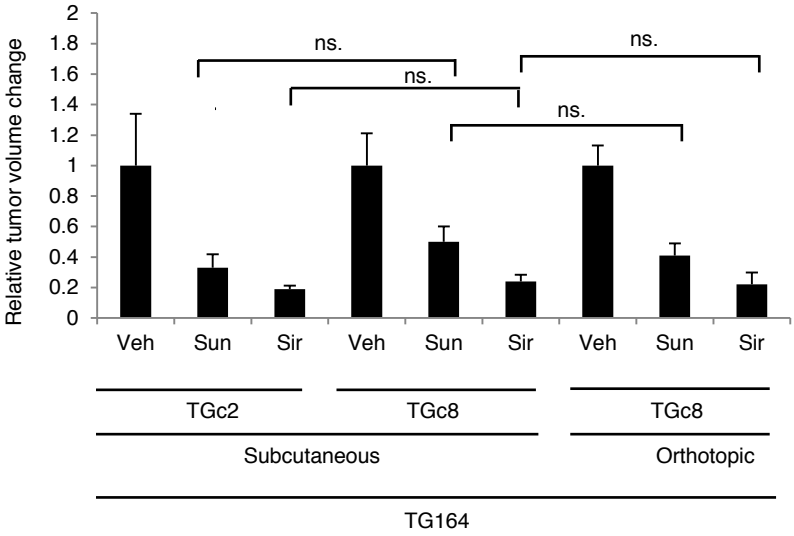

Fig. S1. Evaluation of the effects of implantation site (orthotopically vs subcutaneous) and passage on treatment for tumorgraft line TG164. Data are mean tumor volumes at the end of drug trial + SE (*n*=3 per treatment arm). Veh, vehicle; Sun, sunitinib; Sir, sirolimus; ns., not significant.

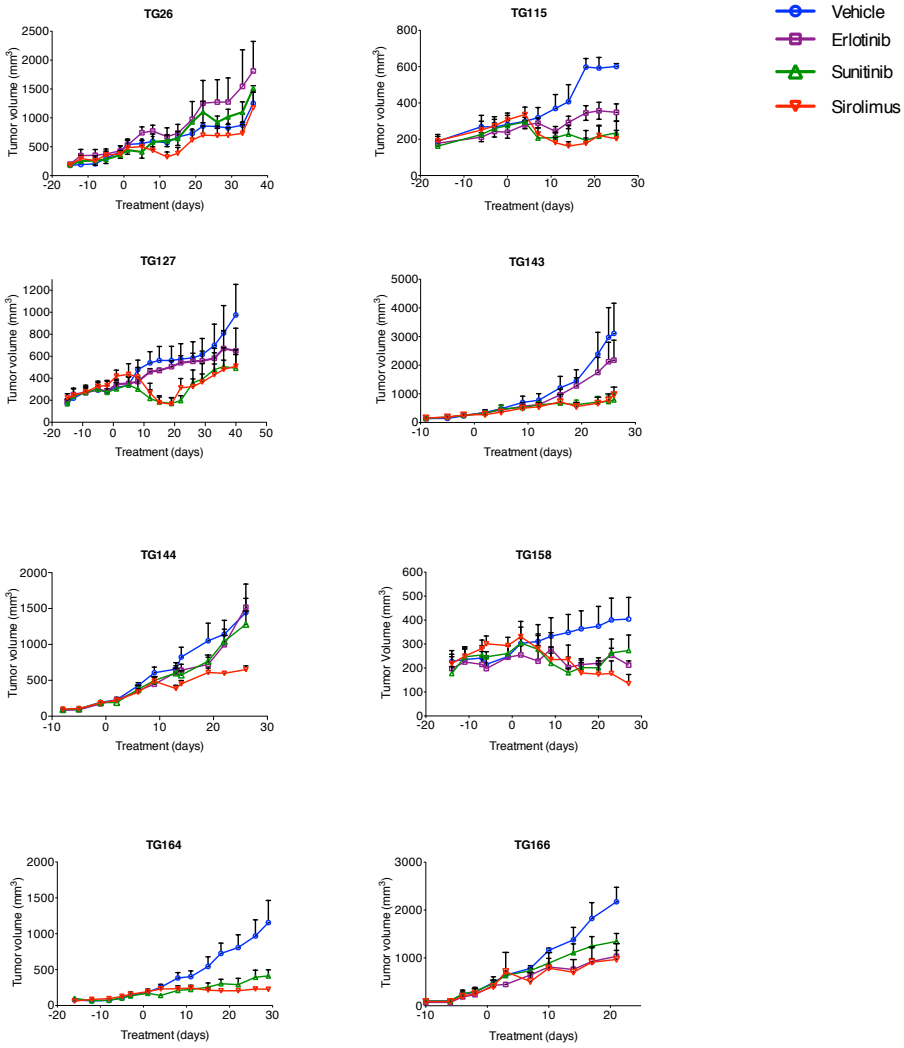

Fig. S2. Sunitinib, sirolimus, and erlotinib drug trials by individual tumorgraft line. Data are means + SE (*n*=3-5 per treatment arm).

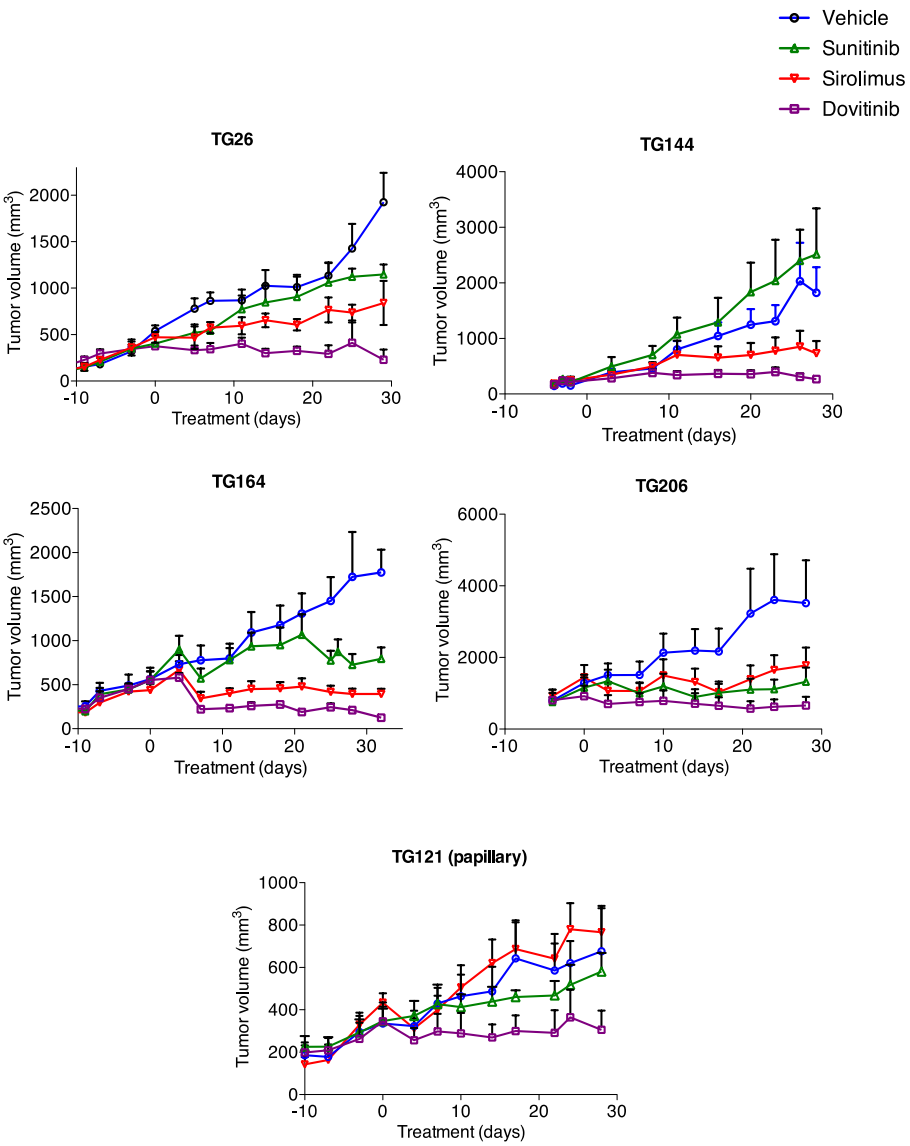

Fig. S3. Dovitinib drug trials by tumorgraft line including a papillary line (TG121). Data are means + SE (*n*=3-5 per treatment arm).

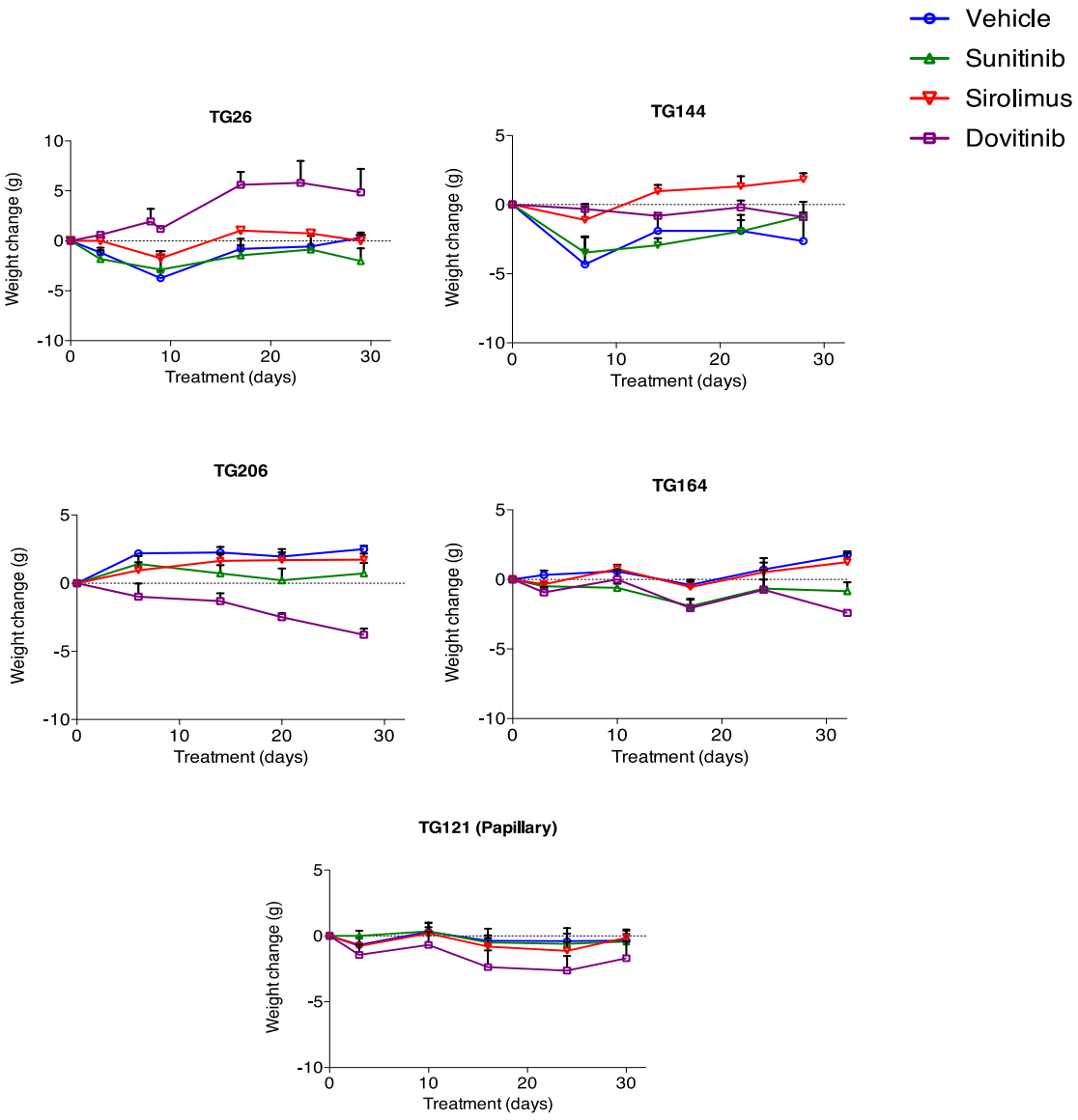

Fig. S4. Treatment effects on mouse weights. Data are means + SE (*n*=3-5 per treatment arm).

Table S1. Histological evaluation of tumor and corresponding tumorgraft cohort

ID	Sample	Histology	Grade	Architecture, morphology or nucleolar features	Cytoplasmic features	Inflammatory cells
TG115	T (diagn.)	clear-cell	3	nested	clear; abundant	lymphocytes
	T (flank.)	clear-cell	3	nested; mostly necrotic	clear	lymphocytes
	TGc1	clear-cell	3	nested; prominent nucleoli	clear	
	TGc2	clear-cell	3	nested	clear; abundant	
	TGc3	clear-cell	3	nested	clear; abundant	
	TGc4	clear-cell	3	nested	clear; abundant	
TG121	T (diagn.)	papillary	3	solid; papillary	eosinophilic	
	T (flank.)	papillary	3	solid; papillary	eosinophilic	
	TGc0	papillary	3	solid; papillary	eosinophilic	
	TGc2	papillary	3	solid; papillary	eosinophilic	
	TGc3	papillary	3	solid; papillary	eosinophilic	
	TGc5	papillary	3	solid; papillary	eosinophilic	
TG127	T (flank.)	clear-cell	3	nested	clear	lymphocytes
	TGc0	clear-cell	2	nested; oval nucleoli	clear	lymphocytes
	TGc1	papillary with clear-cell	2	nested	clear	
	TGc3	papillary with clear-cell	2	nested	clear	
	TGc4	papillary with clear-cell	2	nested	clear	
TG142	T (diagn.)	clear-cell	3	nested	clear	
	T (flank.)	clear-cell	2	nested	clear	
	TGc1	clear-cell	2	nested	clear	
	TGc2	clear-cell	2	nested	clear	
	TGc3	clear-cell	2	nested	clear	
TG143	T (diagn.)	clear-cell with 97% sarcomatoid	4	nested; spindle	clear	
	T (flank.)	papillary with <1% sarcomatoid	4	spindle	eosinophilic	
	TGc0	sarcomatoid	4	spindle	eosinophilic	
	TGc4	sarcomatoid	4	spindle; epithelioid	eosinophilic	
	TGc7	sarcomatoid	4	spindle; epithelioid	eosinophilic	
	TGc14	sarcomatoid	4	spindle; epithelioid	eosinophilic	
TG144	T (diagn.)	clear-cell	3	nested; necrotic	clear	lymphocytes; neutrophils
	T (flank.)	clear-cell	2	nested; necrotic	clear	lymphocytes; neutrophils
	TGc0	clear-cell	3	nested; spindle	clear	neutrophils
	TGc2	clear-cell	3	nested; spindle	clear	neutrophils
	TGc5	clear-cell	3	nested; spindle	clear	neutrophils
	TGc6	clear-cell	3	nested; spindle	clear	neutrophils
	TGc11	clear-cell	3	nested; spindle	clear	neutrophils
TG152	T (diagn.)	poorly differentiated carcinoma	4	spindle; epithelioid; prominent nucleoli; perinuclear clearing	eosinophilic	
	T (flank.)	<5% undifferentiated tumor cells	4	spindle, prominent nucleoli	eosinophilic	
	TGc0	poorly differentiated carcinoma	4	solid; prominent nucleoli	eosinophilic	
	TGc1	poorly differentiated carcinoma	4	solid; perinuclear clearing	eosinophilic	
	TGc2	poorly differentiated carcinoma	4	solid; perinuclear clearing	eosinophilic	
TG156	T (diagn.)	papillary	3	papillary	eosinophilic	
	T (flank.)	papillary	3	papillary	eosinophilic	
	TGc1	papillary	3	papillary	eosinophilic	
	TGc2	papillary	3	papillary	eosinophilic	
TG158	T (diagn.)	clear-cell with focal papillary	3	nested	clear	
	T (flank.)	clear-cell	3	nested	clear	
	TGc0	clear-cell	3	nested	clear	
	TGc1	clear-cell	3	nested	clear	
	TGc2	clear-cell	3	nested	clear; eosinophilic	
TG164	T (diagn.)	sarcomatoid with clear-cell	4	fascicular; spindle	eosinophilic	
	T (flank.)	sarcomatoid	4	fascicular; spindle	eosinophilic	
	TGc0	sarcomatoid	4	fascicular; spindle	eosinophilic	
	TGc2	sarcomatoid	4	fascicular; spindle	eosinophilic	
	TGc5	sarcomatoid	4	fascicular; spindle	eosinophilic	
	TGc6	sarcomatoid	4	fascicular; spindle	eosinophilic	
	TGc11	sarcomatoid	4	fascicular; spindle	eosinophilic	
TG165	T (flank.)	clear-cell	3	nested	clear; eosinophilic	lymphocytes
	TGc0	clear-cell	3	nested	clear	
	TGc1	clear-cell	3	nested	clear	
TG166	T (diagn.)	rhabdoid with sarcomatoid	4	solid	granular eosinophilic	
	T (flank.)	rhabdoid	4	solid; nested	granular eosinophilic; abundant	
	TGc0	rhabdoid	4	solid	granular eosinophilic	
	TGc5	rhabdoid with sarcomatoid	4	solid	granular eosinophilic	
	TGc8	rhabdoid with sarcomatoid	4	solid	granular eosinophilic	
TG168	T (flank.)	unclassified	3	solid; tubular; prominent nucleoli	granular eosinophilic; comedonecrosis	
	TGc0	unclassified	3	solid; tubular; peritubular fibrosis; prominent nucleoli	granular eosinophilic; comedonecrosis	
	TGc1	unclassified	3	solid; tubular; peritubular fibrosis; prominent nucleoli	granular eosinophilic; comedonecrosis	
	TGc2	unclassified	3	solid; tubular; peritubular fibrosis; prominent nucleoli	granular eosinophilic; comedonecrosis	
TG169	T (diagn.)	unclassified	3	solid; tubular; papillary; predominantly necrotic	granular eosinophilic	
	T (flank.)	unclassified	3	solid; tubular; papillary; predominantly necrotic	granular eosinophilic	
	TGc0	unclassified	3	nested	granular eosinophilic	
	TGc1	unclassified	3	solid; predominantly necrotic	granular eosinophilic	
	TGc2	unclassified	3	solid; tubular; papillary; predominantly necrotic	granular eosinophilic	
	TGc3	unclassified	3	solid; tubular; papillary; predominantly necrotic	granular eosinophilic	
TG180	T (flank.)	clear-cell	2	nested	clear	
	TGc0	clear-cell	2	nested	clear	
	TGc1	clear-cell	2	nested	clear	
TG206	T (flank.)	clear-cell	3	solid; nested	clear	
	TGc0	clear-cell	3	solid; nested	clear	
	TGc2	clear-cell	3	solid; nested	clear	
	TGc3	clear-cell	3	solid; nested	clear	
	TGc4	clear-cell	3	solid; nested; some spindle	clear	

T (diagn.), surgical pathology tissue for diagnosis; T (flank.), flanking sections from samples used for tumorgraft generation; TGc#, tumorgraft cohort number

Table S2. Overrepresented Ingenuity Pathways corresponding to probesets upregulated in tumors over tumorgrafts (FDR q <0.05, FC>1.5).

	Ingenuity Canonical Pathways	*p*	Ratio
1	Role of NFAT in Regulation of the Immune Response	**6E-21**	0.28
2	Systemic Lupus Erythematosus Signaling	**6E-20**	0.29
3	Antigen Presentation Pathway	**2E-17**	0.56
4	Dendritic Cell Maturation	**1E-16**	0.25
5	iCOS-iCOSL Signaling in T Helper Cells	**3E-15**	0.30
6	PKCθ Signaling in T Lymphocytes	**5E-15**	0.27
7	CTLA4 Signaling in Cytotoxic T Lymphocytes	**8E-15**	0.34
8	CD28 Signaling in T Helper Cells	**1E-14**	0.29
9	T Helper Cell Differentiation	**3E-14**	0.39
10	Communication between Innate and Adaptive Immune Cells	**4E-14**	0.29
11	Natural Killer Cell Signaling	**4E-14**	0.32
12	Hepatic Fibrosis / Hepatic Stellate Cell Activation	**6E-14**	0.27
13	Type I Diabetes Mellitus Signaling	**8E-14**	0.29
14	Crosstalk between Dendritic Cells and Natural Killer Cells	**3E-13**	0.32
15	Graft-versus-Host Disease Signaling	**4E-13**	0.44
16	T Cell Receptor Signaling	**1E-12**	0.29
17	Primary Immunodeficiency Signaling	**8E-12**	0.35
18	Cytotoxic T Lymphocyte-mediated Apoptosis of Target Cells	**2E-11**	0.32
19	Leukocyte Extravasation Signaling	**3E-11**	0.22
20	Role of Pattern Recognition Receptors in Recognition of Bacteria and Viruses	**4E-11**	0.30
21	Altered T Cell and B Cell Signaling in Rheumatoid Arthritis	**8E-11**	0.29
22	G-Protein Coupled Receptor Signaling	**1E-10**	0.16
23	OX40 Signaling Pathway	**1E-10**	0.29
24	Autoimmune Thyroid Disease Signaling	**1E-10**	0.33
25	Allograft Rejection Signaling	**3E-10**	0.28
26	IL-4 Signaling	**7E-10**	0.32
27	Calcium-induced T Lymphocyte Apoptosis	**1E-09**	0.31
28	Role of Macrophages, Fibroblasts and Endothelial Cells in Rheumatoid Arthritis	**1E-09**	0.17
29	Growth Hormone Signaling	**1E-09**	0.31
30	B Cell Development	**2E-09**	0.43
31	NF-κB Signaling	**2E-09**	0.21
32	Complement System	**6E-09**	0.43
33	Pathogenesis of Multiple Sclerosis	**8E-09**	0.89
34	Role of JAK1 and JAK3 in γc Cytokine Signaling	**2E-08**	0.29
35	Phospholipase C Signaling	**2E-08**	0.17
36	Fcγ Receptor-mediated Phagocytosis in Macrophages and Monocytes	**4E-08**	0.25
37	TREM1 Signaling	**5E-08**	0.27
38	Nur77 Signaling in T Lymphocytes	**7E-08**	0.29
39	Atherosclerosis Signaling	**7E-08**	0.22
40	Acute Phase Response Signaling	**1E-07**	0.19
41	PTEN Signaling	**1E-07**	0.21
42	MSP-RON Signaling Pathway	**2E-07**	0.31
43	B Cell Receptor Signaling	**2E-07**	0.20
44	Glucocorticoid Receptor Signaling	**3E-07**	0.15
45	IL-9 Signaling	**5E-07**	0.33
46	GM-CSF Signaling	**5E-07**	0.27
47	Prolactin Signaling	**5E-07**	0.25
48	Colorectal Cancer Metastasis Signaling	**8E-07**	0.16
49	IL-8 Signaling	**1E-06**	0.17
50	Production of Nitric Oxide and Reactive Oxygen Species in Macrophages	**1E-06**	0.17
51	CCR5 Signaling in Macrophages	**2E-06**	0.20
52	JAK/Stat Signaling	**2E-06**	0.27
53	IL-2 Signaling	**2E-06**	0.28
54	Cdc42 Signaling	**2E-06**	0.17
55	FcγRIIB Signaling in B Lymphocytes	**3E-06**	0.24
56	IGF-1 Signaling	**5E-06**	0.21
57	Fc Epsilon RI Signaling	**5E-06**	0.21
58	IL-15 Signaling	**1E-05**	0.24
59	PDGF Signaling	**1E-05**	0.23
60	Erythropoietin Signaling	**1E-05**	0.22

Ratio, fraction of genes present in the signature list respect to all genes for each specific pathway.

Table S4. Overrepresented Ingenuity Canonical Pathways in RCC compared to normal renal cortices prior and after immune/stroma signature subtraction.

	Pathways prior to immune/stroma subtraction	*p*	Ratio	#
1	ATM Signaling	**4E-14**	0.56	1
2	Role of BRCA1 in DNA Damage Response	**3E-11**	0.46	2
3	**Role of Pattern Recognition Receptors in Recognition of Bacteria**	**8E-10**	0.37	
4	Role of CHK Proteins in Cell Cycle Checkpoint Control	**2E-9**	0.54	3
5	Hereditary Breast Cancer Signaling	**7E-9**	0.31	4
6	**Antigen Presentation Pathway**	**2E-8**	0.47	
7	Cell Cycle Control of Chromosomal Replication	**2E-8**	0.52	5
8	p53 Signaling	**3E-8**	0.34	9
9	DNA Double-Strand Break Repair by Homologous Recombination	**5E-8**	0.65	6
10	Type I Diabetes Mellitus Signaling	**9E-8**	0.30	68
11	Molecular Mechanisms of Cancer	**1E-7**	0.21	11
12	**Dendritic Cell Maturation**	**1E-7**	0.25	
13	**Crosstalk between Dendritic Cells and Natural Killer Cells**	**2E-7**	0.32	
14	Hepatic Fibrosis / Hepatic Stellate Cell Activation	**4E-7**	0.28	26
15	Pancreatic Adenocarcinoma Signaling	**5E-7**	0.29	17
16	**Role of NFAT in Regulation of the Immune Response**	**7E-7**	0.24	
17	**Natural Killer Cell Signaling**	**7E-7**	0.31	
18	Cell Cycle: G2/M DNA Damage Checkpoint Regulation	**9E-7**	0.39	7
19	**iCOS-iCOSL Signaling in T Helper Cells**	**3E-6**	0.27	
20	**T Helper Cell Differentiation**	**5E-6**	0.33	
21	IL-8 Signaling	**7E-6**	0.23	49
22	Death Receptor Signaling	**1E-5**	0.32	14
23	Aryl Hydrocarbon Receptor Signaling	**1E-5**	0.24	8
24	**TREM1 Signaling**	**1E-5**	0.30	
25	**Systemic Lupus Erythematosus Signaling**	**2E-5**	0.22	
26	**Production of Nitric Oxide and Reactive Oxygen Species in Macro**	**2E-5**	0.22	
27	Mitotic Roles of Polo-Like Kinase	**2E-5**	0.32	10
28	Colorectal Cancer Metastasis Signaling	**3E-5**	0.21	50
29	**PKCθ Signaling in T Lymphocytes**	**4E-5**	0.23	
30	Reelin Signaling in Neurons	**5E-5**	0.29	63
31	**IL-4 Signaling**	**5E-5**	0.30	
32	**Acute Myeloid Leukemia Signaling**	**9E-5**	0.28	
33	Ovarian Cancer Signaling	**9E-5**	0.24	22
34	**Fcγ Receptor-mediated Phagocytosis in Macrophages and Monoc**	**1E-4**	0.27	
35	Cyclins and Cell Cycle Regulation	**1E-4**	0.26	12
36	ILK Signaling	**1E-4**	0.22	21
37	**CD28 Signaling in T Helper Cells**	**2E-4**	0.24	
38	**Phospholipase C Signaling**	**2E-4**	0.20	
39	Mismatch Repair in Eukaryotes	**2E-4**	0.38	15
40	Cell Cycle: G1/S Checkpoint Regulation	**2E-4**	0.30	16
41	**Graft-versus-Host Disease Signaling**	**2E-4**	0.32	
42	**OX40 Signaling Pathway**	**2E-4**	0.25	
43	**Cytotoxic T Lymphocyte-mediated Apoptosis of Target Cells**	**2E-4**	0.27	
44	**Leukocyte Extravasation Signaling**	**2E-4**	0.22	
45	**CTLA4 Signaling in Cytotoxic T Lymphocytes**	**2E-4**	0.26	
46	Ephrin Receptor Signaling	**3E-4**	0.20	19
47	**Autoimmune Thyroid Disease Signaling**	**3E-4**	0.26	
48	**B Cell Receptor Signaling**	**4E-4**	0.22	
49	**CCR5 Signaling in Macrophages**	**4E-4**	0.22	
50	Small Cell Lung Cancer Signaling	**4E-4**	0.24	24
51	Glioma Signaling	**4E-4**	0.23	43
52	SAPK/JNK Signaling	**4E-4**	0.25	46
53	Prostate Cancer Signaling	**4E-4**	0.24	23
54	Tumoricidal Function of Hepatic Natural Killer Cells	**5E-4**	0.42	44
55	**Altered T Cell and B Cell Signaling in Rheumatoid Arthritis**	**5E-4**	0.25	
56	HGF Signaling	**5E-4**	0.25	45
57	Germ Cell-Sertoli Cell Junction Signaling	**8E-4**	0.22	35
58	**GM-CSF Signaling**	**9E-4**	0.27	
59	Glioma Invasiveness Signaling	**9E-4**	0.28	66
60	DNA Double-Strand Break Repair by Non-Homologous End Joining	**1E-3**	0.37	18
61	Pyrimidine Metabolism	**1E-3**	0.19	13
62	Melanoma Signaling	**1E-3**	0.30	34
63	Myc Mediated Apoptosis Signaling	**1E-3**	0.28	42
64	**Communication between Innate and Adaptive Immune Cells**	**1E-3**	0.21	
65	Role of PKR in Interferon Induction and Antiviral Response	**1E-3**	0.28	40
66	**T Cell Receptor Signaling**	**1E-3**	0.23	
67	**Cdc42 Signaling**	**1E-3**	0.20	
68	**Calcium-induced T Lymphocyte Apoptosis**	**2E-3**	0.26	
69	**JAK/Stat Signaling**	**2E-3**	0.27	
70	PTEN Signaling	**2E-3**	0.21	53
71	**NF-κB Signaling**	**2E-3**	0.21	
72	Renal Cell Carcinoma Signaling	**2E-3**	0.26	41
73	Hypoxia Signaling in the Cardiovascular System	**2E-3**	0.27	20
74	**HMGB1 Signaling**	**2E-3**	0.23	
75	Breast Cancer Regulation by Stathmin1	**2E-3**	0.20	29
76	PI3K/AKT Signaling	**3E-3**	0.20	47
77	Granzyme B Signaling	**3E-3**	0.44	32
78	**Primary Immunodeficiency Signaling**	**3E-3**	0.24	
79	TNFR1 Signaling	**3E-3**	0.26	28
80	**Interferon Signaling**	**3E-3**	0.31	
81	**Pathogenesis of Multiple Sclerosis**	**3E-3**	0.56	
82	Inhibition of Angiogenesis by TSP1	**3E-3**	0.31	74
83	**Toll-like Receptor Signaling**	**3E-3**	0.26	
84	**Integrin Signaling**	**4E-3**	0.19	
85	**Caveolar-mediated Endocytosis Signaling**	**4E-3**	0.22	

	Pathways after immune/stroma subtraction	*p*	Ratio	#
1	ATM Signaling	**1E-16**	0.56	1
2	Role of BRCA1 in DNA Damage Response	**2E-13**	0.46	2
3	Role of CHK Proteins in Cell Cycle Checkpoint Control	**5E-11**	0.54	4
4	Hereditary Breast Cancer Signaling	**8E-10**	0.29	5
5	Cell Cycle Control of Chromosomal Replication	**1E-9**	0.52	7
6	DNA Double-Strand Break Repair by Homologous Recombination	**5E-9**	0.65	9
7	Cell Cycle: G2/M DNA Damage Checkpoint Regulation	**3E-8**	0.39	18
8	Aryl Hydrocarbon Receptor Signaling	**5E-8**	0.24	23
9	p53 Signaling	**5E-8**	0.30	8
10	Mitotic Roles of Polo-Like Kinase	**8E-7**	0.32	27
11	Molecular Mechanisms of Cancer	**2E-6**	0.17	11
12	Cyclins and Cell Cycle Regulation	**2E-5**	0.25	35
13	Pyrimidine Metabolism	**2E-5**	0.18	61
14	Death Receptor Signaling	**2E-5**	0.28	22
15	Mismatch Repair in Eukaryotes	**3E-5**	0.38	39
16	Cell Cycle: G1/S Checkpoint Regulation	**4E-5**	0.28	40
17	Pancreatic Adenocarcinoma Signaling	**5E-5**	0.22	15
18	DNA Double-Strand Break Repair by Non-Homologous End Joining	**3E-4**	0.37	60
19	Ephrin Receptor Signaling	**4E-4**	0.17	46
20	Hypoxia Signaling in the Cardiovascular System	**5E-4**	0.25	73
21	ILK Signaling	**6E-4**	0.18	36
22	Ovarian Cancer Signaling	**8E-4**	0.19	33
23	Prostate Cancer Signaling	**1E-3**	0.20	53
24	Small Cell Lung Cancer Signaling	**2E-3**	0.19	50
25	Endoplasmic Reticulum Stress Pathway	**2E-3**	0.39	98
26	Hepatic Fibrosis / Hepatic Stellate Cell Activation	**3E-3**	0.18	14
27	Induction of Apoptosis by HIV1	**3E-3**	0.21	86
28	TNFR1 Signaling	**4E-3**	0.23	79
29	Breast Cancer Regulation by Stathmin1	**4E-3**	0.16	75
30	Wnt/β-catenin Signaling	**4E-3**	0.17	92
31	Antiproliferative Role of TOB in T Cell Signaling	**4E-3**	0.31	90
32	Granzyme B Signaling	**4E-3**	0.38	77
33	Bladder Cancer Signaling	**5E-3**	0.20	124
34	Melanoma Signaling	**5E-3**	0.24	62
35	Germ Cell-Sertoli Cell Junction Signaling	**6E-3**	0.17	57
36	CD27 Signaling in Lymphocytes	**6E-3**	0.21	94
37	HIF1α Signaling	**7E-3**	0.19	88
38	Semaphorin Signaling in Neurons	**7E-3**	0.23	100
39	**Estrogen Receptor Signaling**	**7E-3**	0.17	
40	Role of PKR in Interferon Induction and Antiviral Response	**8E-3**	0.22	65
41	Renal Cell Carcinoma Signaling	**8E-3**	0.20	72
42	Myc Mediated Apoptosis Signaling	**8E-3**	0.21	63
43	Glioma Signaling	**8E-3**	0.17	51
44	Tumoricidal Function of Hepatic Natural Killer Cells	**0.010**	0.29	54
45	HGF Signaling	**0.010**	0.18	56
46	SAPK/JNK Signaling	**0.010**	0.18	52
47	PI3K/AKT Signaling	**0.011**	0.16	76
48	Apoptosis Signaling	**0.011**	0.18	125
49	IL-8 Signaling	**0.011**	0.15	21
50	Colorectal Cancer Metastasis Signaling	**0.016**	0.14	28
51	Role of Oct4 in Mammalian Embryonic Stem Cell Pluripotency	**0.017**	0.22	131
52	Huntington's Disease Signaling	**0.020**	0.14	119
53	PTEN Signaling	**0.022**	0.15	70
54	TWEAK Signaling	**0.023**	0.21	109
55	Agrin Interactions at Neuromuscular Junction	**0.028**	0.19	105
56	Glioblastoma Multiforme Signaling	**0.028**	0.15	115
57	**4-1BB Signaling in T Lymphocytes**	**0.029**	0.21	
58	ERK5 Signaling	**0.031**	0.19	137
59	TR/RXR Activation	**0.032**	0.17	132
60	Rac Signaling	**0.032**	0.15	96
61	Non-Small Cell Lung Cancer Signaling	**0.034**	0.17	87
62	**RAN Signaling**	**0.035**	0.22	
63	Reelin Signaling in Neurons	**0.037**	0.17	30
64	Chronic Myeloid Leukemia Signaling	**0.038**	0.15	108
65	FLT3 Signaling in Hematopoietic Progenitor Cells	**0.038**	0.18	91
66	Glioma Invasiveness Signaling	**0.039**	0.18	59
67	ERK/MAPK Signaling	**0.040**	0.14	135
68	Type I Diabetes Mellitus Signaling	**0.041**	0.15	10
69	Retinoic acid Mediated Apoptosis Signaling	**0.043**	0.18	126
70	**Purine Metabolism**	**0.043**	0.12	
71	**Thyroid Cancer Signaling**	**0.044**	0.20	
72	Nicotinate and Nicotinamide Metabolism	**0.045**	0.14	123
73	Axonal Guidance Signaling	**0.048**	0.12	101
74	Inhibition of Angiogenesis by TSP1	**0.049**	0.21	82

Unique pathways are in bold. Ratio, fraction of genes present in the signature list respect to all genes for each specific pathway; #, ranking order in alternate analysis.

Table S5. Deep sequencing of the *TSC1* mutation (TG22).

Tissue	Mutant reads	Wild-type reads	Percent Mutant	
Tumorgraft	1,663,908	39,041	97.707	
Patient tumor (sample 1)	4,687	1,820,112	0.257	p =0.0034
Patient tumor (sample 2)	7,561	2,210,331	0.341	
Patient normal (blood)	256	796,149	0.032	
Patient normal (connective tissue)	313	883,295	0.035	
Unrelated normal sample	271	928,206	0.029	

p value comparing percent mutant reads in tumor vs. normal and unrelated control.