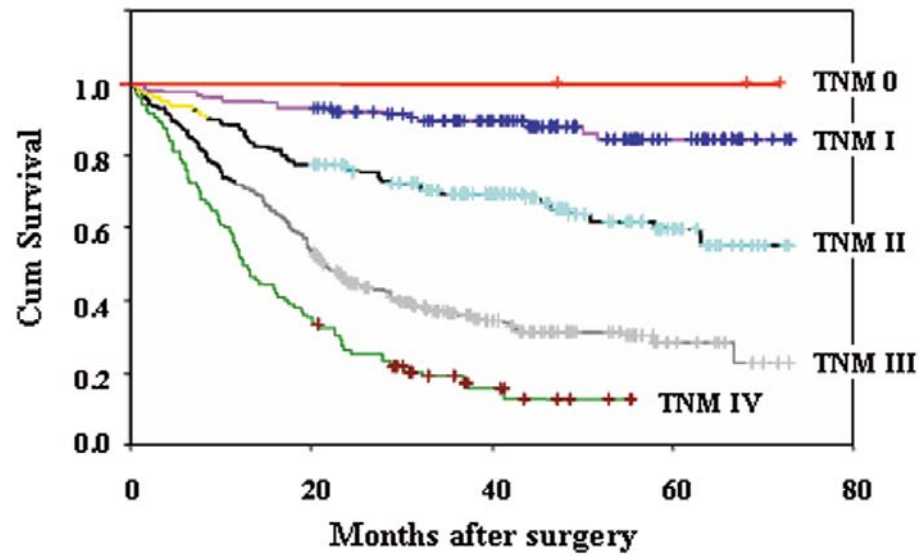
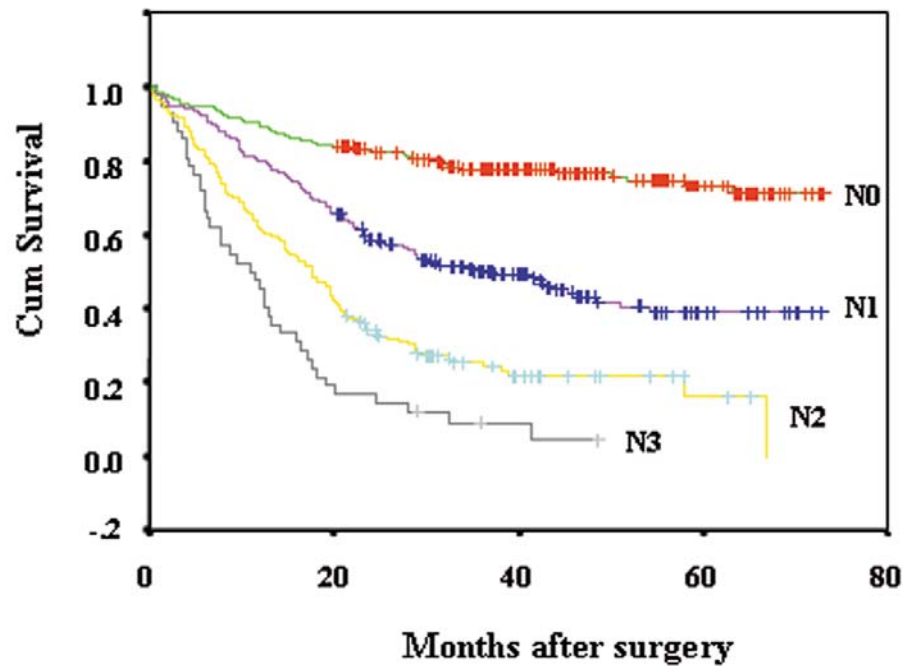


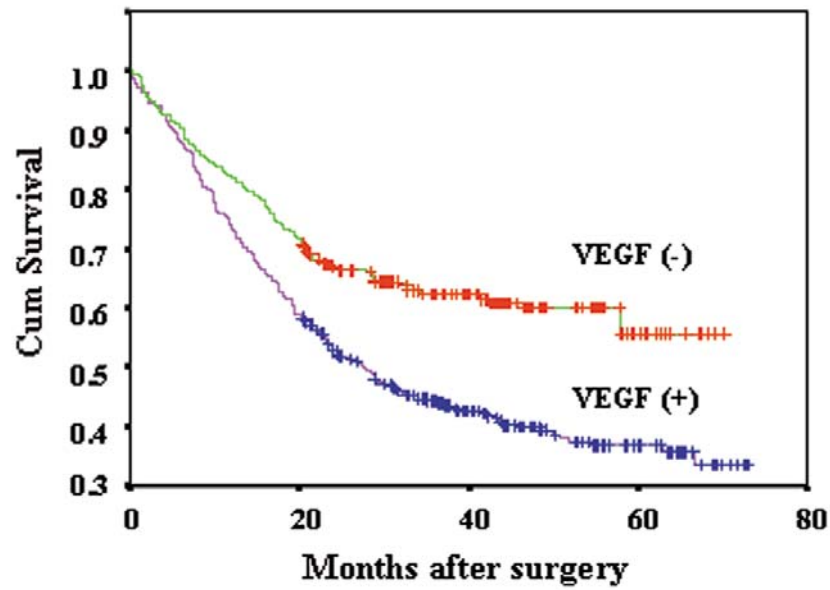
Supplemental Fig. 1. The expression of mTOR, p-mTOR, VEGF and PCNA in 1072 cases of gastric cancer specimens. *Underexpression*, tumor with no staining or staining positivity lower than matched normal tissue; *Normal expression*, tumor with staining positivity similar to matched normal tissue; *Overexpression*, tumor with staining positivity higher than normal. Staining positivity was determined according to the percentage score of positive cells and the score of staining intensity.



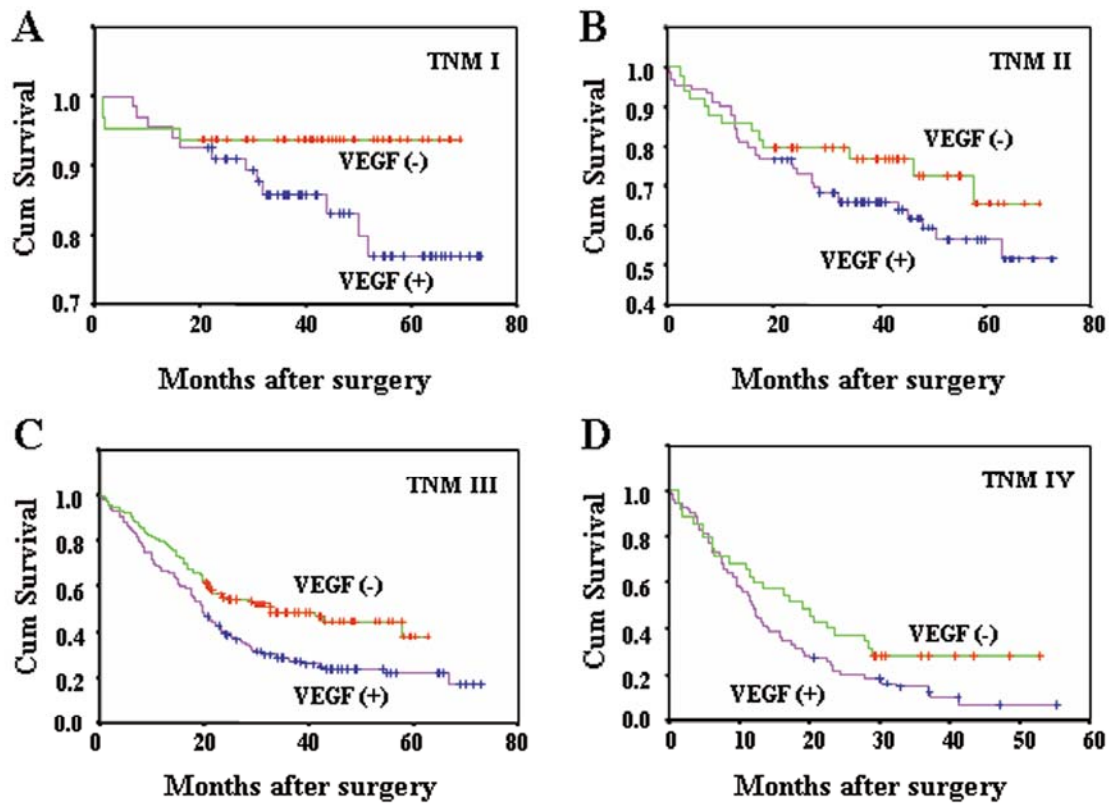
Supplemental Fig. 2. Kaplan-Meier plot of overall survival durations in the patients according to TNM stages. The survival durations were significantly worse in patients of advanced stage disease (a median survival of more than 71 months for stage 0) than those with early stage disease: a median survival of 12 months for stage IV disease; 21 months for stage III disease; >52 months for stage II disease, and >66 months for stage I disease. $P < 0.0001$



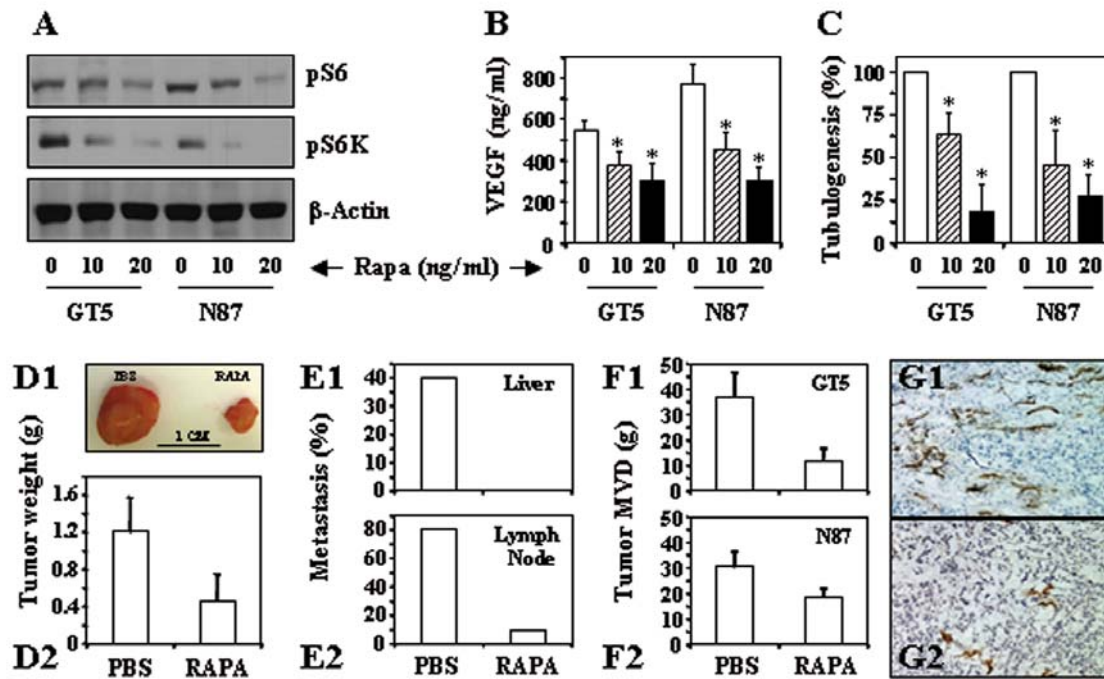
Supplemental Fig. 3. Kaplan-Meier plot of overall survival durations in the patients according to lymph node metastasis. The survival durations were significantly worse in patients with an increasing involvement of lymph node metastasis (a median survival of more than 37 months for N2; 18 months for N2-positive tumors; and 11 months for N3) than those with early stage disease (a median survival of more than 59 months for N0). $P < 0.0001$



Supplemental Fig. 4. Kaplan-Meier plot of overall survival durations in the patients according to VEGF expression. The survival durations were significantly worse in patients with a VEGF overexpression (“+”, a median survival of 28 months) than those without VEGF overexpression (“-”, a median survival of 48 months). $P < 0.0067$



Supplemental Fig. 5. Kaplan-Meier plot of overall survival durations in the patients with different TNM stages according to VEGF expression . The survival durations were significantly worse in patients of stage III and IV with VEGF overexpression (“+”, a median survival of 20 months for stage III and 12 months for stage IV) than those of stage III and IV without VEGF overexpression (“-”, a median survival of 33 months for stage III: $P = 0.001$; and 19 months for stage IV: $P = 0.0500$). However, there was no significant difference in survival durations in patients of stage I and II with VEGF overexpression (a median survival of more than 63 months for stage I and more than 50 months for stage II) than those of stage I and II without VEGF overexpression (a median survival of more than 65 months for stage I: $P = 0.0663$; and more than 55 months for stage II: $P = 0.2243$).



Supplemental Fig. 6. Inhibition of mTOR suppressed angiogenesis and growth of gastric cancer in vitro and in mouse models. N87 and GT5 cells were treated with rapamycin (*Rapa*) for 18 hours. Total protein extracts were prepared for Western blot analysis using specific anti-S6 and anti-pS6K antibodies (**A**). Supernatants were collected for analysis of VEGF secretion using ELISA assay (**B**) and angiogenic potential using tubulogenesis assay (**C**). Gastric cancer cells were injected into the subcutis (N87, **D1**) or the wall of stomach (GT5, **D2**) of nude mice. Groups of nude mice (n=5) received treatment of PBS (control) or rapamycin (RAPA, 2.5 mg/kg, *i.p.*) when tumors reached around 4 mm in diameters as described in the Materials and Methods section. Representative subcutaneous tumors (**D1**) and weights of stomach tumors (**D2**) were presented. In the orthotopic model, metastasis to liver (**E1**) and regional lymph nodes (**E2**) were determined and evaluated. The stomach (GT5, **F1**) and subcutaneous (N87, **F2**) tumor tissues were further processed for MVD assessment. Representative photos of MVD in N87 tumors were shown (**G1** & **G2**). * $P < 0.05$

Supplemental Table 1 Correlation between VEGF expression and clinicopathological factors

Clinicopathological factor	Total (n)	Positive VEGF Expression		
		n	%	P
Age				<0.001
≤ 60 years	537	281	52.3	
> 60 years	535	356	66.5	
Sex				0.004
Male	757	470	62.1	
Female	315	167	53.0	
Location				0.002
Cardia	180	127	70.6	
Corpus	329	182	55.3	
Antrum	519	297	57.2	
Whole	44	31	70.5	
Size (Diameter)				NS
≤ 6 cm	825	489	59.3	
> 6 cm	247	148	59.9	
Tumor type				<0.001
Adenocarcinoma	947	595	62.8	
Mucous carcinoma	78	24	30.8	
Ring-like cell carcinoma	29	9	31.0	
Other	18	7	38.9	
Differentiation				<0.001
Well/moderate	616	431	68.0	
Poorly	456	206	47.0	
Gastric wall invasion				0.030
T1/T2	312	166	53.2	
T3/T4	760	471	62.0	
Nodal metastasis				0.017
Negative	356	195	54.8	
Positive	716	442	61.7	
TNM stage				NS
I/II	427	238	55.7	
III/IV	645	399	61.9	
p53 expression				0.003
Negative	481	263	54.7	
Positive	591	374	63.3	
PCNA expression				<0.001
Negative	115	49	42.6	
Positive	957	588	61.4	

Supplemental Table 2 Direct correlation between the expression of VEGF and mTOR in gastric cancer

		VEGF Expression		Total
		Negative	Positive	
mTOR Expression	Negative	296	231	527
	Positive	139	406	545
Total		435	637	1072

Pearson $\chi^2 = 104.47$, $P < 0.001$

Supplemental Table 3 Direct correlation between the expression of VEGF and p-mTOR in gastric cancer

		VEGF Expression		Total
		Negative	Positive	
p-mTOR Expression	Negative	288	285	573
	Positive	147	352	499
Total		435	637	1072

Pearson $\chi^2 = 47.87$, $P < 0.001$

Supplemental Table 4 Direct correlation between the expression of mTOR and p-mTOR in gastric cancer

		p-mTOR Expression		Total
		Negative	Positive	
mTOR Expression	Negative	365	162	527
	Positive	208	337	545
Total		573	499	1072

Pearson $\chi^2 = 104.12$ $P < 0.001$

Supplemental Table 5 Correlation between mTOR expression and MVD

		MVD			Total
		Low	Moderate	High	
mTOR Expression	Negative	260	168	90	527
	Positive	140	188	226	545
Total		400	356	316	1072

Pearson $\chi^2 = 94.553$ $P < 0.001$

Supplemental Table 6 Correlation between p-mTOR expression and MVD

		MVD			Total
		Low	Moderate	High	
p-mTOR Expression	Negative	300	191	82	573
	Positive	100	165	234	499
Total		400	356	316	1072

Pearson $\chi^2 = 170.718$, $P < 0.001$

Supplemental Table 7 Correlation between VEGF expression and MVD

		MVD			Total
		Low	Moderate	High	
VEGF Expression	Negative	254	118	63	435
	Positive	146	238	253	637
Total		400	356	316	1072

Pearson $\chi^2 = 151.145$, $P < 0.001$