9561	0.7455 to 1.2263	-0.044867	0.12696	0.1249	0.7238	0.881148

<b>RWDD4</b>	<b>Recurrence</b>	<b>TCGA</b>	0.9625	0.7618 to 1.2160	-0.03824	0.1193	0.1027	0.7486	0.89832
<b>ING2</b>	<b>Node Stage</b>	<b>GSE21032</b>	0.9199	0.5321 to 1.5903	-0.083484	0.2793	0.08935	0.765	0.903583
<b>TENM3</b>	<b>Death</b>	<b>TCGA</b>	0.9264	0.5489 to 1.5634	-0.076483	0.267	0.08205	0.7745	0.903583
<b>ACSL1</b>	<b>Recurrence</b>	<b>TCGA</b>	1.0287	0.8299 to 1.2752	0.028338	0.10958	0.06688	0.7959	0.909016
<b>ACSL1</b>	<b>Pathological Stage</b>	<b>TCGA</b>	0.9708	0.7713 to 1.2220	-0.029616	0.11739	0.06365	0.8008	0.909016
<b>CASP3</b>	<b>Death</b>	<b>TCGA</b>	1.0736	0.5595 to 2.0600	0.071012	0.33249	0.04561	0.8309	0.930608
<b>RWDD4</b>	<b>Recurrence</b>	<b>GSE21032</b>	1.0574	0.5965 to 1.8745	0.055837	0.29209	0.03654	0.8484	0.937705
<b>ACSL1</b>	<b>Recurrence</b>	<b>GSE21032</b>	0.9656	0.5973 to 1.5611	-0.034991	0.24508	0.02038	0.8865	0.939659
<b>RWDD4</b>	<b>Death</b>	<b>TCGA</b>	1.0336	0.6280 to 1.7014	0.033073	0.25426	0.01692	0.8965	0.939659
<b>RWDD4</b>	<b>Pathological Stage</b>	<b>TCGA</b>	0.982	0.7893 to 1.2217	-0.018203	0.11146	0.02667	0.8703	0.939659
<b>ACSL1</b>	<b>Metastasis</b>	<b>GSE46691</b>	0.9855	0.7729 to 1.2566	-0.014617	0.12398	0.0139	0.9061	0.939659
<b>CDKN2AIP</b>	<b>Recurrence</b>	<b>GSE46691</b>	0.983	0.7942 to 1.2167	-0.017115	0.10882	0.02474	0.875	0.939659
<b>RWDD4</b>	<b>Pathological Stage</b>	<b>GSE21032</b>	1.0193	0.6295 to 1.6507	0.019147	0.24593	0.006061	0.9379	0.9492
<b>ACSL1</b>	<b>Death</b>	<b>GSE46691</b>	1.0124	0.7554 to 1.3568	0.012302	0.1494	0.00678	0.9344	0.9492
<b>ACSL1</b>	<b>Pathological Stage</b>	<b>GSE21032</b>	1.0116	0.6779 to 1.5096	0.011519	0.20425	0.003181	0.955	0.955

**Table S8. Related to Fig. 5.** Microarray data analysis of dysregulated transcripts in four PC-3 clonal isolates over-expressing *RWDD4*

**Table S9. Related to Fig. 5.** Microarray data analysis of dysregulated transcripts in four PC-3 clonal isolates over-expressing *CENPU*