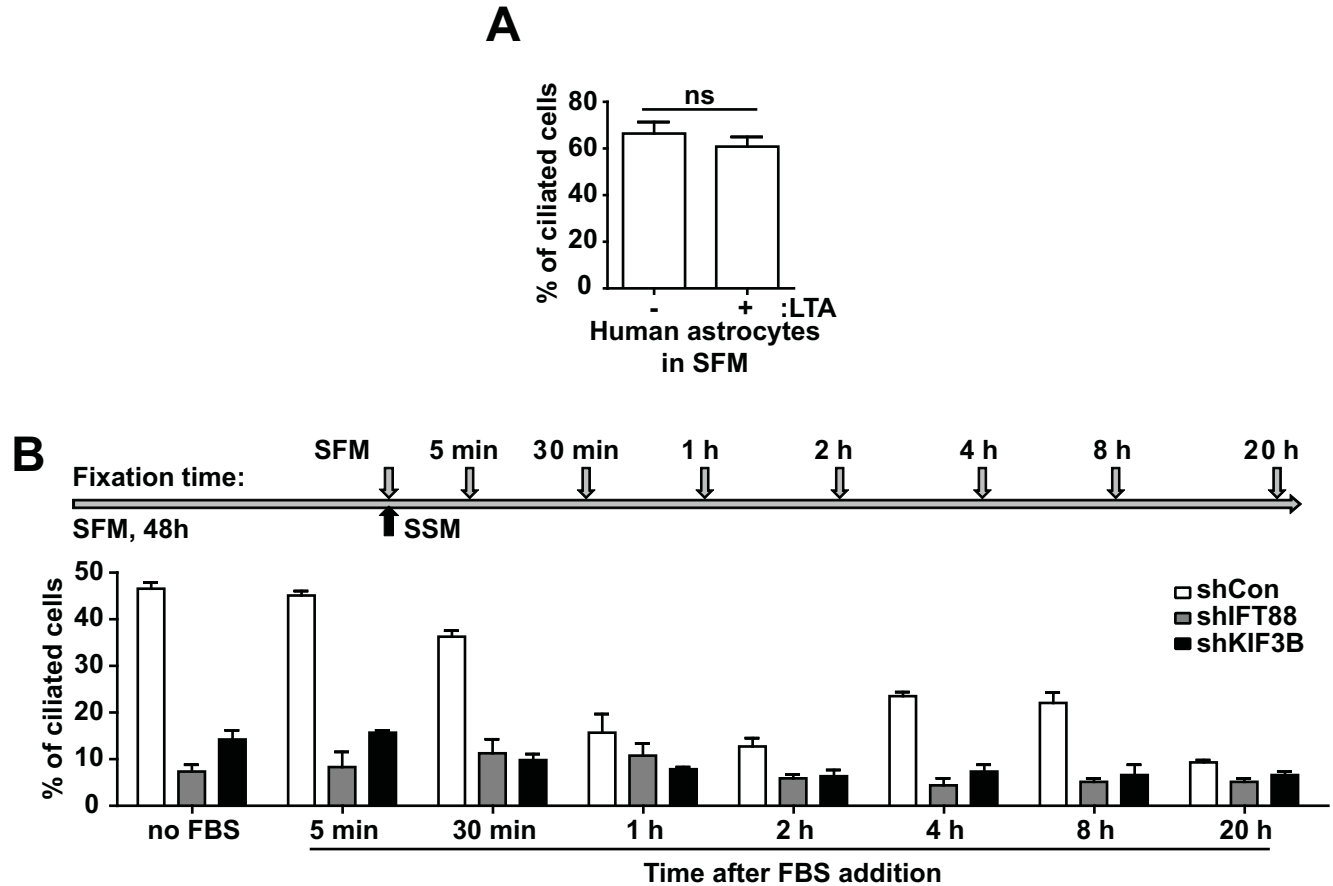
Supplementary Materials and Methods.

Generation of CRISPR-Cas9 driven LPAR1 knock out in astrocytes.

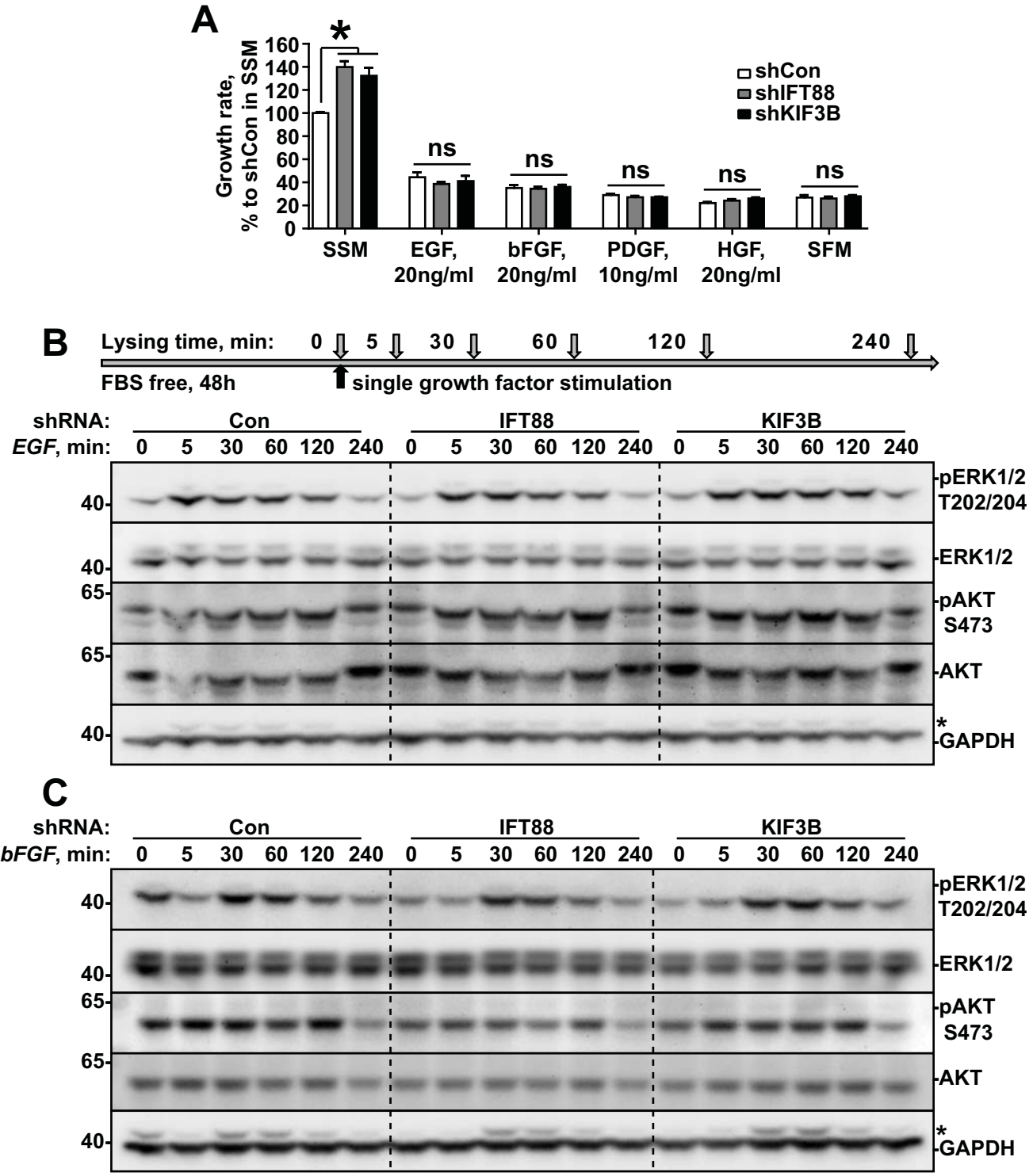
sgRNA targeting LPAR1 were designed using Broad institute web tool: https://portals.broadinstitute.org/gpp/public/analysis-tools/sgrna-design; synthesized as separate oligo nucleotides and cloned into pLentiCRISPR v2 (1) (a gift from Feng Zhang (Addgene plasmid # 52961)). Lentiviral particles were produced as previously described (2). Immortalized astrocytes were infected and selected on 1 µg/ml of puromycin until stable clones were formed. Individual cloned were established and tested for LPAR1 expression.

1. Sanjana NE, Shalem O, Zhang F. Improved vectors and genome-wide libraries for CRISPR screening. Nature methods. 2014;11(8):783-4.
2. Pugacheva EN, Jablonski SA, Hartman TR, Henske EP, Golemis EA. HEF1-dependent Aurora A activation induces disassembly of the primary cilium. Cell. 2007;129(7):1351-63.



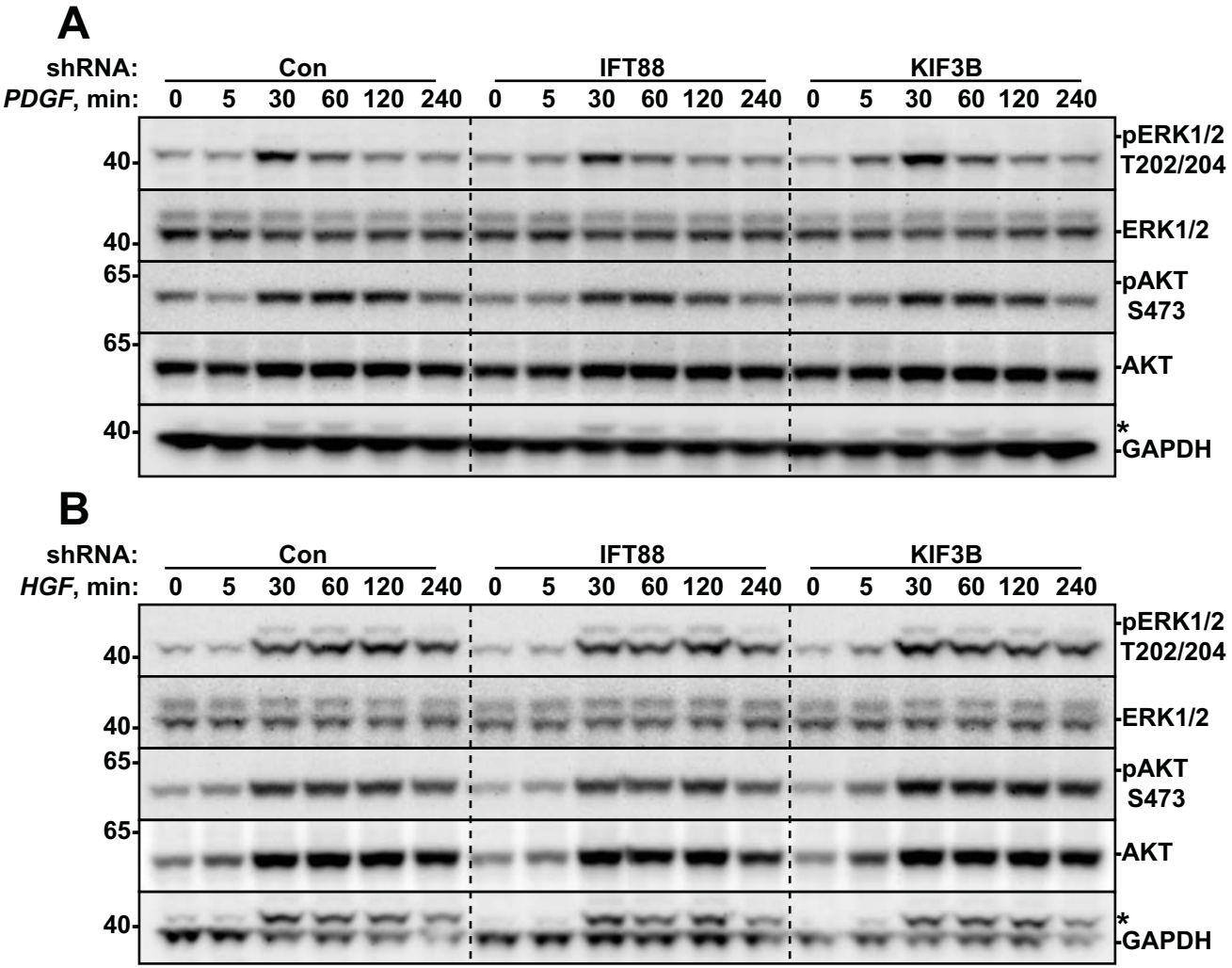
Primary cilia formation in human astrocytes and astrocytes immortalized with large T antigen.
A. Quantification of primary cilia in human astrocytes and human astrocytes immortalized with large T antigen (LTA) in serum-free media (SFM) as in **Fig.1 A-B**; two-tailed Student's *t*-test, n=3, 100 cells per experiment. **B.** Quantification of primary cilia over time in HA-LTA constitutively expressing shCon, shIFT88 or shKIF3B, pre-incubated for 48h with serum-free media (SFM) and stimulated with serum-supplemented media (SSM); experimental design on top, n = 3, per time point.

Supplementary Figure 1. Loskutov



Proliferation and ERK1/2 and AKT phosphorylation in response to single growth factor stimulation of HA-LTA.

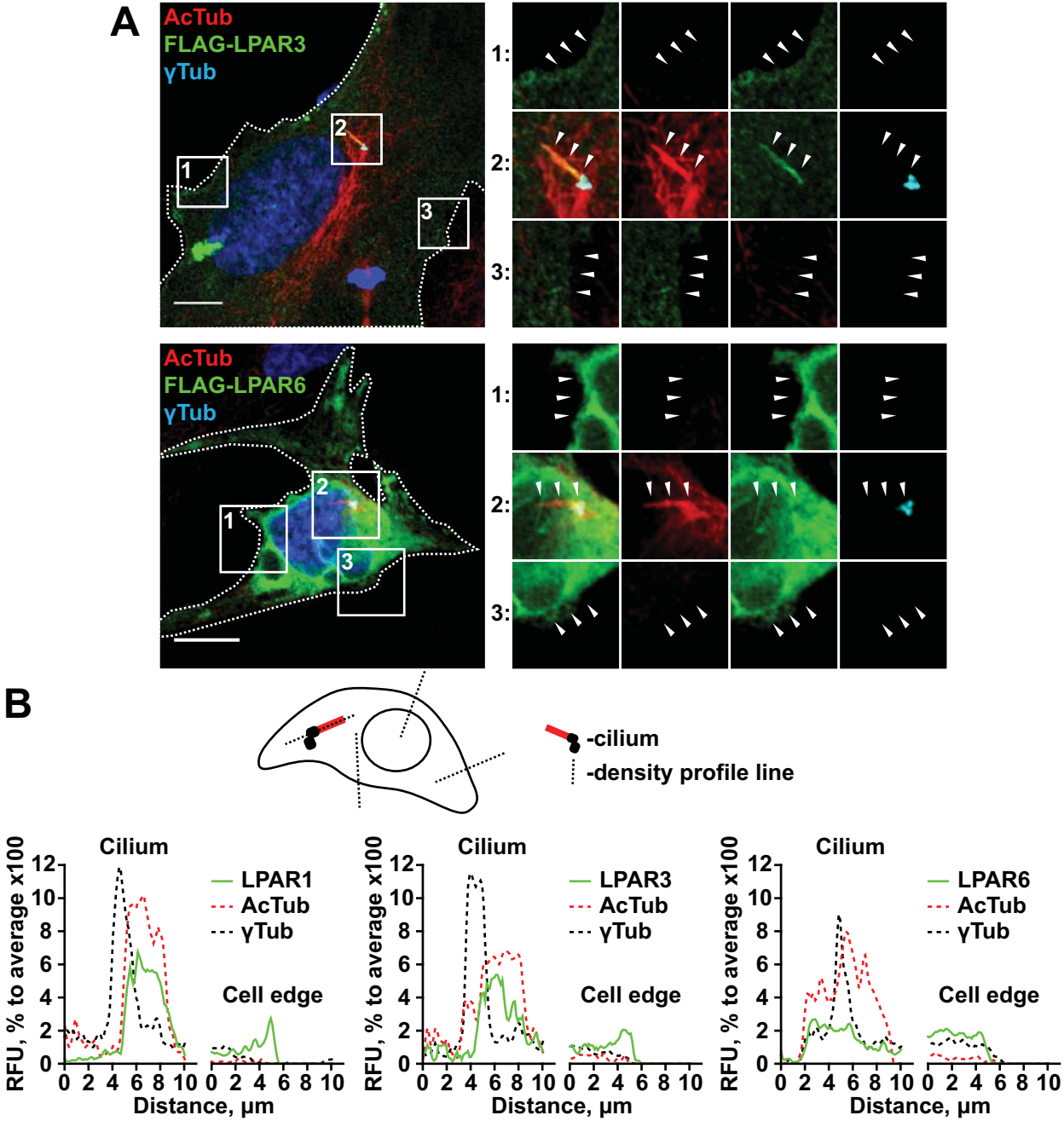
A. Growth rate of HA-LTA with intact (shCon) or impaired (shIFT88, shKIF3B) ciliogenesis in serum-supplemented media (SSM), serum-free media (SFM) or SFM supplemented with indicated single growth factors. One-way ANOVA with Dunnett's post hoc test, *$p < 0.05$; n=3. **B, C.** Representative western blot of response to single growth factor stimulation for cells as in **A**. Experimental set up shown in top **B:** serum-starved cells were treated with 20ng/ml of EGF (bottom **B**), 20ng/ml of bFGF (**C**), lysed in time-dependent manner; and stained with antibodies against Thr202/Tyr204 phosphorylated ERK1/2 (pERK1/2 T202/204), total ERK1/2, Ser473 phosphorylated AKT (pAKT S473), total AKT and GAPDH, as a loading control. * indicates bleed-through of pERK1/2 signal.



Proliferation and ERK1/2 and AKT phosphorylation in response to single growth factor stimulation of HA-LTA.

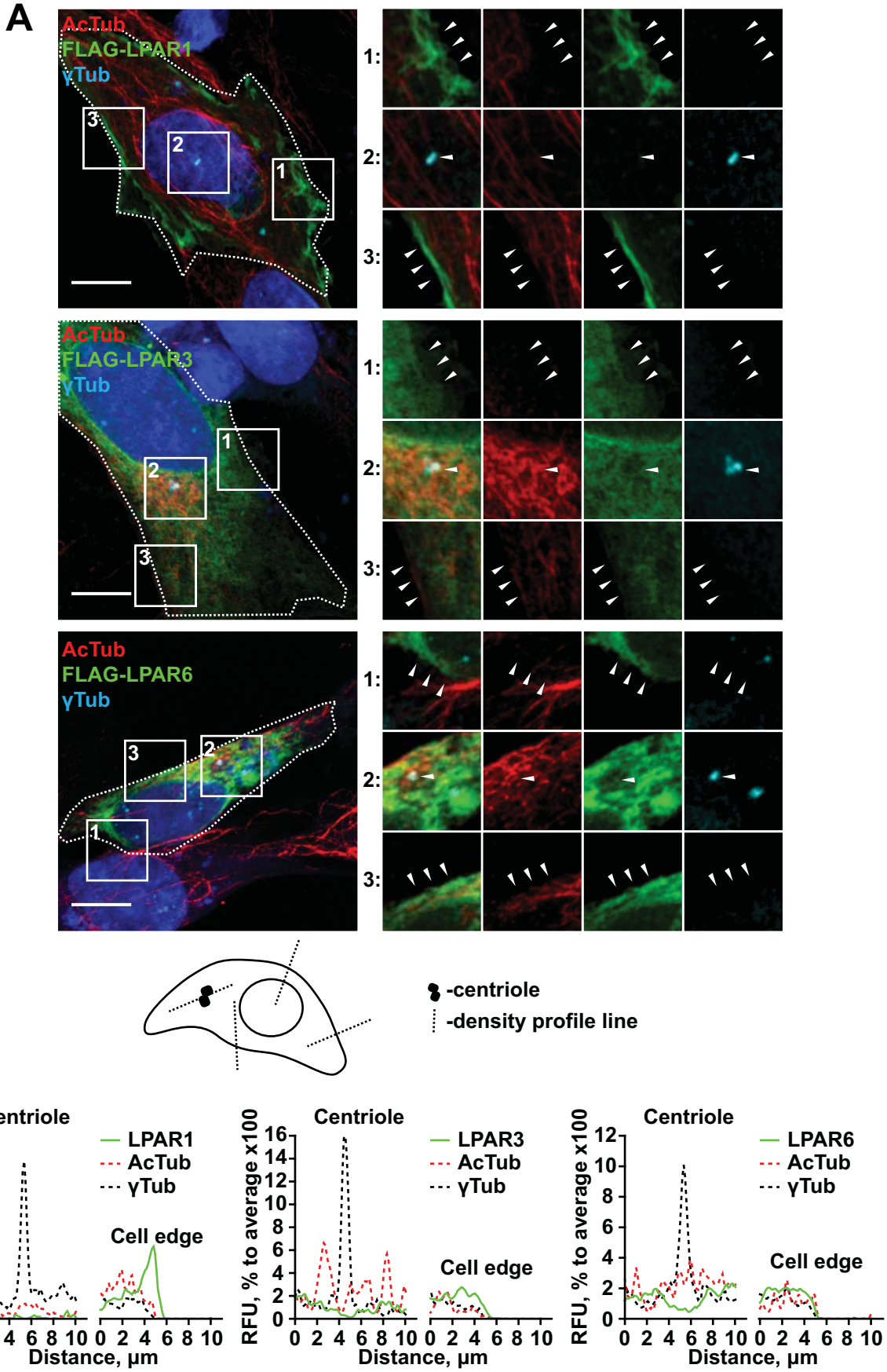
A, B. Representative western blot of response to single growth factor stimulation for cells as in **Fig.S2A**. Experimental set up shown in top **Fig.S2B:** serum-starved cells were treated with 10ng/ml of PDGF-AB (**A**), or 20ng/ml of HGF (**B**), lysed in time-dependent manner; and stained with antibodies against Thr202/Tyr204 phosphorylated ERK1/2 (pERK1/2 T202/204), total ERK1/2, Ser473 phosphorylated AKT (pAKT S473), total AKT and GAPDH, as a loading control. * indicates bleed-through of pERK1/2 signal.

Supplementary Figure 3. Loskutov



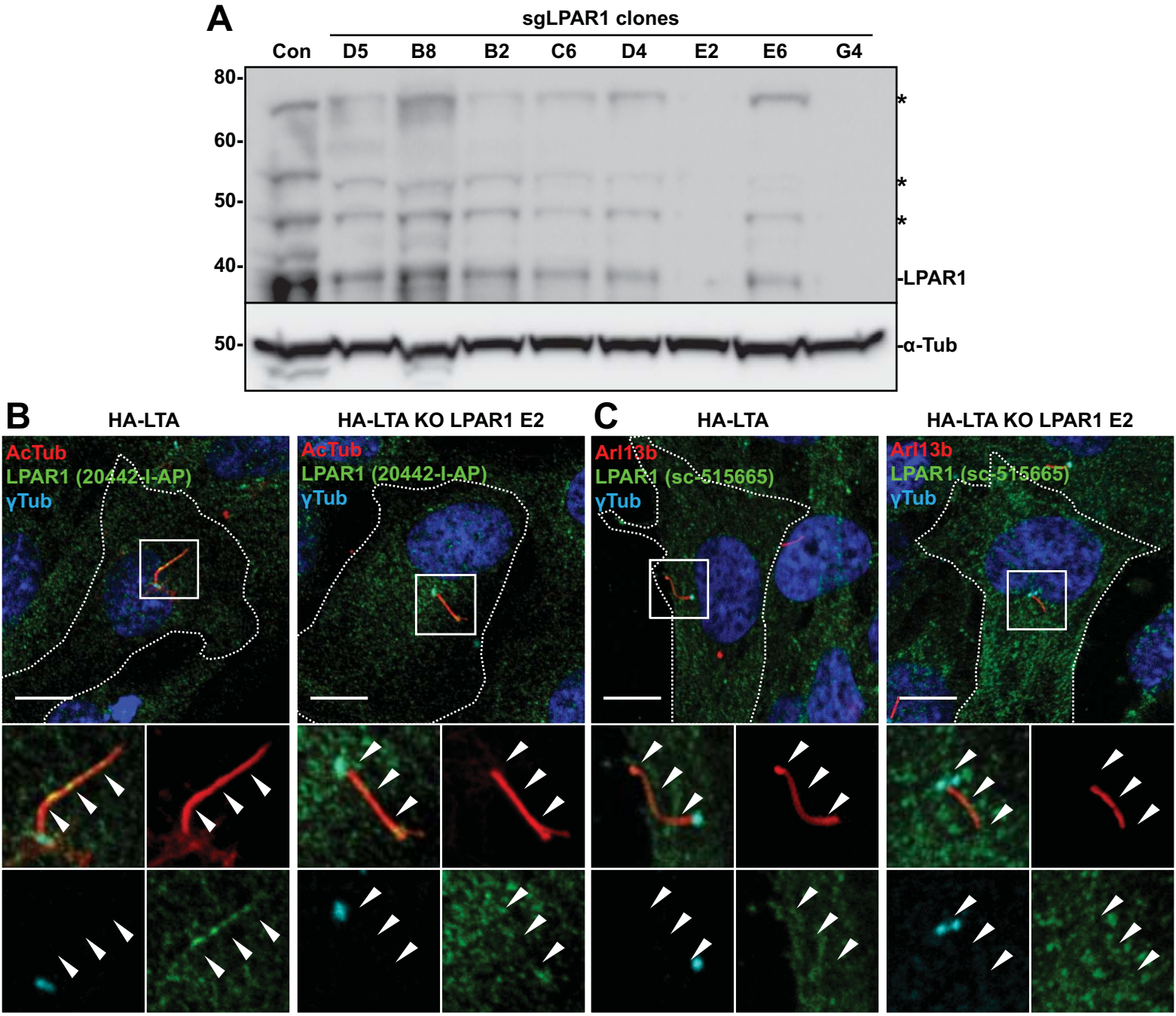
LPAR1, 3 and 6 subcellular localization in cells with assembled primary cilium.
A. Representative images of cells with primary cilia expressing 3xFLAG LPAR3 and LPAR6, stained for FLAG-tag, acetylated α-tubulin (AcTub, cilia marker) and γ-tubulin (γTub, centriole/basal body marker). Scale bar - 10μm. **B.** Signal intensity profile of the primary cilium and cell edge regions of cell in **A** and **Fig.5A**, as shown in pictogram on top.

Supplementary Figure 4. Loskutov



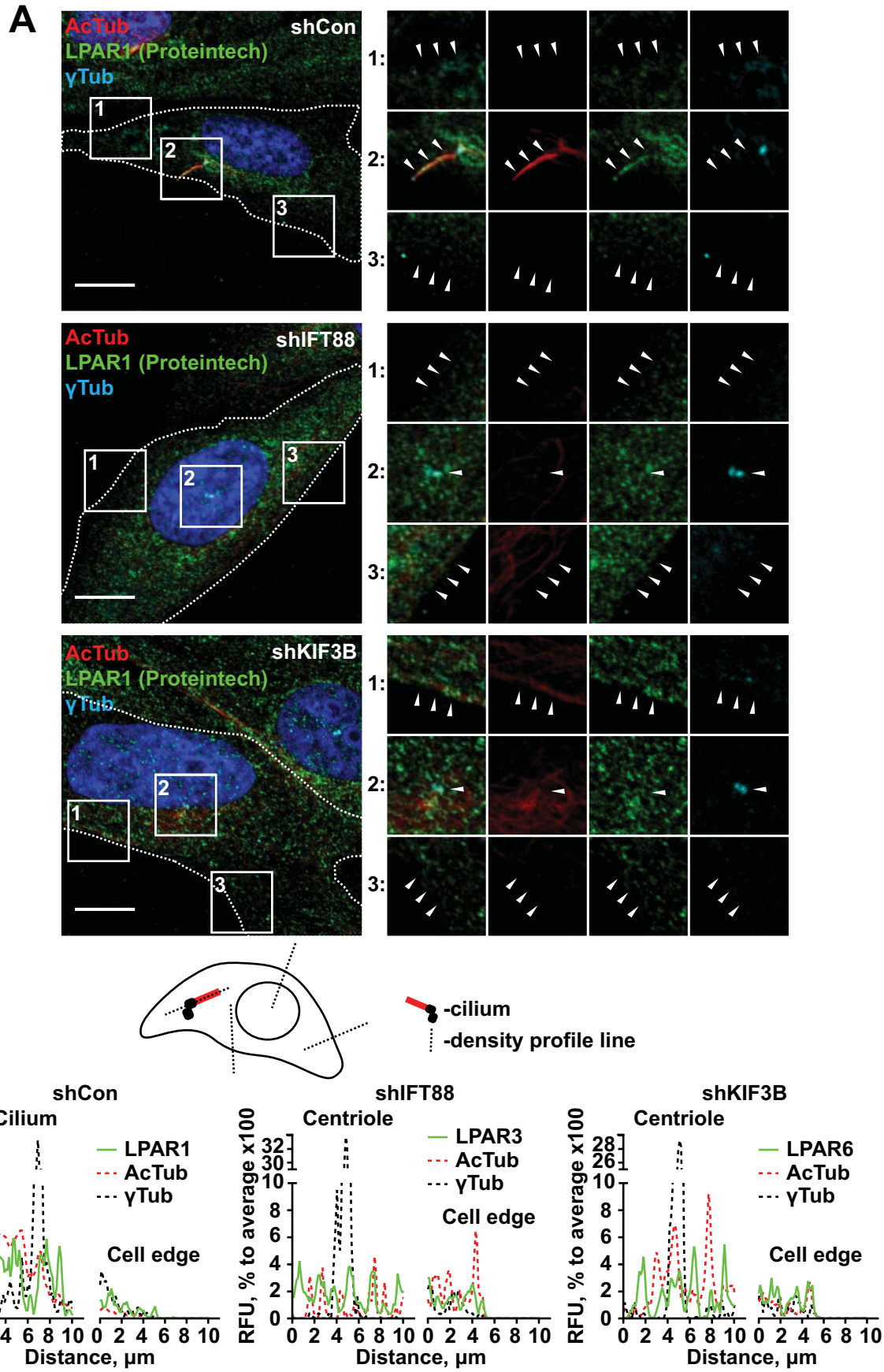
LPAR1, 3 and 6 subcellular localization in cells with disassembled primary cilium.
A. Representative images of cells w/o primary cilia expressing 3xFLAG tagged LPAR1, LPAR3 and LPAR6, stained for FLAG-tag, acetylated α-tubulin (AcTub, cilia marker) and γ-tubulin (γTub, centriole/basal body marker). Scale bar - 10μm. **B.** Signal intensity profile of the centriole and cell edge regions of cell in **A**, as shown in pictogram on top.

Supplementary Figure 5. Loskutov



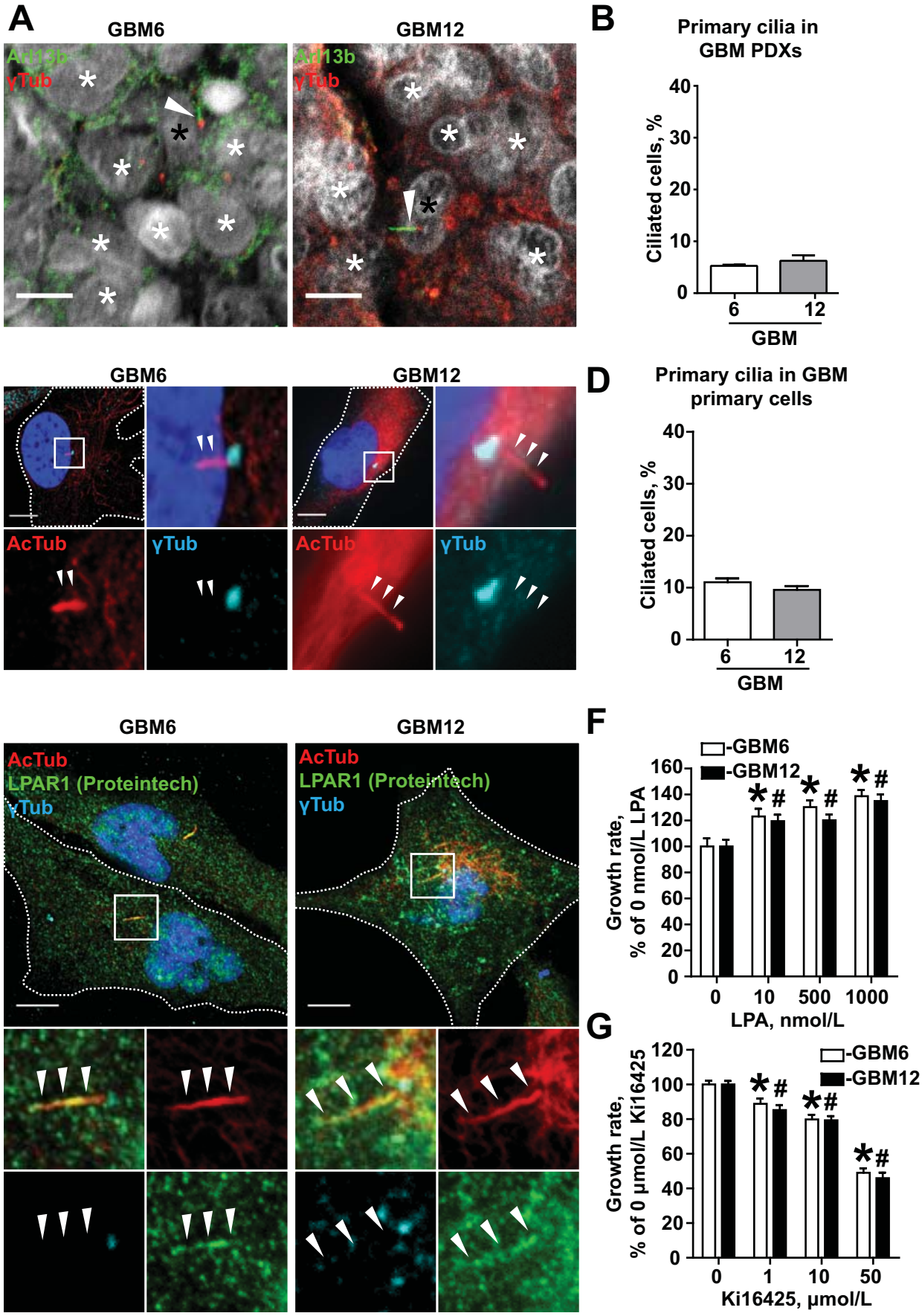
LPAR1 antibodies validation for immunofluorescent staining.
A. Western blot of CRISPR-Cas9 induced knockout of LPAR1 in immortalized astrocytes (HA-LTA) stably expressing sgRNA (Con) or sgRNA against LPAR1. * indicates glycosylated forms of LPAR1. **B-C.** Representative image of HA-LTA, stained for acetylated α-tubulin (AcTub, cilium marker; B) or Arl13b (cilium marker; C), γ-tubulin (γTub, basal body marker) and LPAR1 (B - Proteintech 20442-I-AP, C - SantaCruz sc-515665); scale bar – 10μm.

Supplementary Figure 6. Loskutov



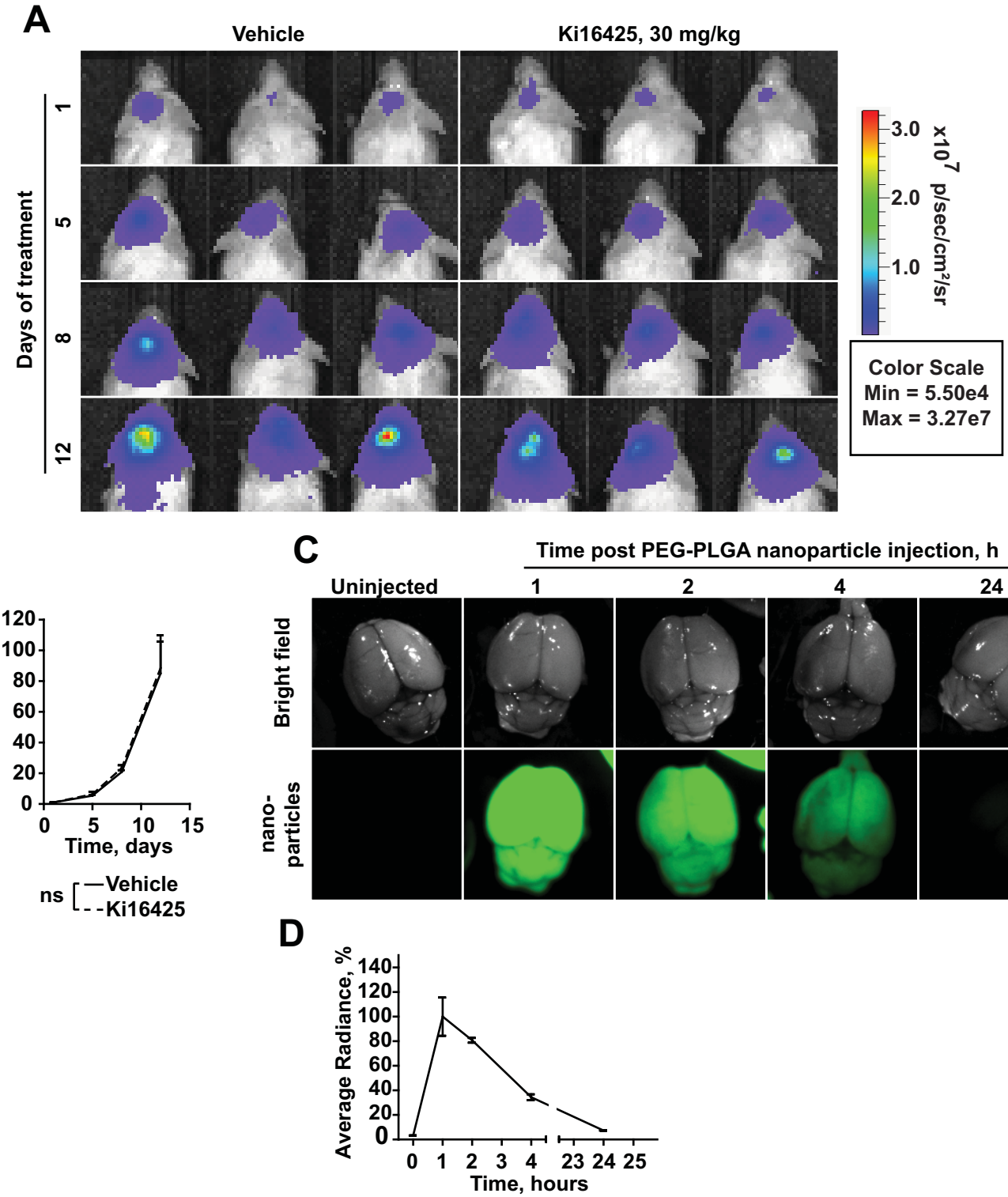
Endogenous LPAR1 localization in cells with and without primary cilium.
A. Representative images of HA-LTA with intact (shCon) or impaired (shIFT88, shKIF3B), stained for LPAR1, acetylated α-tubulin (AcTub, cilia marker) and γ-tubulin (γTub, centriole/basal body marker). Scale bar - 10μm. **B.** Signal intensity profile of the cilium/centriole and cell edge regions of cells in **A**, as shown in pictogram on top.

Supplementary Figure 7. Loskutov



GBM6 and GBM12 have decreased ciliation and utilize LPA as a growth factor.

A. Representative images of GBM6 and GBM12 PDXs stained for Arl13b (marker of cilia) and γ-tubulin (γTub, marker of centriole/basal body). Arrows indicate primary cilia, black asterisks - ciliated cells, white asterisks - deciliated cells. Scale bar - 10μm. **B.** Quantification of primary cilia occurrence in GBM6 and GBM12 xenografts as in **A**; n=3, 100 cells per group. **C.** Representative images of GBM6 and GBM12 cultured primary cells stained for acetylated α-tubulin (AcTub, marker of cilia) and γ-tubulin (γTub, marker of centriole/basal body). Arrows indicate primary cilia. Scale bar - 10μm. **D.** Quantification of primary cilia occurrence in GBM6 and GBM12 primary cells, as in **C**; n=3,100 cells per group. **E.** Representative images of GBM6 and GBM12 cultured primary cells stained for acetylated α-tubulin (AcTub, marker of cilia), LPAR1 and γ-tubulin (γTub, marker of centriole/basal body). Arrows indicate primary cilia. Scale bar - 10μm. **F.** Growth rate of GBM6 and GBM12 primary cells in serum-free media supplemented with 20ng/ml of EGF, 20ng/ml of bFGF, B27 supplement and indicated concentrations of LPA. One-way ANOVA with Dunnett's post hoc test; *, $^{\#}p<0.05$ for GBM6 and GBM12 respectively, compared to no LPA control; n=3. **G.** Growth rate of GBM6 and GBM12 primary cells in 2% serum-supplemented media and in presence of indicated concentrations of Ki16425. One-way ANOVA with Dunnett's post hoc test; *, $^{\#}p<0.05$ for GBM6 and GBM12 respectively, compared to no Ki16425 control; n=3.



Administration of Ki16425 has no effect on intracranial tumor growth.
A. Representative images of GBM12 growing in brains of mice treated with Vehicle-control or Ki16425. **B.** Quantification of bioluminescence, as in **A**; two-way ANOVA, Tukey post hoc test; n = 5. **C.** Representative images of mice brains injected with PEG-PLGA nanoparticles loaded with fluorescent dye. **D.** Quantification of fluorescence from brains as in **C**; n=2.

Supplementary Figure 9. Loskutov

target	cat.#	host species	company	application	dilution
acetyated alpha tubulin	T6793	mouse	Sigma	IF, F-IHC	1:1000
acetyated alpha tubulin	5335S	rabbit	Cell Signaling	IF	1:500
gamma tubulin	sc-7396	goat	Santa Cruz	IF, F-IHC	1:500
IFT88	60227-1-Ig	mouse	Proteintech	WB	1:1000
Kif3B	sc-50456	rabbit	Santa Cruz	WB	1:500
alpha tubulin	16199	mouse	Sigma	WB	1:40000
pERK1/2 T202/204	9101	rabbit	Cell Signaling	IF, WB	1:200, 1:1000
ERK1/2	4695	rabbit	Cell Signaling	WB	1:1000
GAPDH	MAB374	mouse	Millipore	WB	1:80000
pAKT S473	AF887	rabbit	R&D Systems	IF, WB	1:100, 1:500
AKT	2920	mouse	Cell Signaling	WB	1:1000
FLAG	F1804	mouse	Sigma	IF, WB	1:500, 1:1000
FLAG	PA1-984B	rabbit	Thermo Fisher Scientific	IF, WB	1:500, 1:1000
G alpha s	sc-135914	mouse	Santa Cruz	IF, WB	1:100, 1:500
G alpha q	sc-393	rabbit	Santa Cruz	IF, WB	1:200, 1:1000
G alpha 12	sc-409	rabbit	Santa Cruz	IF, WB	1:100, 1:200
G alpha i1	sc-391	rabbit	Santa Cruz	IF, WB	1:100, 1:500
Arl13b	17711-1-AP	rabbit	Proteintech	IF, F-IHC	1:400, 1:200
LPAR1	20442-1-AP	rabbit	Proteintech	IF	1:100
LPAR1	10005280	rabbit	Cyman chemicals	WB	1:250
LPAR1	sc-515665	mouse	Santa Cruz	IF	1:100

Supplementary table 1

name	clone ID	targeting sequence	vector	company
shIFT88#1	V3LHS_338157	GGAATAACACTGACCACCT	pGIPZ	Dharmacon
shIFT88#2	V3LHS_338155	AGCATCTGAATACTGACCA	pGIPZ	Dharmacon
shKif3B#1	V3LHS_644788	TTGCTAGTCTCTTCTCTCA	pGIPZ	Dharmacon
shKif3B#2	V3LHS_635533	ATCTCATCTTCATCCTGCA	pGIPZ	Dharmacon

Supplementary table 2

name	sequence	company
BamHI-LPAR1	ATTGGATCCATGGCTGCCATCTCTACTTCC	IDT Technologies
LPAR1-TGA-XhoI	ATTCTCGAGTCAAACCACAGAGTGGTCATTGC	Invitrogen
BamHI-LPAR3	ATTGGATCCATGAATGAGTGTCACTATGACAAGC	IDT Technologies
LPAR3-TGA-XhoI	ATTCTCGAGTCAGGAAGTGCTTTTATTGCAGACTG	Invitrogen
BamHI-LPAR6	ATTGGATCCATGGTAAGCGTTAACAGCTCC	IDT Technologies
LPAR6-TGA-XhoI	ATTCTCGAGTCAGGCAGCAGATTCATTGTCAAATATC	Invitrogen
ER-3xFlag-MSC (forward strand)	GATCCTAAGCTTACCGGTATGAAGACGATCATCGCCCTGAGCT ACATCTTCTGCCTGGTATTCGCCATGGACTACAAAGACCATGAC GGTGATTATAAAGATCATGACATCGATTACAAGGATGACGATGA CAAGGGAGGTGGAGGCGGTGGAGGATCCTGTACAGCTAGCGA ATTCTGCAGATATCGGCGCGCCGTTTAAACACGCGTCTCGAGT GATTAATTAAGGTCGACGATCCT	Invitrogen
sgLPAR1_F	caccgTCTTTGGCTATGTTCGCCAG	Invitrogen
sgLPAR1_R	aaacCTGGCGAACATAGCCAAAGAc	Invitrogen

Supplementary table 3