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SUPPLEMENTARY MATERIAL

corresponding to:

**Expression and evolution of *Tiki1* and *Tiki2* genes
in vertebrates**

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Signal peptide

Exon 1 | 2

Human TIK11 (1) ----MSPWSEWLLQLCCLPTGACRRGAPGIANCELKFOSSLSNLSFLWTKRRPPSYFPGTIHVYPTRWVDFIPNSKAFHSSIVYFELDLDTPYT

Macaque TIK11 (1) ----MSPWSEWLLQLCCLPTGACRRGAPGIANCELKFOSSLSNLSFLWTKRRPPSYFPGTIHVYPTRWVDFIPNSKAFHSSIVYFELDLDTPYT

Rabbit Tiki1 (1) ----MSPWSEWLLQLCCLPTGACRRGAPGIANCELKFOSSLSNLSFLWTKRRPPSYFPGTIHVYPTRWVDFIPNSKAFHSSIVYFELDLDTPYT

Chicken Tiki1 (1) ----MSPWSEWLLQLCCLPTGACRRGAPGIANCELKFOSSLSNLSFLWTKRRPPSYFPGTIHVYPTRWVDFIPNSKAFHSSIVYFELDLDTPYT

Xenopus Tiki1 (1) ----MSPWSEWLLQLCCLPTGACRRGAPGIANCELKFOSSLSNLSFLWTKRRPPSYFPGTIHVYPTRWVDFIPNSKAFHSSIVYFELDLDTPYT

Human TIK12 (1) ----MHAALAGPLLAALLATARAROPPPDGGCCRPFGSORLNSFLWTKRRPPSYFPGTIHVYPTRWVDFIPNSKAFHSSIVYFELDLDTPYT

Macaque Tiki2 (1) ----MHAALAGPLLAALLATARAROPPPDGGCCRPFGSORLNSFLWTKRRPPSYFPGTIHVYPTRWVDFIPNSKAFHSSIVYFELDLDTPYT

Mouse Tiki2 (1) ----MHAALAGPLLAALLATARAROPPPDGGCCRPFGSORLNSFLWTKRRPPSYFPGTIHVYPTRWVDFIPNSKAFHSSIVYFELDLDTPYT

Rat Tiki2 (1) ----MHAALAGPLLAALLATARAROPPPDGGCCRPFGSORLNSFLWTKRRPPSYFPGTIHVYPTRWVDFIPNSKAFHSSIVYFELDLDTPYT

Guinea Pig Tiki2 (1) ----MHAALAGPLLAALLATARAROPPPDGGCCRPFGSORLNSFLWTKRRPPSYFPGTIHVYPTRWVDFIPNSKAFHSSIVYFELDLDTPYT

Squirrel Tiki2 (1) ----MHAALAGPLLAALLATARAROPPPDGGCCRPFGSORLNSFLWTKRRPPSYFPGTIHVYPTRWVDFIPNSKAFHSSIVYFELDLDTPYT

Rabbit Tiki2 (1) ----MHAALAGPLLAALLATARAROPPPDGGCCRPFGSORLNSFLWTKRRPPSYFPGTIHVYPTRWVDFIPNSKAFHSSIVYFELDLDTPYT

Chicken Tiki2 (1) ----MHAALAGPLLAALLATARAROPPPDGGCCRPFGSORLNSFLWTKRRPPSYFPGTIHVYPTRWVDFIPNSKAFHSSIVYFELDLDTPYT

Xenopus Tiki2 (1) MKGTMTARAVHFCFSGVTLLNQEVLTRRIEVDLGGCGGLRSESSLSNLSFLWTKRRPPSYFPGTIHVYPTRWVDFIPNSKAFHSSIVYFELDLDTPYT

Human TIK11 (96) ISALRSCQMLPCCGNLQDVLPRDIYRLKRHLHYKIMMFWMTPTQRCGLYADYLFNAIAGNWERKREWVMLMVNSLTEIKSRGVVPLDLAQAQ

Macaque Tiki1 (96) ISALRSCQMLPCCGNLQDVLPRDIYRLKRHLHYKIMMFWMTPTQRCGLYADYLFNAIAGNWERKREWVMLMVNSLTEIKSRGVVPLDLAQAQ

Rabbit Tiki1 (96) ISALRSCQMLPCCGNLQDVLPRDIYRLKRHLHYKIMMFWMTPTQRCGLYADYLFNAIAGNWERKREWVMLMVNSLTEIKSRGVVPLDLAQAQ

Chicken Tiki1 (93) ISALRSCQMLPCCGNLQDVLPRDIYRLKRHLHYKIMMFWMTPTQRCGLYADYLFNAIAGNWERKREWVMLMVNSLTEIKSRGVVPLDLAQAQ

Xenopus Tiki1 (95) ISALRSCQMLPCCGNLQDVLPRDIYRLKRHLHYKIMMFWMTPTQRCGLYADYLFNAIAGNWERKREWVMLMVNSLTEIKSRGVVPLDLAQAQ

Human TIK12 (94) ISLASQCLLPFGCNLQDVLPRELYRLKRHLHYKIMMFWMTPTQRCGLYADYLFNAIAGNWERKREWVMLMVNSLTEIKSRGVVPLDLAQAQ

Macaque Tiki2 (94) ISLASQCLLPFGCNLQDVLPRELYRLKRHLHYKIMMFWMTPTQRCGLYADYLFNAIAGNWERKREWVMLMVNSLTEIKSRGVVPLDLAQAQ

Mouse Tiki2 (94) ISLASQCLLPFGCNLQDVLPRELYRLKRHLHYKIMMFWMTPTQRCGLYADYLFNAIAGNWERKREWVMLMVNSLTEIKSRGVVPLDLAQAQ

Rat Tiki2 (94) ISLASQCLLPFGCNLQDVLPRELYRLKRHLHYKIMMFWMTPTQRCGLYADYLFNAIAGNWERKREWVMLMVNSLTEIKSRGVVPLDLAQAQ

Guinea Pig Tiki2 (94) ISLASQCLLPFGCNLQDVLPRELYRLKRHLHYKIMMFWMTPTQRCGLYADYLFNAIAGNWERKREWVMLMVNSLTEIKSRGVVPLDLAQAQ

Squirrel Tiki2 (94) ISLASQCLLPFGCNLQDVLPRELYRLKRHLHYKIMMFWMTPTQRCGLYADYLFNAIAGNWERKREWVMLMVNSLTEIKSRGVVPLDLAQAQ

Rabbit Tiki2 (94) ISLASQCLLPFGCNLQDVLPRELYRLKRHLHYKIMMFWMTPTQRCGLYADYLFNAIAGNWERKREWVMLMVNSLTEIKSRGVVPLDLAQAQ

Chicken Tiki2 (96) ISGLASQCLLPFGCNLQDVLPRELYRLKRHLHYKIMMFWMTPTQRCGLYADYLFNAIAGNWERKREWVMLMVNSLTEIKSRGVVPLDLAQAQ

Xenopus Tiki2 (101) ISALRSCQMLPCCGNLQDVLPRDIYRLKRHLHYKIMMFWMTPTQRCGLYADYLFNAIAGNWERKREWVMLMVNSLTEIKSRGVVPLDLAQAQ

Exon 2 | 3 3 | 4

Human TIK11 (196) ABRLLRKTGAVRVEEQCHPLNGLNSQVIFALNQTLQCESVRAGSQAQSYITEDLKHYNCGDLSLISHDSQVNFNATLPPEQVTAQEQID

Macaque Tiki1 (196) ABRLLRKTGAVRVEEQCHPLNGLNSQVIFALNQTLQCESVRAGSQAQSYITEDLKHYNCGDLSLISHDSQVNFNATLPPEQVTAQEQID

Rabbit Tiki1 (196) ABRLLRKTGAVRVEEQCHPLNGLNSQVIFALNQTLQCESVRAGSQAQSYITEDLKHYNCGDLSLISHDSQVNFNATLPPEQVTAQEQID

Chicken Tiki1 (193) ABRLLRKTGAVRVEEQCHPLNGLNSQVIFALNQTLQCESVRAGSQAQSYITEDLKHYNCGDLSLISHDSQVNFNATLPPEQVTAQEQID

Xenopus Tiki1 (195) ABRLLRKTGAVRVEEQCHPLNGLNSQVIFALNQTLQCESVRAGSQAQSYITEDLKHYNCGDLSLISHDSQVNFNATLPPEQVTAQEQID

Human TIK12 (194) ABRLLRKTGAVRVEEQCHPLNGLNSQVIFALNQTLQCESVRAGSQAQSYITEDLKHYNCGDLSLISHDSQVNFNATLPPEQVTAQEQID

Macaque Tiki2 (194) ABRLLRKTGAVRVEEQCHPLNGLNSQVIFALNQTLQCESVRAGSQAQSYITEDLKHYNCGDLSLISHDSQVNFNATLPPEQVTAQEQID

Mouse Tiki2 (194) ABRLLRKTGAVRVEEQCHPLNGLNSQVIFALNQTLQCESVRAGSQAQSYITEDLKHYNCGDLSLISHDSQVNFNATLPPEQVTAQEQID

Rat Tiki2 (194) ABRLLRKTGAVRVEEQCHPLNGLNSQVIFALNQTLQCESVRAGSQAQSYITEDLKHYNCGDLSLISHDSQVNFNATLPPEQVTAQEQID

Guinea Pig Tiki2 (194) ABRLLRKTGAVRVEEQCHPLNGLNSQVIFALNQTLQCESVRAGSQAQSYITEDLKHYNCGDLSLISHDSQVNFNATLPPEQVTAQEQID

Squirrel Tiki2 (194) ABRLLRKTGAVRVEEQCHPLNGLNSQVIFALNQTLQCESVRAGSQAQSYITEDLKHYNCGDLSLISHDSQVNFNATLPPEQVTAQEQID

Rabbit Tiki2 (194) ABRLLRKTGAVRVEEQCHPLNGLNSQVIFALNQTLQCESVRAGSQAQSYITEDLKHYNCGDLSLISHDSQVNFNATLPPEQVTAQEQID

Chicken Tiki2 (196) ABRLLRKTGAVRVEEQCHPLNGLNSQVIFALNQTLQCESVRAGSQAQSYITEDLKHYNCGDLSLISHDSQVNFNATLPPEQVTAQEQID

Xenopus Tiki2 (201) ABRLLRKTGAVRVEEQCHPLNGLNSQVIFALNQTLQCESVRAGSQAQSYITEDLKHYNCGDLSLISHDSQVNFNATLPPEQVTAQEQID

Exon 4 | 5 5 | 6

Human TIK11 (295) YLRRELYKRNRMGRVRLLEEFDFKGFPAFAGAGHFGNNTVLDLREGVEVEHPAGRIHKKGSKKTSTR-----PTLSTFALAVPTLEVFA

Macaque Tiki1 (295) YLRRELYKRNRMGRVRLLEEFDFKGFPAFAGAGHFGNNTVLDLREGVEVEHPAGRIHKKGSKKTSTR-----PTLSTFALAVPTLEVFA

Rabbit Tiki1 (295) YLRRELYKRNRMGRVRLLEEFDFKGFPAFAGAGHFGNNTVLDLREGVEVEHPAGRIHKKGSKKTSTR-----PTLSTFALAVPTLEVFA

Chicken Tiki1 (292) YLRRELYKRNRMGRVRLLEEFDFKGFPAFAGAGHFGNNTVLDLREGVEVEHPAGRIHKKGSKKTSTR-----PTLSTFALAVPTLEVFA

Xenopus Tiki1 (294) YLRRELYKRNRMGRVRLLEEFDFKGFPAFAGAGHFGNNTVLDLREGVEVEHPAGRIHKKGSKKTSTR-----PTLSTFALAVPTLEVFA

Human TIK12 (294) YLRRELYKRNRMGRVRLLEEFDFKGFPAFAGAGHFGNNTVLDLREGVEVEHPAGRIHKKGSKKTSTR-----PTLSTFALAVPTLEVFA

Macaque Tiki2 (294) YLRRELYKRNRMGRVRLLEEFDFKGFPAFAGAGHFGNNTVLDLREGVEVEHPAGRIHKKGSKKTSTR-----PTLSTFALAVPTLEVFA

Mouse Tiki2 (293) YLRRELYKRNRMGRVRLLEEFDFKGFPAFAGAGHFGNNTVLDLREGVEVEHPAGRIHKKGSKKTSTR-----PTLSTFALAVPTLEVFA

Rat Tiki2 (293) YLRRELYKRNRMGRVRLLEEFDFKGFPAFAGAGHFGNNTVLDLREGVEVEHPAGRIHKKGSKKTSTR-----PTLSTFALAVPTLEVFA

Guinea Pig Tiki2 (293) YLRRELYKRNRMGRVRLLEEFDFKGFPAFAGAGHFGNNTVLDLREGVEVEHPAGRIHKKGSKKTSTR-----PTLSTFALAVPTLEVFA

Squirrel Tiki2 (293) YLRRELYKRNRMGRVRLLEEFDFKGFPAFAGAGHFGNNTVLDLREGVEVEHPAGRIHKKGSKKTSTR-----PTLSTFALAVPTLEVFA

Rabbit Tiki2 (293) YLRRELYKRNRMGRVRLLEEFDFKGFPAFAGAGHFGNNTVLDLREGVEVEHPAGRIHKKGSKKTSTR-----PTLSTFALAVPTLEVFA

Chicken Tiki2 (295) YLRRELYKRNRMGRVRLLEEFDFKGFPAFAGAGHFGNNTVLDLREGVEVEHPAGRIHKKGSKKTSTR-----PTLSTFALAVPTLEVFA

Xenopus Tiki2 (300) YLRRELYKRNRMGRVRLLEEFDFKGFPAFAGAGHFGNNTVLDLREGVEVEHPAGRIHKKGSKKTSTR-----PTLSTFALAVPTLEVFA

Exon 6 | 7

Human TIK11 (389) PEAVSSGSHTEPFWSRPGSADTPEAQRFRFRKRRRSORRRPRLRQFSDLWVRDEESAVVPQLOVVEVLDRHISTELRIERRGHSHSSQVASSACL

Macaque Tiki1 (386) PEAVSSGSHTEPFWSRPGSADTPEAQRFRFRKRRRSORRRPRLRQFSDLWVRDEESAVVPQLOVVEVLDRHISTELRIERRGHSHSSQVASSACL

Rabbit Tiki1 (386) ALAPAEGLAAHAMPSHVSPCCSVELPEPEPKRKRKPKORRQFSDLWVRDEESAVVPQLOVVEVLDRHISTELRIERRGHSHSSQVASSACL

Chicken Tiki1 (385) PVEHLTKPEEDELPHLLPEGIDVLEKVEKVKKKKQKORRQFSDLWVRDEESAVVPQLOVVEVLDRHISTELRIERRGHSHSSQVASSACL

Xenopus Tiki1 (392) RIKQINSHKQDESIDLLEDDIDQKDER---KVKKQKORRQFSDLWVRDEESAVVPQLOVVEVLDRHISTELRIERRGHSHSSQVASSACL

Human TIK12 (392) VTEPTAPEDEDDALSPHLLPDSLQLEFEGRCQKWHKRSQTHORERQFNDLWVRDEESAVVPQLOVVEVLDRHISTELRIERRGHSHSSQVASSACL

Macaque Tiki2 (392) VTEPTAPEDEDDALSPHLLPDSLQLEFEGRCQKWHKRSQTHORERQFNDLWVRDEESAVVPQLOVVEVLDRHISTELRIERRGHSHSSQVASSACL

Mouse Tiki2 (393) ATEPTAPEDEDDALSPHLLPDSLQLEFEGRCQKWHKRSQTHORERQFNDLWVRDEESAVVPQLOVVEVLDRHISTELRIERRGHSHSSQVASSACL

Rat Tiki2 (392) VTEPTAPEDEDDALSPHLLPDSLQLEFEGRCQKWHKRSQTHORERQFNDLWVRDEESAVVPQLOVVEVLDRHISTELRIERRGHSHSSQVASSACL

Guinea Pig Tiki2 (391) VTEPTAPEDEDDALSPHLLPDSLQLEFEGRCQKWHKRSQTHORERQFNDLWVRDEESAVVPQLOVVEVLDRHISTELRIERRGHSHSSQVASSACL

Squirrel Tiki2 (391) VTEPTAPEDEDDALSPHLLPDSLQLEFEGRCQKWHKRSQTHORERQFNDLWVRDEESAVVPQLOVVEVLDRHISTELRIERRGHSHSSQVASSACL

Rabbit Tiki2 (391) ATEPTAPEDEDDALSPHLLPDSLQLEFEGRCQKWHKRSQTHORERQFNDLWVRDEESAVVPQLOVVEVLDRHISTELRIERRGHSHSSQVASSACL

Chicken Tiki2 (393) PSLKPLQDEDEDSPHLLPDSLQLEFEGRCQKWHKRSQTHORERQFNDLWVRDEESAVVPQLOVVEVLDRHISTELRIERRGHSHSSQVASSACL

Xenopus Tiki2 (394) AAVSVCPEDEDDALSPHLLPDSLQLEFEGRCQKWHKRSQTHORERQFNDLWVRDEESAVVPQLOVVEVLDRHISTELRIERRGHSHSSQVASSACL

Human TIK11 (486) LWTPV----FWLVLAFOQETEDL

Macaque Tiki1 (486) LWTPV----FWLVLAFOQETEDL

Rabbit Tiki1 (486) LWTPV----FWLVLAFOQETEDL

Chicken Tiki1 (484) SHSLI---LSLITSAHLMRL

Xenopus Tiki1 (489) SHPSA---FLTAMCFQVAVLQ

Human TIK12 (491) SHPTL---GLTEPATITAVCFLLSLGSP

Macaque Tiki2 (491) SHPTL---GLTEPATITAVCFLLSLGSP

Mouse Tiki2 (491) SHPTL---GLTEPATITAVCFLLSLGSP

Rat Tiki2 (490) SHPTL---GLTEPATITAVCFLLSLGSP

Guinea Pig Tiki2 (490) SHPTL---GLTEPATITAVCFLLSLGSP

Squirrel Tiki2 (490) SHPTL---GLTEPATITAVCFLLSLGSP

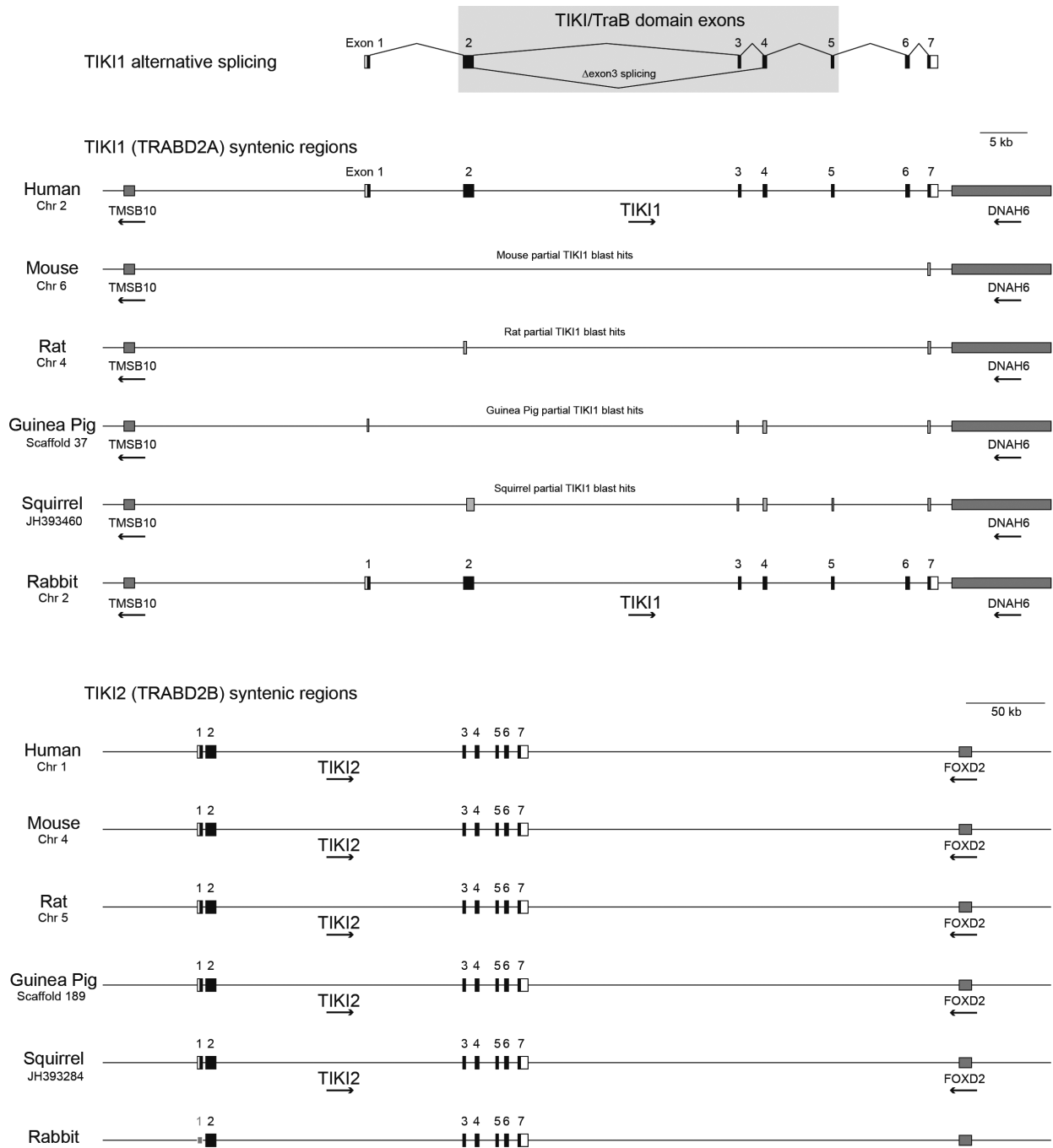
Rabbit Tiki2 (490) SHPTL---GLTEPATITAVCFLLSLGSP

Chicken Tiki2 (492) PTTASATILWSPVPLVVAISPLNLLP

Xenopus Tiki2 (493) SNSSPK---CLSASPFYTLVTLTITMRTS

(Transmembrane)

Supplementary Fig. S1. ClustalW alignment of TIK1 proteins from Human, Macaque, Rabbit, Chicken, Xenopus and for rodent Tiki2: Mouse, Rat, Guinea Pig and Squirrel. Black, grey, and light grey represent identical, conservative, and similar amino acid residues, respectively. The alignment is annotated with exon/intron boundaries, predicted signal peptide cleavage sites and predicted transmembrane regions. Conserved cysteines are highlighted in yellow below the alignment. Protein sequence details and accession numbers are listed in the Materials and Methods section.



Supplementary Fig. S2. Genomic structures of *TIK1* genes and syntenic regions. (A) Vertebrate *TIK1* genes are encoded by seven exons, with the conserved *TIK1/TraB* domain mainly contained within exons 2-5. Exon coding regions are displayed in black and non-coding regions in white. Exon 3 is 147 base pairs and encodes 49 amino acids within the *TIK1/TraB* domain and contains one of four conserved cysteine residues (see Fig S1). Human *TIK1* has an alternative spliced transcript that lacks exon 3 (NM_001080824.2, NP_001074293.1) without altering the reading frame of the remaining 3' exons. We have independently cloned this form of *Tiki1* cDNA lacking exon3 from Human, Rabbit and Chicken. **(B)** Syntenic genomic regions annotated and scaled to the Human *TIK1* locus based on the current genomic assemblies. For simplicity, genomic regions are presented with the *TIK1* genes 5' to 3'. Flanking genes *TMSB10* (*Thymosin beta-10*) and *DNAH6* (*Dynein heavy chain 6, axonemal*) were identified in the "*Tiki1*" genomic region of all rodents. Genomic distances between *TMSB10* and *DNAH6* (Human 96kb, Mouse 59kb, Rat 51kb, Guinea Pig 119kb, Squirrel 106kb, Rabbit 113kb) reveal a greater number of intergenic deletions in the mouse and the rat. BLASTN alignment of the Human *TIK1* cDNA with the rodent *Tiki1* genomic regions unveils the remnants of the *Tiki1* exons (shown with gray boxes and positioned relative to Human *TIK1*) although many coding changes are observed and the reading frame is not maintained in the rodent exon fragments. **(C)** The syntenic *TIK2* genomic region annotated and scaled to Human *TIK2*. The neighboring gene *FOXD2* (*Forkhead box D2*) is shown to verify the *TIK2* genomic region. The mouse, rat, guinea pig and squirrel contain a full-length *Tiki2* genes in the current genomic assemblies. A gap in the genomic Rabbit *Tiki2* exon1 region is shaded gray. This region is GC rich and frequently absent in other mammalian genome assemblies.

SUPPLEMENTARY TABLE S1

ALTERED EXPRESSION OF TIK1 AND TIK2 IN CANCERS AND OTHER DISEASES

Human TIK1 (TRABD2A)

Tissue/cell type	Comparison groups (a vs b)	log2foldchange		Sample size (a vs b)	DataSet accession	Design Element/reporter
		(a/b)	p-value			
gastric tissue	Gastric Cancer vs. Normal	1.95	1,00E-03	12 vs 3	GSE19826	227867_at
endometrial tissues	disease state: 'ovarian endometriosis' vs 'normal'	1.83	7,19E-05	10 vs 10	GDS2835	227867_at
testicular parenchyma	Testicular Seminoma vs. Normal	1.81	2,90E-02	3 vs 3	GSE1818	BC051789
gastric vs. mucosa	Gastric Mixed Adenocarcinoma vs. Normal mucosa	1.28	4,10E-02	4 vs 31	GSE13911	227867_at
kidney	Papillary Renal Cell Carcinoma vs. Normal	1.18	9,00E-03	19 vs 3	GSE11151	227867_at
prostate gland	Prostate Carcinoma vs. Normal	1.04	4,80E-02	7 vs 6	GSE3325	227867_at
B-lymphocytes	Follicular Lymphoma vs. Normal	1.03	9,57E-15	38 vs 20	GSE12195	227867_at
gastric vs. mucosa	Gastric Intestinal Type Adenocarcinoma vs. Normal mucosa	1.02	3,00E-03	26 vs 31	GSE13911	227867_at
B-lymphocytes	Activated B-Cell-Like Diffuse Large B-Cell Lymphoma vs. Normal	0.88	1,25E-05	17 vs 20	GSE12195	227867_at
colon vs. mucosa	Colon Adenoma vs. Normal mucosa	0.76	1,14E-04	5 vs 10	GSE20916	227867_at
colon vs. mucosa	Colon Carcinoma vs. Normal mucosa	0.65	7,00E-05	5 vs 10	GSE20916	227867_at
bone marrow	Monoclonal Gammopathy of Undetermined Significance vs. Normal	0.64	2,57E-04	44 vs 22	GSE5900	227867_at
thyroid gland	Thyroid Gland Papillary Carcinoma vs. Normal	0.61	2,70E-02	14 vs 4	GSE6004	227867_at
B-lymphocytes	Diffuse Large B-Cell Lymphoma vs. Normal	0.61	1,66E-08	44 vs 20	GSE12195	227867_at
umbilical cord tissues (higher gestational age)	disease state: 'bronchopulmonary dysplasia' vs 'control'	0.61	3,63E-02	5 vs 21	GDS3356	227867_at
T-lymphocyte	Angioimmunoblastic T-Cell Lymphoma vs. Normal	-0.60	3,60E-02	6 vs 20	GSE6338	227867_at
colon	Cecum Adenocarcinoma vs. Normal	-0.62	7,11E-04	17 vs 5	GSE5206	227867_at
colon	Rectal Adenocarcinoma vs. Normal	-0.63	1,20E-02	8 vs 5	GSE5206	227867_at
bone marrow	Acute Myeloid Leukemia vs. Normal	-0.66	1,50E-13	542 vs 74	GSE13159	227867_at
brain	Anaplastic Astrocytoma vs. Normal	-0.69	3,88E-06	19 vs 23	GSE4290	227867_at
lung	Large Cell Lung Carcinoma vs. Normal	-0.69	2,04E-08	19 vs 65	GSE19188	227867_at
brain	Glioblastoma vs. Normal	-0.70	2,67E-07	81 vs 23	GSE4290	227867_at
colon	Rectosigmoid Adenocarcinoma vs. Normal	-0.70	1,00E-03	10 vs 5	GSE5206	227867_at
breast	Invasive Breast Carcinoma vs. Normal	-0.70	1,00E-05	76 vs 61	TCGA RNA-seq	A_24_P268487
bone marrow	Pro-B Acute Lymphoblastic Leukemia vs. Normal	-0.75	2,64E-15	70 vs 74	GSE13159	227867_at
bone marrow	T-Cell Acute Lymphoblastic Leukemia vs. Normal	-0.76	9,68E-16	174 vs 74	GSE13159	227867_at
brain	Oligodendroglioma vs. Normal	-0.76	8,02E-07	50 vs 23	GSE4290	227867_at
bone marrow	Chronic Myelogenous Leukemia vs. Normal	-0.77	5,22E-14	76 vs 74	GSE13159	227867_at
ovarian surface epithelium	Ovarian Mucinous Adenocarcinoma vs. Normal	-0.91	1,30E-02	9 vs 5	Lu KH et al., 2004	51270_at
brain	Diffuse Astrocytoma vs. Normal	-0.91	2,60E-02	7 vs 23	GSE4290	227867_at
breast	Invasive Ductal Breast Carcinoma vs. Normal	-0.96	3,00E-03	23 vs 2	GSE1477	AA399461
colon	Colon Mucinous Adenocarcinoma vs. Normal	-0.96	6,86E-05	13 vs 5	GSE5206	227867_at
ovarian surface epithelium	Ovarian Clear Cell Adenocarcinoma vs. Normal	-1.02	8,00E-03	7 vs 5	Lu KH et al., 2004	51270_at
rectum and colon	Rectosigmoid Adenocarcinoma vs. Normal	-1.14	2,60E-02	3 vs 22	TCGA RNA-seq	A_23_P255897
breast	Invasive Ductal Breast Carcinoma vs. Normal	-1.14	6,76E-13	389 vs 61	TCGA RNA-seq	A_23_P56703
ovarian surface epithelium	Ovarian Endometrioid Adenocarcinoma vs. Normal	-1.28	4,00E-03	9 vs 5	Lu KH et al., 2004	51270_at
ovarian surface epithelium	Ovarian Serous Adenocarcinoma vs. Normal	-1.34	4,00E-03	20 vs 5	Lu KH et al., 2004	51270_at
breast	Male Breast Carcinoma vs. Normal	-1.46	2,00E-03	3 vs 61	TCGA RNA-seq	A_24_P268487
breast	Mucinous Breast Carcinoma vs. Normal	-1.55	5,80E-15	4 vs 61	TCGA RNA-seq	A_24_P268487
breast	Invasive Mixed Breast Carcinoma vs. Normal	-1.63	3,60E-02	3 vs 8	GSE1477	H53191
bone	disease:'osteosarcoma' vs 'normal' on A-AFFY-44	-1.85	1,43E-06	14 vs 4	E-MEXP-3628	227867_at

Human TIK2 (TRABD2A)

Tissue/cell type	Comparison groups (a vs b)	log2foldchange		Sample size (a vs b)	DataSet accession	Design Element/reporter
		(a/b)	p-value			
peripheral blood from multiple sclerosis patients	genotype/variation: 'high serum Sema4A' vs 'low serum Sema4A'	2.35	3,79E-02	3 vs 3	GDS4152	241707_at
skin	Skin Basal Cell Carcinoma vs. Normal	1.78	4,00E-03	15 vs 4	GSE7553	241707_at
skin	Skin Squamous Cell Carcinoma vs. Normal	1.52	1,00E-02	11 vs 4	GSE7553	241707_at
cancer stroma vs. normal breast	Invasive Breast Carcinoma Stroma vs. Normal	1.36	7,62E-05	53 vs 6	GSE9014	A_32_P232214
breast	Invasive Mixed Breast Carcinoma vs. Normal	1.30	1,40E-02	3 vs 7	GSE1477	AW291482
vulva	Vulvar Intraepithelial Neoplasia vs. Normal	1.25	1,00E-02	9 vs 10	GSE5563	241707_at
kidney	Clear Cell Renal Cell Carcinoma vs. Normal	1.10	7,14E-05	26 vs 3	GSE11151	241707_at
gastric tissue	Gastric Cancer vs. Normal	1.06	1,50E-02	12 vs 3	GSE19826	244472_at
skin	Cutaneous Melanoma vs. Normal	1.05	3,60E-02	14 vs 4	GSE7553	241707_at
breast	Ductal Breast Carcinoma in Situ vs. Normal	1.04	3,40E-02	3 vs 7	GSE1477	AW291482
testis	Yolk Sac Tumor, NOS vs. Normal	1.01	6,81E-09	9 vs 6	GSE3218	241707_at
breast	Invasive Lobular Breast Carcinoma vs. Normal	0.98	4,10E-02	6 vs 7	GSE1477	AW291482
gastric vs. mucosa	Gastric Intestinal Type Adenocarcinoma vs. Normal mucosa	0.65	2,00E-02	26 vs 31	GSE13911	244472_at
rectum and colon	Rectal Adenocarcinoma vs. Normal	-0.59	1,00E-03	60 vs 22	TCGA RNA-seq	A_32_P232218
prostate gland	Prostate Carcinoma vs. Normal	-0.71	3,20E-02	7 vs 6	GSE3325	244472_at
gastric tissue	Gastric Cancer vs. Normal	-0.72	2,70E-02	12 vs 3	GSE19826	241707_at
breast	Ductal Breast Carcinoma vs. Normal	-0.72	6,00E-03	40 vs 7	GSE3744	244472_at
bone marrow	Smoldering Myeloma vs. Normal	-0.77	6,00E-03	12 vs 22	GSE5900	244472_at
rectum and colon	Colon Adenocarcinoma vs. Normal	-0.80	1,63E-05	101 vs 22	TCGA RNA-seq	A_32_P232218
synovial tissues	disease state: 'rheumatoid arthritis' vs 'normal'	-0.89	2,70E-02	4 vs 4	GDS1857	12558
rectum and colon	Rectal Mucinous Adenocarcinoma vs. Normal	-1.00	1,70E-02	6 vs 22	TCGA RNA-seq	A_32_P232218
breast	Invasive Breast Carcinoma vs. Normal	-1.31	6,83E-10	76 vs 61	TCGA RNA-seq	A_32_P232214
skin	Cutaneous Melanoma vs. Normal	-1.45	1,80E-02	14 vs 4	GSE7553	244472_at
breast	Invasive Ductal Breast Carcinoma vs. Normal	-1.51	4,83E-22	389 vs 61	TCGA RNA-seq	A_32_P232218
ductal breast cell	Invasive Ductal Breast Carcinoma vs. Normal	-2.00	4,30E-02	5 vs 10	GSE5764	244472_at
bone	disease:'osteosarcoma' vs 'normal' on A-AFFY-44	-2.44	1,10E-05	14 vs 4	E-MEXP-3628	244472_at
breast	Mucinous Breast Carcinoma vs. Normal	-2.46	6,00E-03	4 vs 61	TCGA RNA-seq	A_32_P232218

In order to gain insights into the expression alteration of *TIK1* (TRABD2A) and *TIK2* (TRABD2B) in human diseases, a gene-based analysis was performed using public accessible databases of NCBI Geo Profiles (Barrett et al., 2013), ArrayExpress (Parkinson et al., 2011), and OncoPrint (Rhodes et al., 2007). A threshold of 1.5 times fold change ($|\log_2(\text{fold change})| > 0.585$) and $p\text{-value} < 0.05$ was applied to identify differential gene expression. The result, ranked by gene expression fold changes, is summarized in the table. According to this analysis, *TIK1* and *TIK2* are both down-regulated in breast and colon carcinoma, up-regulated in kidney and testis tumors, which may reflect altered Wnt signaling in these diseases. In addition, *TIK1* expression increases in gastric cancer, endometrial tissue of patients with endometriosis, prostate carcinoma, and thyroid gland papillary carcinoma, and decreases in osteosarcoma, ovarian adenocarcinoma, and brain tumors. The differential expression of *TIK1* in various kinds of lymphoma and leukemia might result from the population drift of different B cell or T cell subtypes (Piccaluga et al., 2007). *TIK2* increases in skin carcinoma, melanoma, and vulvar neoplasia, while it decreases in osteosarcomas, rheumatoid arthritis and gastric cancer. Similar to that seen with other Wnt inhibitors, *TIK2* downregulation appears to correlate with osteosarcoma growth (Li et al., 2014).