

Supplemental Information

A molecular signature in superficial bladder carcinoma predicts clinical outcome

Lars Dyrskjøt, Karsten Zieger, Mogens Kruhøffer, Thomas Thykjaer, Jens L. Jensen, Hanne Primdahl, Natasha Aziz, Niels Marcussen, Klaus Møller & Torben F. Ørntoft

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Supplemental Table 1

Risk score description.

Risk factor	Score		
	0	1	0.5
Stage	Ta	T1	Suspected superficial invasion
Grade (Bergkvist)	1 or 2	3	2-3
Tumor size	All Ta grade 1 Grade 2/3 < 3 cm	> 3 cm (grade 3)	~ 3 cm (grade 3) > 3 cm (grade 2)
Concomitant CIS	Not present	Present	Assumed
Multiplicity and recurrence, grade 3	Single/none	Multiple/frequent grade 3 tumors	grade 2 tumors with <u>one</u> grade 3 tumor

Supplemental Table 2

Clinical data on all patients involved in the training and test sets

Training set						
Group	Sample ¹	Histology	Progressed to:	Time to progression (months)	Follow-up time (months) ²	Total follow-up time (months) ³
No progression	150-6	Ta gr3	-	-	76	138
No progression	997-1	Ta gr2	-	-	53	53
No progression	833-2	Ta gr3	-	-	73	154
No progression	1070-1	Ta gr3	-	-	51	51
No progression	968-1	Ta gr2	-	-	56	56
No progression	815-1	Ta gr2	-	-	50	50
No progression	861-1	Ta gr2	-	-	65	65
No progression	669-1	Ta gr2	-	-	81	81
No progression	368-4	Ta gr2	-	-	16	53
No progression	898-1	Ta gr2	-	-	74	81
No progression	576-6	Ta gr2	-	-	56	90
No progression	625-1	T1 gr3	-	-	44	44
No progression	880-1	T1 gr3	-	-	67	67
Progression	747-3	Ta gr2	T1 gr3	7	-	7
Progression	956-2	Ta gr3	T1 gr3	27	-	27
Progression	1083-1	T1 gr2	T4a gr2	1	-	1
Progression	686-3	Ta gr2	T1 gr2	6	-	84
Progression	795-13	Ta gr2	T1 gr3	4	-	181
Progression	865-1	Ta gr2	T1 gr2	8	-	139
Progression	112-2	Ta gr3	T1 gr3	7	-	36
Progression	825-3	Ta gr3	T1 gr3	7	-	36
Progression	679-2	Ta gr2	T4a gr3	32	-	22
Progression	941-4	Ta gr3	T3 gr3	10	-	14
Progression	607-1	T1 gr2	T2+ gr3	8	-	30
Progression	1017-1	T1 gr3	T2+ gr3	8	-	8
Progression	1276-1	T1 gr3	T2+ gr3	7	-	12
Progression	501-1	T1 gr3	T2+ gr3	26	-	26
Progression	744-1	T1 gr3	T2+ gr3	14	-	14
Progression	839-1	T1 gr3	T2+ gr3	13	-	13

1. Patient number followed by visit number (1= first visit to the dept. of Urology).
2. The follow-up time from sampling visit.
3. The follow-up time from first visit to the clinic.

Test set

Sample ¹	Histology	Progressed to:	Time to progression (months)	Follow-up (months) ²	Total follow-up ³	Progression prediction	Stage classification	Clinical risk at sampling ⁴	Clinical risk at end-point ⁵
926-1	Ta gr2	-	-	67	67	No progression	No progression	low	low
1012-1	Ta gr1	-	-	39	39	No progression	No progression	low	medium
521-1	Ta gr1	-	-	47	47	No progression	No progression	low	medium
1008-1	Ta gr2	-	-	66	66	No progression	Progression	low	low
1211-1	Ta gr1	-	-	50	50	No progression	No progression	low	low
793-1	Ta gr1	-	-	81	81	No progression	No progression	low	low
916-1	Ta gr1	-	-	68	68	No progression	No progression	low	low
1352-1	Ta gr2	-	-	38	38	No progression	No progression	low	medium
927-1	T1 gr3	-	-	68	68	No progression	No progression	medium	medium
682-2	Ta gr1	-	-	65	65	No progression	No progression	low	low
1255-1	Ta gr2	-	-	49	49	No progression	No progression	low	low
1303-1	Ta gr2	-	-	40	40	No progression	No progression	low	medium
812-1	T1 gr3	-	-	78	78	No progression	No progression	medium	medium
1346-1	Ta gr2	-	-	41	41	No progression	No progression	low	medium
539-1	Ta gr2	-	-	98	98	No progression	No progression	low	medium
841-1	Ta gr1	-	-	58	58	No progression	No progression	low	low
1060-1	Ta gr2	-	-	62	62	No progression	Progression	low	low
407-1	Ta gr2	-	-	110	110	No progression	No progression	low	low
1250-1	Ta gr1	-	-	44	44	No progression	No progression	low	medium
1093-1	Ta gr3	T1 gr3	6	59	59	No progression	Progression	medium	high
332-1	Ta gr2	-	-	67	178	No progression	Progression	low	low
1086-1	Ta gr2	-	-	53	53	Not classified	No progression	low	low
1131-1	Ta gr1	-	-	48	48	Not classified	Progression	low	low
1354-1	Ta gr3	T2+ gr3	9	-	9	Not classified	No progression	low	high
1335-1	Ta gr2	-	-	42	42	Not classified	No progression	low	medium
797-1	Ta gr3	-	-	78	78	Not classified	Progression	medium	high
1375-1	T1 gr2	-	-	39	39	Not classified	No progression	low	high
1415-1	Ta gr3	T4b	22	-	99	Not classified	No progression	medium	high
1280-1	T1 gr3	-	-	47	47	Not classified	No progression	low	medium
1146-1	Ta gr2	-	-	49	49	Not classified	Progression	low	low
703-1	Ta gr1	-	-	64	64	Not classified	Progression	low	low
746-1	Ta gr2	-	-	80	80	Not classified	Progression	low	low
1282-1	T1 gr2	-	-	46	46	Not classified	No progression	medium	high
1105-1	Ta gr2	-	-	32	32	Not classified	Progression	low	medium
843-1	Ta gr2	T2+ gr3	17	-	17	Not classified	Progression	low	high
942-1	Ta gr2	-	-	63	63	Not classified	Progression	low	low
1158-1	Ta gr2	-	-	54	214	Not classified	Progression	low	low
1379-1	Ta gr2	T1 gr2	33	39	39	Not classified	No progression	low	high
692-1	Ta gr2	-	-	41	41	Not classified	Progression	low	medium
876-1	Ta gr2	-	-	74	74	Not classified	No progression	low	medium
1053-1	T1 gr2	-	-	64	277	Not classified	No progression	low	high
1077-1	T1 gr 2	-	-	62	208	Not classified	No progression	low	low
823-2	Ta gr2	-	-	61	61	Not classified	Progression	low	medium
1210-1	Ta gr2	-	-	43	43	Not classified	Progression	low	medium
763-1	Ta gr2	-	-	83	83	Progression	Progression	low	low
829-1	Ta gr2	-	-	76	76	Progression	Progression	low	low
925-7	Ta gr2	T1 gr3	3	68	68	Progression	Progression	low	medium
760-1	T1 gr3*	-	-	84	84	Progression	Progression	high	high
684-1	T1 gr3*	-	-	74	93	Progression	No progression	high	high
1066-1	Ta gr3	-	-	53	53	Progression	Progression	medium	medium
972-1	Ta gr1	-	-	45	45	Progression	Progression	low	medium
1036-1	T1 gr3*	-	-	57	81	Progression	No progression	high	high
1024-1	T1 gr3	-	-	52	52	Progression	No progression	high	high
1656-1	Ta gr2	T1 gr3	7	12	12	Progression	Progression	medium	high
1342-1	Ta gr1	-	-	42	42	Progression	Progression	low	medium
1031-1	T1 gr3*	-	-	65	65	Progression	Progression	medium	high
441-1	Ta gr2	T1 gr3	68	99	99	Progression	Progression	low	medium
1252-1	T1 gr3*	-	-	48	48	Progression	Progression	high	high
1206-1	Ta gr1	-	-	51	51	Progression	Progression	low	low
1062-2	Ta gr3	T2+ gr3	17	-	47	Progression	Progression	medium	high
1574-1	T1 gr3	T2+ gr3	1	-	4	Progression	Progression	high	high
1349-1	Ta gr3	-	-	30	30	Progression	No progression	medium	high
1345-1	T1 gr3	T4a gr3	28	-	28	Progression	No progression	high	high
1182-1	T1 gr3	-	-	53	53	Progression	No progression	high	high
1145-1	Ta gr2	-	-	46	46	Progression	Progression	low	medium
1191-1	T1 gr4	T2 gr4	1	-	41	Progression	Progression	high	high
775-1	Ta gr3	-	-	41	41	Progression	Progression	medium	high
962-10	T1 gr2	T4a gr2-3	1	-	93	Progression	Progression	medium	high
1189-1	Ta gr1	-	-	50	50	Progression	Progression	low	medium
1330-1	Ta gr3	-	-	42	42	Progression	Progression	low	high
1290-1	Ta gr2	T1 gr3	29	44	44	Progression	Progression	low	high
1293-1	T1 gr3	-	-	45	45	Progression	No progression	high	high
780-1	Ta/T1 gr3	-	-	51	51	Progression	No progression	medium	high
1367-1	T1 gr3*	-	-	37	37	Progression	No progression	medium	high

1. Patient number followed by visit number (1= first visit to the dept. of Urology).
2. The follow-up time from sampling visit.
3. The follow-up time from first visit to the clinic.
4. The clinical risk score determined at the time of array analysis. The score is based on the clinical and histopathological information available at time of analysis.
5. The clinical risk score determined at end of follow-up or before just before progression.

Supplemental Table 3

The optimal 45 genes for predicting disease progression.

Unigene cluster (build 168)	Description	T-test ¹	5% perm ²	Gene Name	Exemplar Accession	CV
Hs.75216	protein tyrosine phosphatase, receptor type, F	4.57	4.39	<i>PTPRF</i>	AW170332	29
Hs.196914	minor histocompatibility antigen HA-1	4.20	4.09	<i>HA-1</i>	AW505086	29
Hs.106415	peroxisome proliferative activated receptor, delta	5.76	5.64	<i>PPARD</i>	AA721217	29
Hs.112160	DNA helicase homolog PIF1	3.88	3.61	<i>PIF1</i>	AF108138	29
Hs.240013	catechol-O-methyltransferase	3.49	3.17	<i>COMT</i>	AA447648	28
Hs.1578	baculoviral IAP repeat-containing 5 (survivin)	2.68	2.56	<i>BIRC5</i>	AW409701	28
Hs.27769	chromosome 14 open reading frame 69	4.04	3.80	<i>C14orf69</i>	AA610175	26
Hs.378766	hypothetical protein FLJ11323	3.73	3.46	<i>FLJ11323</i>	AK002185	25
Hs.268016	mitochondrial ribosomal protein S6	3.10	3.02	<i>MRPS6</i>	R26969	24
Hs.153752	cell division cycle 25B	3.46	3.16	<i>CDC25B</i>	S78187	24
Hs.387443	MSTP131 (MST131) mRNA, complete cds	4.37	4.23	-	AW954938	23
Hs.95231	formin homology 2 domain containing 1	3.90	3.63	<i>FHOD1</i>	NM_013241	22
Hs.53250	bone morphogenetic protein receptor, type II (serine/threonine kinase)	3.44	2.88	<i>BMPR2</i>	AA040311	29
Hs.360026	baculoviral IAP repeat-containing 6 (apollon)	3.83	3.03	<i>BIRC6</i>	AF265555	29
Hs.83532	membrane cofactor protein (CD46, trophoblast-lymphocyte cross-reactive antigen)	4.26	3.37	<i>MCP</i>	BE243982	29
Hs.389438	KIAA0590 gene product	2.33	1.95	<i>KIAA0590</i>	AI277829	29
Hs.433332	mitogen-activated protein kinase kinase 1 interacting protein 1	5.24	4.53	<i>MAP2K1IP1</i>	W23814	29
Hs.55279	serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 5	4.89	4.11	<i>SERPINB5</i>	W74001	29
Hs.439599	mannosidase, alpha, class 2A, member 1	4.95	4.31	<i>MAN2A1</i>	AI955579	29
Hs.79404	DNA segment on chromosome 4 (unique) 234 expressed sequence	6.03	5.51	<i>D4S234E</i>	BE262478	29
Hs.373588	PDZ domain containing guanine nucleotide exchange factor (GEF) 1	3.77	3.18	<i>PDZGEF1</i>	NM_014247	28
Hs.334826	splicing factor 3b, subunit 1, 155kDa	2.40	2.03	<i>SF3B1</i>	AF054284	28
Hs.5548	F-box and leucine-rich repeat protein 5	2.48	2.09	<i>FBXL5</i>	AF142481	28
Hs.414362	cytochrome b5 reductase b5R.2	4.28	3.41	<i>CYB5R2</i>	AF169802	28
Hs.303154	iduronate 2-sulfatase (Hunter syndrome)	4.86	4.04	<i>IDS</i>	H14843	28
Hs.438159	sortilin-related receptor, L (DLR class) A repeats-containing	4.65	3.79	<i>SORL1</i>	T51454	28
Hs.181461	ariadne homolog, ubiquitin-conjugating enzyme E2 binding protein, 1 (Drosophila)	3.77	3.15	<i>ARIH1</i>	AJ243190	27
Hs.84087	KIAA0143 protein	4.62	3.76	<i>KIAA0143</i>	D63477	27
Hs.307033	pleckstrin homology domain containing, family B (evectins) member 2	3.50	2.93	<i>PLEKHB2</i>	W28614	26
Hs.152925	KIAA1268 protein	3.52	2.95	<i>KIAA1268</i>	AI634522	26
Hs.20950	phospholysine phosphohistidine inorganic pyrophosphate phosphatase	3.89	3.07	<i>LHPP</i>	AA379353	26
Hs.440734	alpha thalassemia/mental retardation syndrome X-linked (RAD54 homolog, S. cerevisiae)	3.39	2.85	<i>ATRX</i>	U72937	26
Hs.446427	ornithine decarboxylase antizyme 1	4.61	3.71	<i>OAZ1</i>	BE299590	26
Hs.348514	clone IMAGE:4052238, mRNA, partial cds	4.21	3.32	-	AA037683	25
Hs.436186	type 1 tumor necrosis factor receptor shedding aminopeptidase regulator	3.59	2.99	<i>ARTS-1</i>	AI634860	25
Hs.30340	Nedd4 family interacting protein 2	3.62	3.01	<i>NDFIP2</i>	AW770994	25
Hs.11923	hypothetical protein DJ167A19.1	3.71	3.11	<i>DJ167A19.1</i>	BE156256	24
Hs.146180	hypothetical protein LOC161291	4.59	3.67	<i>LOC161291</i>	BE159718	24
Hs.416495	chromosome 1 open reading frame 8	4.89	4.17	<i>C1orf8</i>	AW327695	23
Hs.436349	reticulon 4	4.15	3.38	<i>RTN4</i>	AW239226	23
Hs.446476	succinate-CoA ligase, GDP-forming, beta subunit	4.61	3.72	<i>SUCLG2</i>	AV650537	23
Hs.372571	muscleblind-like 2 (Drosophila)	4.65	3.82	<i>MBNL2</i>	N71848	23
Hs.495628	hypothetical protein MGC4248	4.29	3.42	<i>MGC4248</i>	AW410714	22
Hs.371468	cyclin D1 (PRAD1: parathyroid adenomatosis 1)	4.35	3.49	<i>CCND1</i>	AU077231	22
Hs.439599	mannosidase, alpha, class 2A, member 1	4.71	3.84	<i>MAN2A1</i>	D63998	22

1. Result of the t-test statistics used for identifying differentially expressed genes
2. The 5% permutation level

Supplemental Table 4

The 200 best markers of progression

Unigene cluster (build 168)	Description	T-test ¹	5% perm ²	Gene Symbol	Exemplar accession
Hs.79404	DNA segment on chromosome 4 (unique) 234 expressed sequence	6.03	5.62	D4S234E	BE262478
Hs.8148	selenoprotein T	5.98	5.06	SELT	AL037800
Hs.145575	ubiquitin-like 3	5.9	4.88	UBL3	AA149707
Hs.277324	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 1 (GalNAc-T1)	5.52	4.67	GALNT1	U41514
Hs.433332	mitogen-activated protein kinase kinase 1 interacting protein 1	5.24	4.51	MAP2K1IP1	W23814
Hs.381430	Homo sapiens cDNA FLJ26252 fis, clone DMC03335	5.23	4.44	-	AA256641
Hs.439599	mannosidase, alpha, class 2A, member 1	4.95	4.39	MAN2A1	AI955579
Hs.438827	leucyl/cystinyl aminopeptidase	4.94	4.31	LNPEP	AW894856
Hs.396161	hypothetical protein FLJ21870	4.9	4.26	FLJ21870	BE176980
Hs.416495	chromosome 1 open reading frame 8	4.89	4.17	C1orf8	AW327695
Hs.55279	serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 5	4.89	4.13	SERPINB5	W74001
Hs.131842	chromosome 6 open reading frame 133	4.87	4.08	C6orf133	AB002347
Hs.303154	iduronate 2-sulfatase (Hunter syndrome)	4.86	4.03	IDS	H14843
Hs.443943	KIAA0977 protein	4.86	4.00	KIAA0977	AB023194
Hs.93354	platelet-activating factor acetylhydrolase, isoform Ib, beta subunit 30kDa	4.82	3.97	PAFAH1B2	AW390601
Hs.408096	fragile X mental retardation, autosomal homolog 1	4.8	3.93	FXR1	AI815732
Hs.183435	NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 1, 7kDa	4.78	3.92	NDUFB1	AA535762
Hs.512642	necdin-like 2	4.77	3.90	NDNL2	AA356694
Hs.26704	cytoplasmic FMR1 interacting protein 1	4.72	3.86	CYFIP1	AW068349
Hs.439599	mannosidase, alpha, class 2A, member 1	4.71	3.84	MAN2A1	D63998
Hs.372571	muscleblind-like 2 (Drosophila)	4.65	3.82	MBNL2	N71848
Hs.438159	sortilin-related receptor, L(DLR class) A repeats-containing	4.65	3.82	SORL1	T51454
Hs.171262	ets variant gene 6 (TEL oncogene)	4.62	3.79	ETV6	AI301558
Hs.84087	KIAA0143 protein	4.62	3.78	KIAA0143	D63477
Hs.446476	succinate-CoA ligase, GDP-forming, beta subunit	4.61	3.74	SUCLG2	AV650537
Hs.446427	ornithine decarboxylase antizyme 1	4.61	3.74	OAZ1	BE299590
Hs.412707	hypoxanthine phosphoribosyltransferase 1 (Lesch-Nyhan syndrome)	4.6	3.70	HPRT1	BE548641
Hs.146180	hypothetical protein LOC161291	4.59	3.68	LOC161291	BE159718
Hs.438159	sortilin-related receptor, L(DLR class) A repeats-containing	4.57	3.66	SORL1	-
Hs.172028	a disintegrin and metalloproteinase domain 10	4.53	3.65	ADAM10	NM_001110
Hs.355983	basic leucine zipper and W2 domains 1 (BZW1)	4.47	3.63	BZW1	N89487
Hs.461178	eukaryotic translation initiation factor 1A, Y-linked	4.45	3.62	EIF1AY	AA321238
Hs.54642	methionine adenosyltransferase II, beta	4.43	3.59	MAT2B	AW966728
Hs.201085	poly(A) polymerase alpha	4.43	3.56	PAPOLA	BE539101
Hs.132955	BCL2/adenovirus E1B 19kDa interacting protein 3-like	4.37	3.56	BNIP3L	AL121317
Hs.28285	ring finger 139	4.37	3.54	RNF139	AF064801
Hs.6856	ash2 (absent, small, or homeotic)-like (Drosophila)	4.37	3.52	ASH2L	AW960782
Hs.271742	ADP-ribosyltransferase (NAD+; poly (ADP-ribose) polymerase)-like 3	4.36	3.52	ADPRTL3	W19144
Hs.349256	paired immunoglobulin-like type 2 receptor beta	4.35	3.51	PILRB	AU077231
Hs.1420	fibroblast growth factor receptor 3 (achondroplasia, thanatophoric dwarfism)	4.34	3.50	FGFR3	AL119671
Hs.7037	pallidin homolog (mouse)	4.32	3.49	PLDN	AW340708
Hs.386802	hepatocellular carcinoma susceptibility protein	4.32	3.48	HCCA3	AF168712
Hs.13351	LanC lantibiotic synthetase component C-like 1 (bacterial)	4.31	3.46	LANCL1	NM_006055
Hs.495628	hypothetical protein MGC4248	4.29	3.45	MGC4248	AW410714
Hs.414362	cytochrome b5 reductase b5R.2	4.28	3.44	CYB5R2	AF169802
Hs.418581	FLJ20160 protein	4.28	3.43	FLJ20160	AW369278
Hs.198998	conserved helix-loop-helix ubiquitous kinase	4.28	3.42	CHUK	AF080157

Hs.31731	peroxiredoxin 5	4.27	3.41	PRDX5	AI805664
Hs.112694	CGI-18 protein	4.26	3.40	CGI-18	NM_015947
Hs.83532	membrane cofactor protein (CD46, trophoblast-lymphocyte cross-reactive antigen)	4.26	3.39	MCP	BE243982
Hs.438838	TAF7 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 55kDa	4.25	3.38	TAF7	AV649864
Hs.278896	UDP glycosyltransferase 1 family, polypeptide A6	4.23	3.37	UGT1A6	AV660038
Hs.101840	major histocompatibility complex, class I-related	4.23	3.37	MR1	AF010446
Hs.136295	guanine nucleotide binding protein (G protein), alpha activating activity polypeptide, olfactory type	4.22	3.35	GNAL	AV647686
Hs.348514	Homo sapiens, clone IMAGE:4052238, mRNA, partial cds	4.21	3.35	-	AA037683
Hs.178470	hypothetical protein FLJ22662	4.21	3.34	FLJ22662	AW970786
Hs.35254	zinc finger CCH type, antiviral 1	4.16	3.34	ZC3HAV1	AW580830
Hs.437606	HMG-box transcription factor 1	4.15	3.33	HBP1	AF019214
Hs.362974	hypothetical protein FKSG44	4.14	3.32	FKSG44	AW130242
Hs.272210	activating transcription factor 7 interacting protein	4.13	3.31	ATF7IP	AI873871
Hs.96996	heterogeneous nuclear ribonucleoprotein A0	4.1	3.30	HNRPA0	BE386038
Hs.16886	clone IMAGE:3352913, mRNA	4.09	3.29	-	AA053601
Hs.445264	hypothetical protein BC004507	4.09	3.29	LOC90313	AL133649
Hs.440961	calpastatin	4.08	3.28	CAST	D16217
Hs.24758	zinc finger protein 36 (KOX 18)	4.06	3.28	ZNF36	AI167810
Hs.438159	sortilin-related receptor, L(DLR class) A repeats-containing	4.06	3.27	SORL1	-
Hs.136309	SH3-domain GRB2-like endophilin B1	4.05	3.27	SH3GLB1	AA164516
Hs.434283	hypothetical protein MGC14276	4.04	3.27	MGC14276	AA774247
Hs.226581	COX15 homolog, cytochrome c oxidase assembly protein (yeast)	4.04	3.24	COX15	NM_004376
Hs.146668	tumor differentially expressed 2	4.02	3.24	TDE2	AI929568
Hs.94896	transmembrane protein 14A	3.99	3.22	TMEM14A	NM_014051
Hs.77542	Homo sapiens transcribed sequence with weak similarity to protein ref:NP_071385.1 (H.sapiens) hypothetical protein FLJ20958 [Homo sapiens]	3.98	3.21	-	AI458213
Hs.509050	tetraspanin similar to TM4SF9	3.97	3.21	DC-TM4F2	AI751157
Hs.454528	vacuolar protein sorting 35 (yeast)	3.96	3.21	VPS35	AF175265
Hs.356190	ubiquitin B	3.96	3.19	UBB	BE300110
Hs.412597	desmoglein 2	3.95	3.19	DSG2	Z26317
Hs.9343	KIAA1999 protein	3.94	3.18	KIAA1999	BE536739
Hs.167700	MAD, mothers against decapentaplegic homolog 5 (Drosophila)	3.92	3.17	MADH5	AA373452
Hs.356076	baculoviral IAP repeat-containing 4	3.92	3.17	BIRC4	H09548
Hs.438904	retinoic acid induced 1	3.92	3.16	RAI1	AL132665
Hs.104640	HIV-1 inducer of short transcripts binding protein	3.91	3.15	FBI1	AF000561
Hs.46366	zinc finger protein 91 homolog (mouse)	3.91	3.14	ZFP91	AL045404
Hs.79187	coxsackie virus and adenovirus receptor	3.9	3.13	CXADR	N34895
Hs.438159	sortilin-related receptor, L(DLR class) A repeats-containing	3.9	3.13	SORL1	-
Hs.20950	phospholysine phosphohistidine inorganic pyrophosphate phosphatase	3.89	3.12	LHPP	AA379353
Hs.318603	myristoylated alanine-rich protein kinase C substrate	3.88	3.12	MARCKS	C15105
Hs.166994	FAT tumor suppressor homolog 1 (Drosophila)	3.86	3.11	FAT	X87241
Hs.278411	NCK-associated protein 1	3.86	3.10	NCKAP1	AI479813
Hs.422340	sorcin	3.85	3.10	SRI	R20909
Hs.13500	cDNA FLJ31593 fis, clone NT2RI2002481	3.83	3.09	-	AW613780
Hs.360026	baculoviral IAP repeat-containing 6 (apollon)	3.83	3.08	BIRC6	AF265555
Hs.349109	insulin-like growth factor 2 (somatomedin A)	3.83	3.08	IGF2	-
Hs.180479	chromosome 20 open reading frame 42	3.82	3.08	C20orf42	AK000123
Hs.438159	sortilin-related receptor, L(DLR class) A repeats-containing	3.82	3.08	SORL1	-
Hs.293970	aldehyde dehydrogenase 6 family, member A1	3.81	3.07	ALDH6A1	BE297886
Hs.438970	likely ortholog of mouse IRA1 protein	3.81	3.06	IRA1	AW263124
Hs.442669	glutamate-ammonia ligase (glutamine synthase)	3.8	3.06	GLUL	W23184
Hs.21356	SWI/SNF-related, matrix-associated actin-dependent regulator of chromatin, subfamily a, containing DEAD/H box 1	3.79	3.06	SMARCAD1	AB032948
Hs.108923	RAB38, member RAS oncogene family	3.79	3.06	RAB38	N20169
Hs.373588	PDZ domain containing guanine nucleotide exchange factor (GEF) 1	3.77	3.05	PDZGEF1	NM_014247
Hs.106415	peroxisome proliferative activated receptor, delta	5.76	5.50	PPARD	AA721217

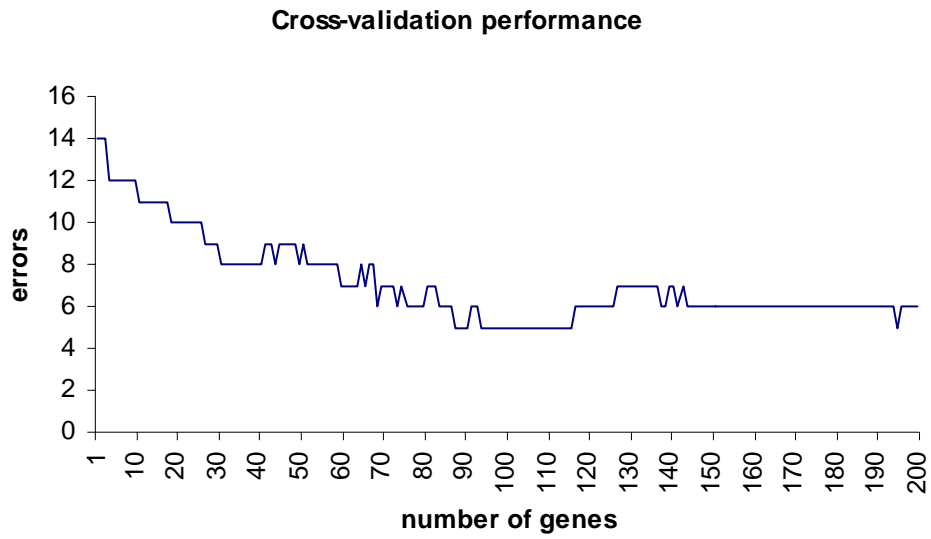
Hs.442658	aurora kinase B	5.41	5.03	AURKB	AW411425
Hs.75216	protein tyrosine phosphatase, receptor type, F	4.57	4.80	PTPRF	AW170332
Hs.408136	Homo sapiens transcribed sequence with weak similarity to protein ref:NP_060312.1 (H.sapiens) hypothetical protein FLJ20489 [Homo sapiens]	4.49	4.59	-	AW979008
Hs.15670	Homo sapiens transcribed sequences	4.42	4.50	-	AI002106
Hs.387443	Homo sapiens MSTP131 (MST131) mRNA, complete cds	4.37	4.40	-	AW954938
Hs.102336	Rho GTPase activating protein 8	4.22	4.32	ARHGAP8	-
Hs.196914	minor histocompatibility antigen HA-1	4.2	4.26	HA-1	AW505086
Hs.133352	KIAA1111 protein	4.16	4.24	KIAA1111	AW249934
Hs.134093	splicing factor, arginine/serine-rich 14	4.14	4.19	SFRS14	AW085131
Hs.396393	ubiquitin-conjugating enzyme E2S	4.11	4.10	UBE2S	BE270447
Hs.301685	plexin D1	4.1	4.07	PLXND1	AB014520
Hs.27769	chromosome 14 open reading frame 69	4.04	4.02	C14orf69	AA610175
Hs.170915	hypothetical protein FLJ10948	4.01	4.00	FLJ10948	AK001810
Hs.143601	paired immunoglobulin-like type 2 receptor beta	4.01	3.98	PILRB	AV647015
Hs.279766	kinesin family member 4A	3.98	3.96	KIF4A	AA307703
Hs.117864	Homo sapiens transcribed sequences	3.97	3.91	-	AA677934
Hs.26023	KIAA1041 protein	3.95	3.88	KIAA1041	AA228357
Hs.404525	ubiquitin fusion degradation 1-like	3.94	3.86	UFD1L	AI435128
Hs.284232	KIAA0720 protein	3.93	3.81	KIAA0720	AB018263
Hs.407912	collagen, type IV, alpha 2	3.93	3.79	COL4A2	BE501689
Hs.95231	formin homology 2 domain containing 1	3.9	3.77	FHOD1	NM_013241
Hs.112160	DNA helicase homolog PIF1	3.88	3.75	PIF1	AF108138
Hs.132977	DKFZp564J157 protein	3.87	3.74	DKFZP564J157	AA789133
Hs.491214	Homo sapiens transcribed sequence with weak similarity to protein ref:NP_060312.1 (H.sapiens) hypothetical protein FLJ20489 [Homo sapiens]	3.84	3.70	-	AI904891
Hs.380008	hypothetical protein MGC40042	3.82	3.68	MGC40042	AI627565
Hs.439505	DAZ associated protein 1	3.8	3.66	DAZAP1	AW663317
Hs.267749	unc-93 homolog A (C. elegans)	3.8	3.65	UNC93A	W92071
Hs.380810	Homo sapiens mRNA; cDNA DKFZp686G12112 (from clone DKFZp686G12112)	3.79	3.64	-	H38914
Hs.165725	CCR4-NOT transcription complex, subunit 2	3.75	3.60	CNOT2	AW973426
Hs.91521	hypothetical protein DKFZP761M1511	3.74	3.59	DKFZP761M1511	AW248434
Hs.8375	TNF receptor-associated factor 4	3.74	3.58	TRAF4	AI751601
Hs.378766	hypothetical protein FLJ11323	3.73	3.55	FLJ11323	AK002185
Hs.12420	PHD protein Jade-1	3.73	3.55	JADE1	AA954566
Hs.444400	Homo sapiens cDNA FLJ42310 fis, clone TRACH2007733	3.72	3.53	-	R44007
Hs.155106	receptor (calcitonin) activity modifying protein 2	3.71	3.51	RAMP2	NM_005854
Hs.274363	neuroglobin	3.71	3.49	NGB	R36571
Hs.211046	hypothetical protein LOC126248	3.67	3.48	LOC126248	AI825732
Hs.345588	hypothetical protein MGC45871	3.67	3.45	MGC45871	AW076098
Hs.380851	Homo sapiens, Similar to RIKEN cDNA 2610524G09 gene, clone IMAGE:4149891, mRNA	3.66	3.45	-	BE382685
Hs.117558	Homo sapiens transcribed sequences	3.65	3.43	-	AA379306
Hs.95424	mitogen-activated protein kinase kinase kinase 1	3.64	3.43	MAP4K1	-
Hs.103267	RAB3A interacting protein (rabin3)	3.64	3.42	RAB3IP	AW247012
Hs.18457	hypothetical protein FLJ20315	3.64	3.42	FLJ20315	AK000322
Hs.405819	Homo sapiens transcribed sequence with weak similarity to protein ref:NP_060312.1 (H.sapiens) hypothetical protein FLJ20489 [Homo sapiens]	3.63	3.41	-	BE079602
Hs.128392	activated p21cdc42Hs kinase	3.62	3.40	ACK1	NM_005781
Hs.55044	DKFZP586H2123 protein	3.6	3.39	DKFZP586H2123	AL050214
Hs.182099	Homo sapiens transcribed sequences	3.6	3.37	-	AI248322
Hs.131905	cation channel, sperm associated 2	3.6	3.36	CATSPER2	AW971983
Hs.372463	microtubule-actin crosslinking factor 1	3.59	3.35	MACF1	AB029290
Hs.433701	ribosomal protein L37a (RPL37A)	3.58	3.34	RPL37A	X90725
-	RC2-ST0158-091099-011-d05 ST0158 Homo sapiens cDNA, MRNA sequence	3.57	3.33	-	AW811633
Hs.106124	full length insert cDNA clone YA77F06	3.56	3.32	-	R26240
Hs.345588	hypothetical protein MGC45871	3.55	3.32	MGC45871	AA306090
Hs.195614	splicing factor 3b, subunit 3, 130kDa	3.54	3.31	SF3B3	BE260120

Hs.398102	Homo sapiens mRNA; cDNA DKFZp686L05235 (from clone DKFZp686L05235)	3.53	3.31	-	AW236939
Hs.511915	enolase 2, (gamma, neuronal)	3.52	3.30	ENO2	NM_001975
Hs.136574	arachidonate 12-lipoxygenase, 12R type	3.52	3.29	ALOX12B	-
Hs.104520	cDNA FLJ13694 fis, clone PLACE2000115	3.52	3.29	-	AI807519
Hs.136295	CHMP1.5 protein	3.52	3.28	CHMP1.5	AV647184
Hs.278839	chromosome 20 open reading frame 77	3.51	3.26	C20orf77	W74157
Hs.240013	catechol-O-methyltransferase	3.49	3.26	COMT	AA447648
Hs.46366	ciliary neurotrophic factor	3.48	3.25	CNTF	AL040328
Hs.76415	inter-alpha (globulin) inhibitor H4 (plasma Kallikrein-sensitive glycoprotein)	3.48	3.25	ITIH4	-
Hs.101474	microtubule associated testis specific serine/threonine protein kinase	3.47	3.23	MAST205	AB018350
Hs.153752	cell division cycle 25B	3.46	3.22	CDC25B	S78187
Hs.60659	similar to Rho GTPase activating protein 12	3.46	3.21	LOC201176	AA015912
Hs.129037	Homo sapiens transcribed sequences	3.46	3.20	-	AI126162
Hs.444994	Homo sapiens transcribed sequences	3.45	3.19	-	AW973078
Hs.366546	mitogen-activated protein kinase kinase 2	3.45	3.19	MAP2K2	BE302900
Hs.72222	fer-1-like 4 (C. elegans)	3.45	3.18	FER1L4	AI219207
Hs.445264	hypothetical protein BC004507	3.43	3.17	-	AL137404
-	-	3.42	3.16	-	-
Hs.110457	Wolf-Hirschhorn syndrome candidate 1	3.4	3.15	WHSC1	AJ007042
Hs.6451	PRO0659 protein	3.39	3.14	PRO0659	AW875398
Hs.74369	integrin, alpha 7	3.38	3.14	ITGA7	NM_002206
Hs.23823	hairly/enhancer-of-split related with YRPW motif-like	3.37	3.13	HEYL	R27319
Hs.273397	ubiquitin specific protease 52	3.35	3.12	USP52	AA248060
Hs.431099	membrane-associated protein 17	3.34	3.11	MAP17	NM_005764
Hs.512094	MAP kinase-interacting serine/threonine kinase 2	3.34	3.10	MKNK2	-
Hs.278027	LIM domain kinase 2	3.33	3.10	LIMK2	-
Hs.132545	Homo sapiens transcribed sequences	3.32	3.09	-	AI261960
Hs.86859	growth factor receptor-bound protein 7	3.3	3.09	GRB7	BE247550
-	-	3.3	3.08	-	-
Hs.66219	hypothetical protein FLJ31528	3.29	3.08	FLJ31528	AW502869
Hs.154525	KIAA1076 protein	3.28	3.07	KIAA1076	AB028999
Hs.123253	likely ortholog of mouse Shc SH2-domain binding protein 1	3.28	3.07	SHCBP1	AW402593
Hs.82906	CDC20 cell division cycle 20 homolog (S. cerevisiae)	3.28	3.06	CDC20	BE250127
Hs.195471	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3	3.27	3.05	PFKFB3	U15177
Hs.55044	DKFZP586H2123 protein	3.27	3.04	DKFZP586H2123	AL047332
Hs.445932	Homo sapiens transcribed sequence with weak similarity to protein ref:NP_060265.1 (H.sapiens) hypothetical protein FLJ20378 [Homo sapiens]	3.27	3.03	-	AW977370
Hs.54941	phosphorylase kinase, alpha 2 (liver)	3.27	3.03	PHKA2	D38616
Hs.270920	death associated protein 3	3.26	3.03	DAP3	AI433694
Hs.8121	Notch homolog 2 (Drosophila)	3.25	3.02	NOTCH2	-
Hs.302034	phospholipase A2, group IIF	3.23	3.02	PLA2G2F	-
-	-	3.23	3.01	-	-
Hs.438720	MCM7 minichromosome maintenance deficient 7 (S. cerevisiae)	3.22	3.01	MCM7	AW410976
Hs.32148	selenoprotein S	3.22	3.00	SELS	AA356389
Hs.127327	Homo sapiens transcribed sequence with moderate similarity to protein ref:NP_056472.1 (H.sapiens) ATP-binding cassette, sub-family A (ABC1), member 12; DKFZP434G232 protein; ATP-binding cassette transporter family A member 12 [Homo sapiens]	3.21	2.98	-	AI798039
Hs.444840	chromosome 7 open reading frame 24	3.2	2.97	C7orf24	AA378776

1. Result of the t-test statistics used for identifying differentially expressed genes
2. The 5% permutation level

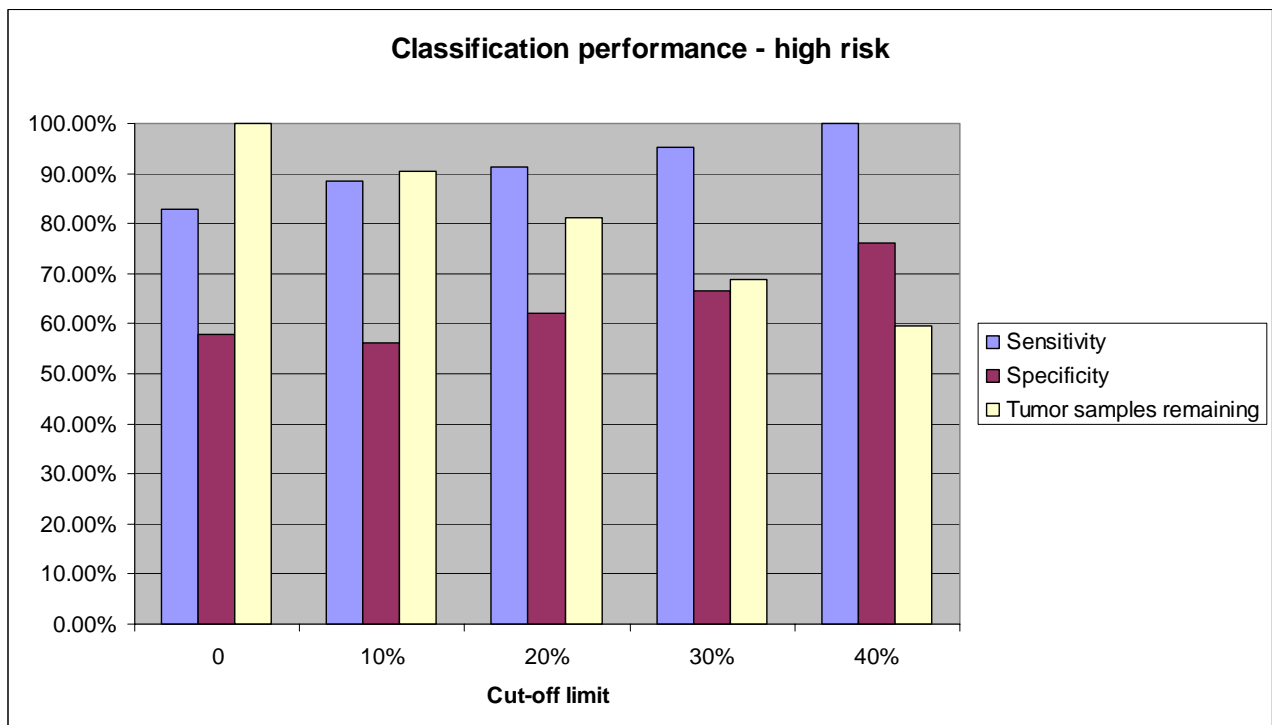
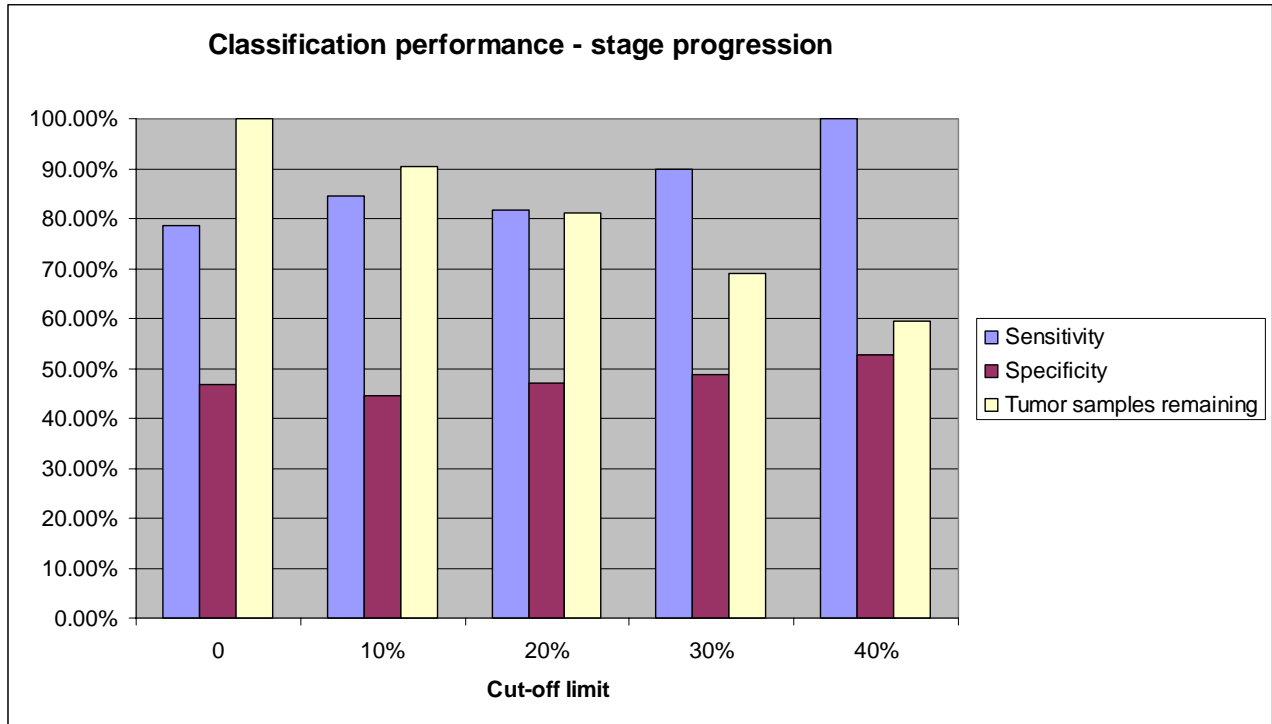
Supplemental Figure 1

Cross-validation performance when using from 1 to 200 genes in the CV-loops.



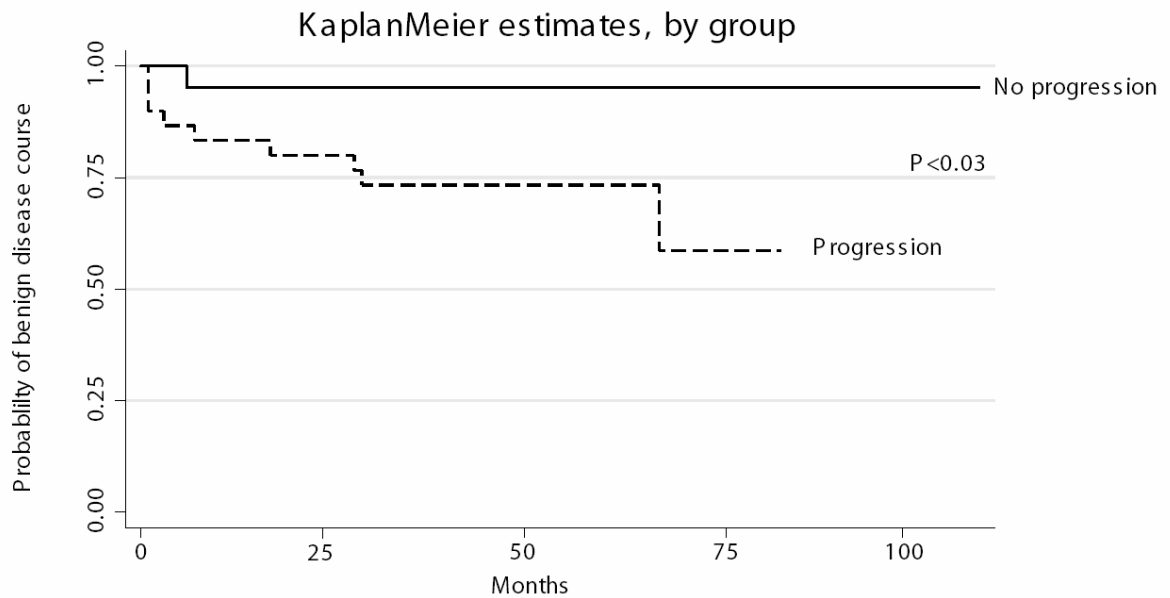
Supplemental Figure 2

Classification performance when applying from 0% to 40% cut-off limits. Graphs for both stage progression and high risk as end points are shown. The number of remaining tumor samples for classification is decreasing from 100% with no cut-off limit to 60% when applying a 40% cut-off limit.



Supplemental Figure 3

Kaplan-Meier progression estimates showing the difference in progression rates between the group classified as no progression (solid line) and the group classified as progression (dotted line). In the no progression group only one patient was scored as high risk at end of follow-up. In the progression group 20 patients were scored as high risk at end of follow-up.



No. at risk

No progression group	21	20	20	20	20
Progression group	30	24	13	3	0