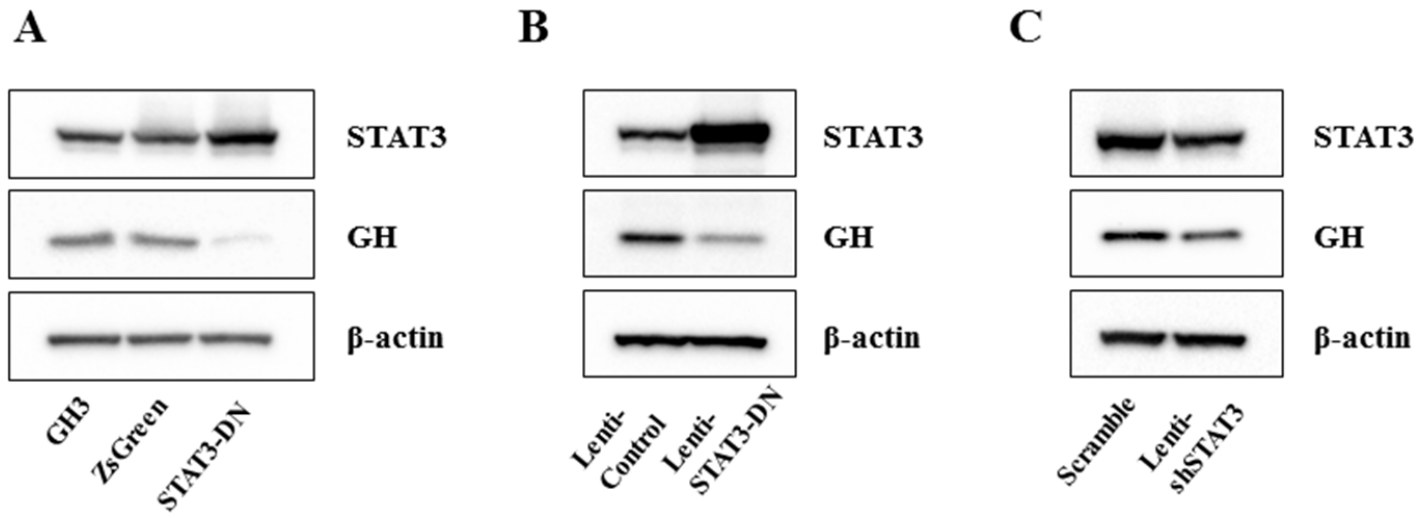
Supplemental Table 1. Twenty-one acromegaly patients

Patient #	Age	Gender	Tumor size	Resected pituitary adenoma immunochemistry	Serum GH (normal < 2ng/ml)		Additional treatments
					Pre-surgery	Post-surgery	
1	55	F	Macro	GH(+), ACTH(partial+), FSH(±), LH(-), PRL(-),TSH(-), P53(-), Ki-67<1%	7.6	0.9	
2	35	M	Macro	GH(+), PRL(+), ACTH(-), FSH(-), LH(-), TSH(-), P53(-), Ki-67 1%	33.0	22.1	Octreotide and surgery 1 year prior
3	42	M	Macro	GH(+), PRL(+), ACTH(-), FSH(-), LH(-), TSH(-), P53(-), Ki-67 <1%	5.4	0.6	Gamma knife 1 year prior
4	27	M	Micro	GH(+), PRL(partial+), ACTH (partial+), LH (partial+), TSH(-), P53(-), Ki-67 2%	14.3	1.3	
5	51	F	Macro	GH(+), PRL(-), ACTH(-), FSH(-), LH(-), TSH(-), P53(-), Ki-67 2%	5.0	1.3	
6	42	F	Macro	GH(+), PRL(+), ACTH(-), FSH(-), LH(-), TSH(-), P53(-), Ki-67 3%	5.2	0.9	Bromocriptine
7	22	F	Macro	GH(+), PRL(+), ACTH(-), FSH(-), LH(-), TSH(-), P53(-), Ki-67 <1%	65.9	74.7	Octreotide before surgery
8	41	F	Macro	GH(+), PRL(+), ACTH(-), FSH(-), LH(-), TSH(-), P53(-), Ki-67 2%	59.7	4.8	
9	60	M	Macro	GH(+), PRL(+), FSH(scattered +), ACTH(-), LH(-), TSH(-), P53(-), Ki-67 1%	7.1	2.1	
10	37	M	Macro	GH(+), PRL(-), ACTH(-), FSH(-), LH(-), TSH(-), P53(-), Ki-67 <1%	8.5	0.4	Octreotide before surgery
11	56	F	Macro	GH(+), PRL(+), ACTH(-), FSH(-), LH(-), TSH(-), P53(-), Ki-67 1%	31.4	8.6	
12	24	M	Macro	GH(+), PRL(+), ACTH(-), FSH(-), LH(-), TSH(-), P53(-), Ki-67 5%	84.5	1.6	

13	56	F	Macro	GH(+), PRL(few+), ACTH(-), FSH(-), LH(-), TSH(-), P53(-), Ki-67 Negative	3.5	1.3	Octreotide before surgery
14	59	F	Macro	GH(+), PRL(-), ACTH(-), FSH(-), LH(-), TSH(-), P53(-), Ki-67 2%	42.7	1.9	
15	37	M	Macro	GH(+), PRL(+), ACTH(-), FSH(-), LH(-), TSH(-), P53(-), Ki-67 2%	7.7	1.3	
16	41	M	Macro	GH(+), PRL(+), ACTH(-), FSH(-), LH(-), TSH(-), P53(-), Ki-67 <1%	24.5	1.4	
17	44	F	Macro	GH(+), PRL(+), ACTH(-), FSH(-), LH(-), TSH(-), P53(-), Ki-67 3%	25.0	0.8	
18	36	M	Micro	GH(+), PRL(+), ACTH(-), FSH(-), LH(-), TSH(-), P53(-), Ki-67 3%	6.3	1.9	
19	24	F	Macro	GH(+), PRL(+), ACTH(-), FSH(-), LH(-), TSH(-), P53(-), Ki-67 <1%	292.0	8.8	Octreotide before surgery
20	36	M	Macro	GH(+), PRL(partial+), ACTH(-), FSH(-), LH(-), TSH(-), P53(-), Ki-67 2%	33.3	6.3	
21	41	M	Macro	GH(+), PRL(+), ACTH(-), FSH(-), LH(-), TSH(partial+), P53(+), Ki-67 1%	8.3	1.0	

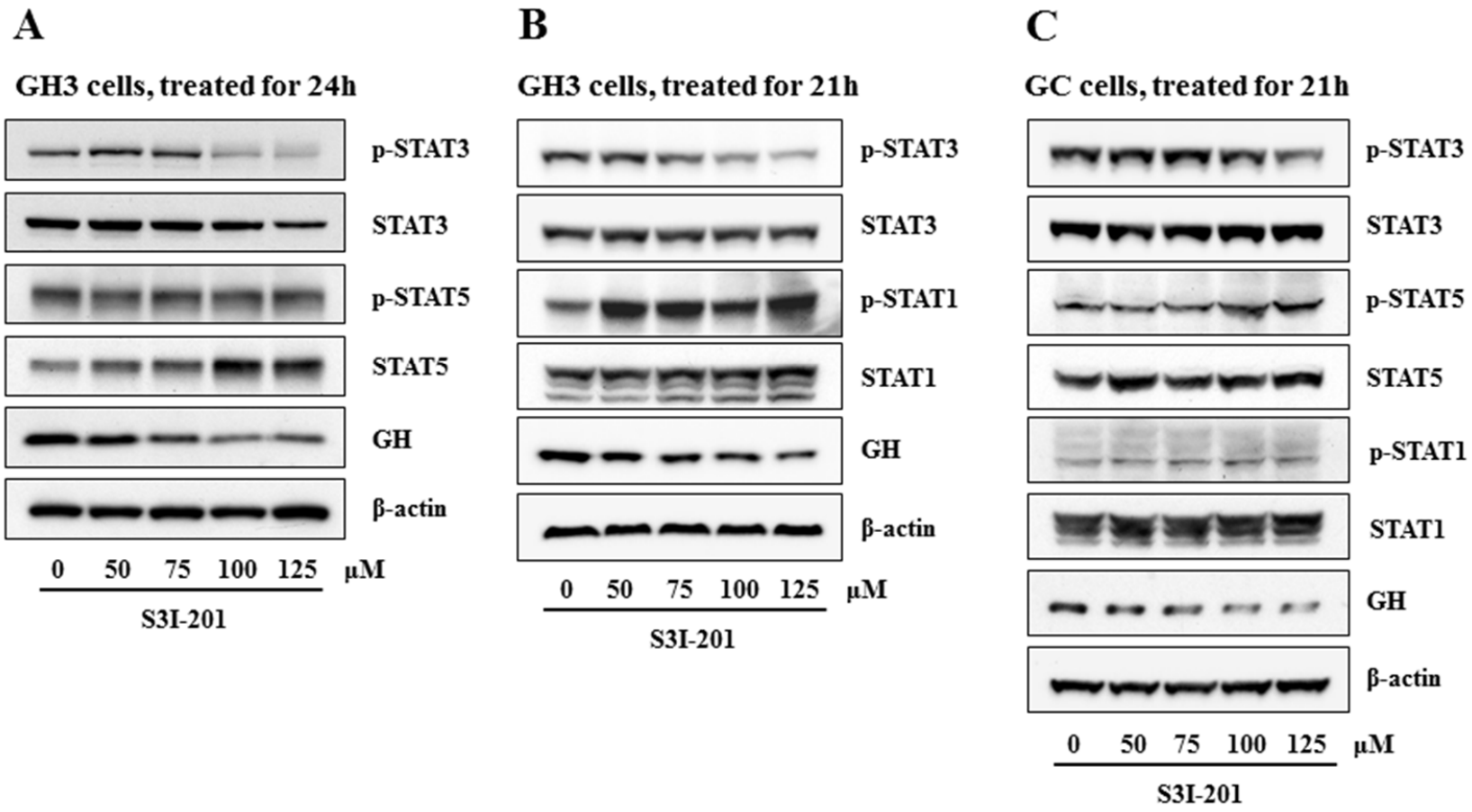
M: male; F: female; Micro: micro-adenoma, tumor largest diameter < 10 mm; Macro: macro-adenoma, tumor largest diameter > 10 mm.

Supplementary Figure 1



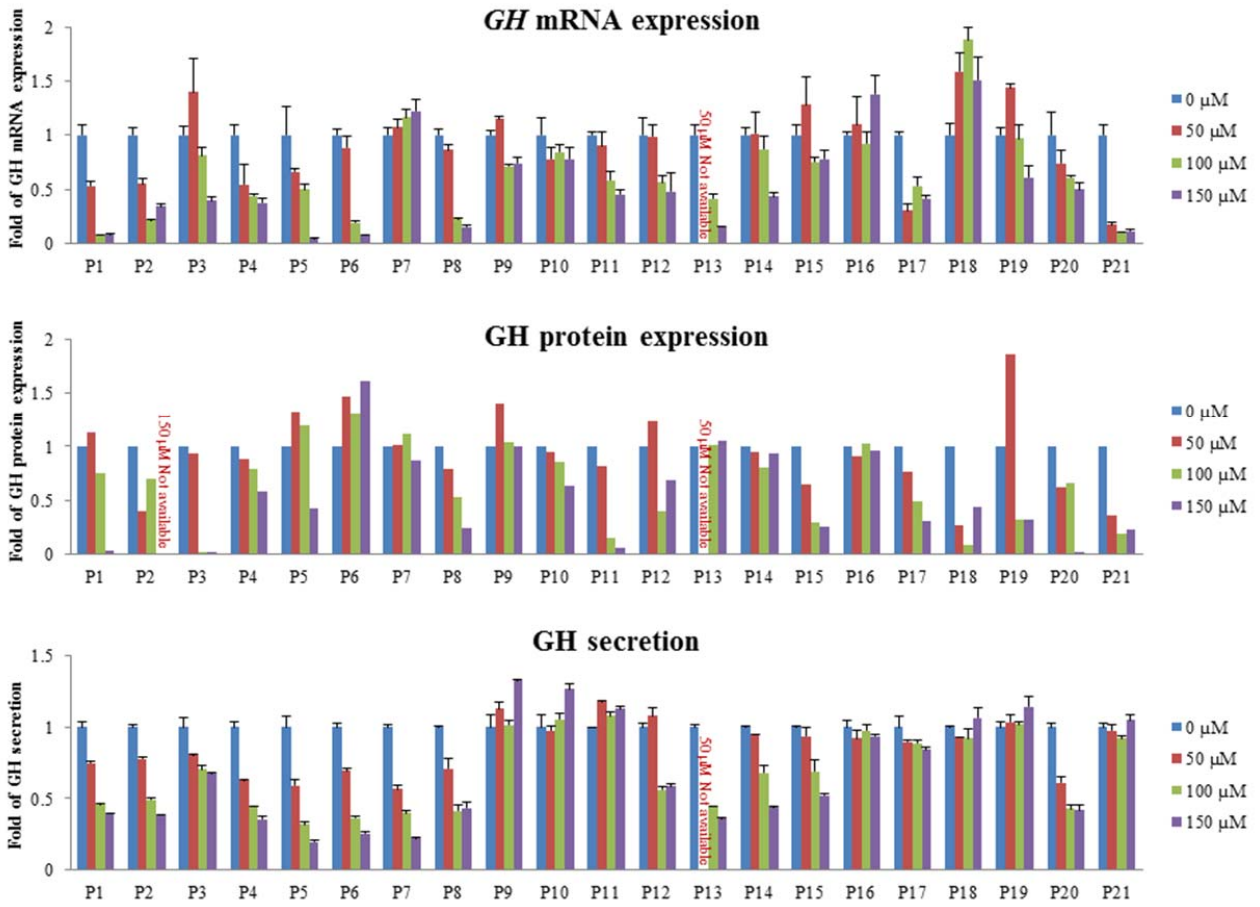
Supplementary Figure 1. STAT3-DN or *Stat3* shRNA expression attenuates GH in GH3 cells as assessed by Western blotting. (A) Gh expression is decreased in STAT3-DN stable transfectants. STAT3-DN stable cells were sorted to ensure strong STAT3-DN expression. GH3: non-transfected GH3 cell lysate. (B) GH expression is decreased in Lenti-STAT3-DN infected cells. (C) GH expression is decreased with attenuating endogenous STAT3 by lenti-shSTAT3 infection. Infected cells were harvested 6 days after infection and proteins extracted. Experiments were repeated 2 or 3 times and figures A-C show representative results.

Supplementary Figure 2



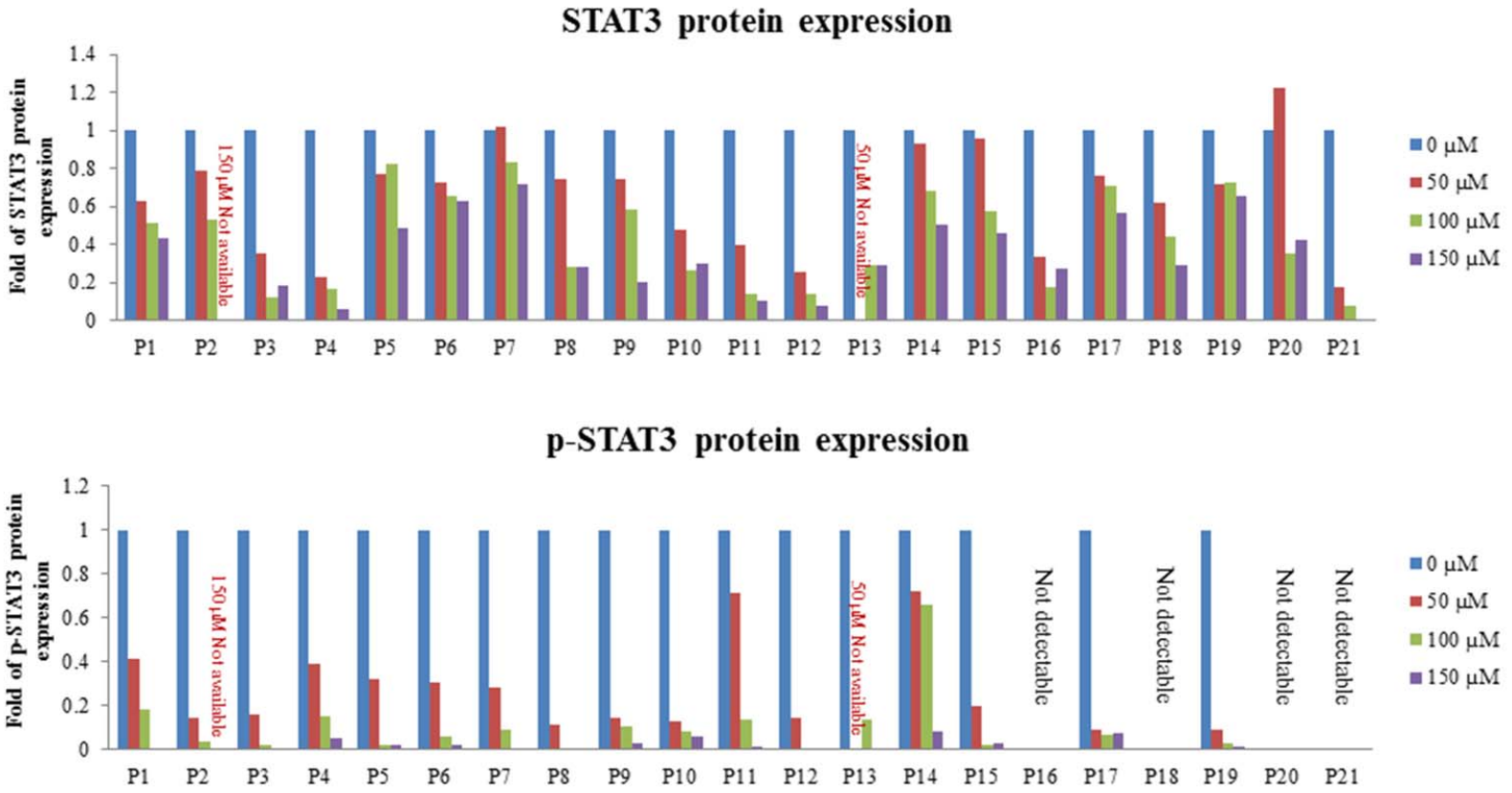
Supplementary Figure 2. Expression of STAT1, 3, 5 and GH in S3I-201 treated GH3 and GC cells as assessed by Western blotting. (A) GH3 cells were treated with increasing amounts of S3I-201 (0-125 μM) for 24 h, and STAT3, 5 and GH expression assessed. (B) GH3 cells were treated with increasing amounts of S3I-201 (0-125 μM) for 21 h, and STAT1, 3 and GH expression assessed. (C) GC cells were treated with increasing amounts of S3I-201 (0-125 μM) for 21 h, and STAT1, 3, 5 and GH expression assessed. Experiments were repeated 2 times and figures show representative results.

Supplementary Figure 3



Supplementary Figure 3. GH mRNA, protein expression and secretion in primary cell cultures derived from 21 human somatotroph adenomas. Cells were treated by S3I-201at 0-150 μM for 48 hours. mRNA expression were assessed by real-time PCR in triplicate wells, data shown as mean ± SD. *RPL13A* and *18S* were used as internal controls. GH protein expression was detected by Western blotting using total protein as normalized control. Medium GH concentrations were measured from 4 parallel wells, data presented as mean ± SE. Western blot sample of P2 at 150 μM, and all samples of P13 at 50 μM were not available.

Supplementary Figure 4



Supplementary Figure 4. STAT3 phosphorylation and expression in primary cell cultures derived from 21 human somatotroph adenomas. Cells were treated by S3I-201at 0-150 μM for 48 hours. Protein expression was assessed by Western blotting, using total protein as normalized controls. Samples of P2 at 150 μM and P13 at 50 μM were not available. STAT3 phosphorylation of P16, P18, P20 and P21 were not detectable.