Supplemental Table 1. Oligonucleotide primers used for qRT-PCR analysis

Gene symbol	Primer direction	Primer sequence
MCM2	Forward	5' - CCAGGCCTCTCTTGATGTCT - 3'
	Reverse	5' - TAGCCTCTCCAAGGATCAGC - 3'
MCM3	Forward	5' - CCAGTGTTCGGGCTGTAACT - 3'
	Reverse	5' - GGCCACCTACATTGCAGAAG - 3'
MCM4	Forward	5' - CGAATAGGCACAGCTCGATA - 3'
	Reverse	5' - GGCAGACACCACACACAGTT - 3'
MCM5	Forward	5' - AGGGATCTTCACCAGGTGTG - 3'
	Reverse	5' - GACATCCAGGTCATGCTCAA - 3'
MCM6	Forward	5' - TCTACTATGCGCCTGGCAAT - 3'
	Reverse	5' - TTGTCAGCTCCCATCATGTC - 3'
MCM7	Forward	5' - GGTCAGTTCTCCACTCACGG - 3'
	Reverse	5' - CATACATTGATCGACTGGCG - 3'
MCM10	Forward	5' - GCGGTCAGCAGAGACAGATT - 3'
	Reverse	5' - CGGCCAAGATTCTACATTGC - 3'
ACAT2	Forward	5' - TGCCATTTTGTGGCTACATT - 3'
	Reverse	5' - GGTGAGATGCCACTGACTGA - 3'
HMGCS1	Forward	5' - TGGCAGGGAGTCTTGGTACT - 3'
	Reverse	5' - TCCCACTCCAAATGATGACA - 3'
HMGCR	Forward	5' - TGTCCCCACTATGACTTCCC - 3'
	Reverse	5' - TCGGTGGCCTCTAGTGAGAT - 3'
FDFT1	Forward	5' - GCAAATGTCGGCAATCACT - 3'
	Reverse	5' - GGTTCATGGAGAGCAAGGAG - 3'
PGGT1B	Forward	5' - AGCCTTTGATGGATTGAACG - 3'
	Reverse	5' - GGTCCTTCCCACAGAAGACA - 3'
RABGGTB	Forward	5' - AGGACCCACCATGAGTAGCA - 3'
	Reverse	5' - TTTACTTGGCTGGTGGCTTT - 3'
MAP1LC3A (LC3A)	Forward	5' - ATGATCACCGGGATTTTGC - 3'
	Reverse	5' - CTCAGACCGGCCTTTCAA - 3'
MAP1LC3B (LC3B)	Forward	5' - GAGAAGACCTTCAAGCAGCG - 3'
	Reverse	5' - AAGCTGCTTCTCACCCTTGT - 3'

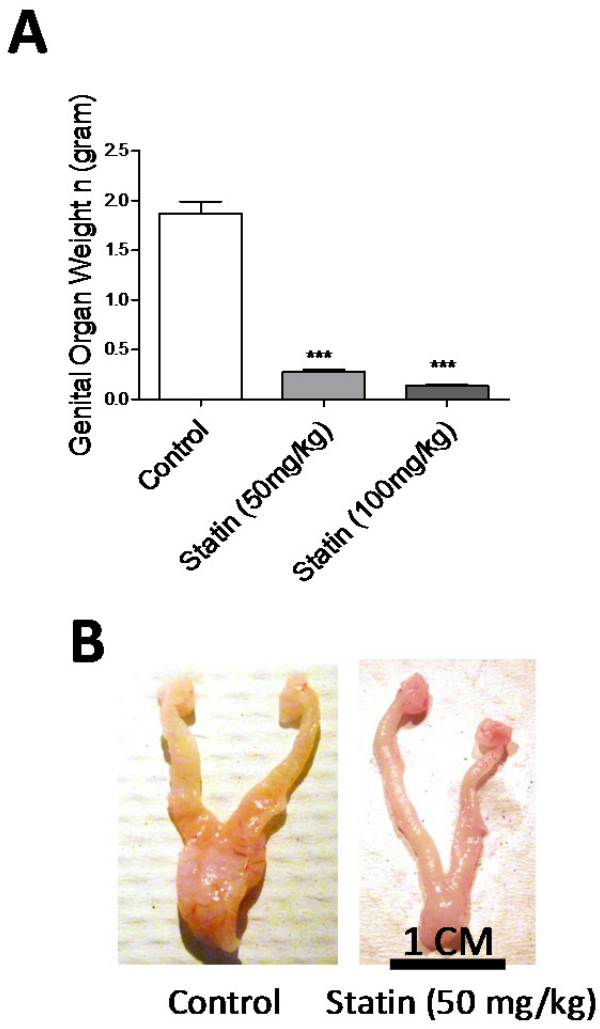
Supplemental Table 2. GSEA enrichment of KEGG functional pathways in lovastatin-regulated genes

	NAME	NOM p-val	FDR q-val
SKOV3 Down-regulated by statin	KEGG_DNA_REPLICATION	0.000	0.000
	KEGG_HOMOLOGOUS_RECOMBINATION	0.001	0.002
	KEGG_MISMATCH_REPAIR	0.000	0.003
	KEGG_BETA_ALANINE_METABOLISM	0.002	0.002
	KEGG_NUCLEOTIDE_EXCISION_REPAIR	0.000	0.014
	KEGG_CELL_CYCLE	0.000	0.012
	KEGG_RNA_POLYMERASE	0.000	0.011
	KEGG_BASE_EXCISION_REPAIR	0.000	0.027
	KEGG_SPLICEOSOME	0.000	0.024
	KEGG_BUTANOATE_METABOLISM	0.024	0.066
	KEGG_LYSINE_DEGRADATION	0.004	0.075
	KEGG_PROGESTERONE_MEDIATED_OOCYTE_ MATURATION	0.001	0.083
	KEGG_PROTEASOME	0.003	0.080
	KEGG_PYRIMIDINE_METABOLISM	0.000	0.076
	KEGG_RIBOSOME	0.000	0.074
	KEGG_PENTOSE_AND_GLUCURONATE_ INTERCONVERSIONS	0.133	0.093
	KEGG_RNA_DEGRADATION	0.006	0.091
	KEGG_ONE_CARBON_POOL_BY_FOLATE	0.147	0.091
SKOV3 Up-regulated by statin	KEGG_TYPE_I_DIABETES_MELLITUS	0.000	0.006
	KEGG_GRAFT_VERSUS_HOST_DISEASE	0.001	0.012
	KEGG_ALLOGRAFT_REJECTION	0.000	0.013
	KEGG_AUTOIMMUNE_THYROID_DISEASE	0.002	0.036
	KEGG_GLYCOSAMINOGLYCAN_DEGRADATION	0.013	0.037
	KEGG_STEROID_BIOSYNTHESIS	0.032	0.054
	KEGG_COMPLEMENT_AND_COAGULATION_CASCADES	0.003	0.047
	KEGG_PRION_DISEASES	0.006	0.055
	KEGG_SNARE_INTERACTIONS_IN_VESICULAR_ TRANSPORT	0.001	0.075
	KEGG_LEISHMANIA_INFECTION	0.001	0.071
	KEGG_PPAR_SIGNALING_PATHWAY	0.000	0.087
OVCAR5 Down-regulated by statin	KEGG_DNA_REPLICATION	0.000	0.000
	KEGG_MISMATCH_REPAIR	0.000	0.003
	KEGG_NUCLEOTIDE_EXCISION_REPAIR	0.000	0.015
	KEGG_RNA_POLYMERASE	0.000	0.032
	KEGG_HOMOLOGOUS_RECOMBINATION	0.007	0.037
	KEGG_SPLICEOSOME	0.000	0.065
	KEGG_PRIMARY_IMMUNODEFICIENCY	0.108	0.074
	KEGG_PYRIMIDINE_METABOLISM	0.000	0.086
OVCAR5 Up-regulated by statin	KEGG_STEROID_HORMONE_BIOSYNTHESIS	0.000	0.007
	KEGG_METABOLISM_OF_XENOBIOTICS_BY_CYTOCHROM E_P450	0.000	0.013

Supplemental Table 3. Lovastatin affects expression of genes in glycolysis/gluconeogenesis pathway

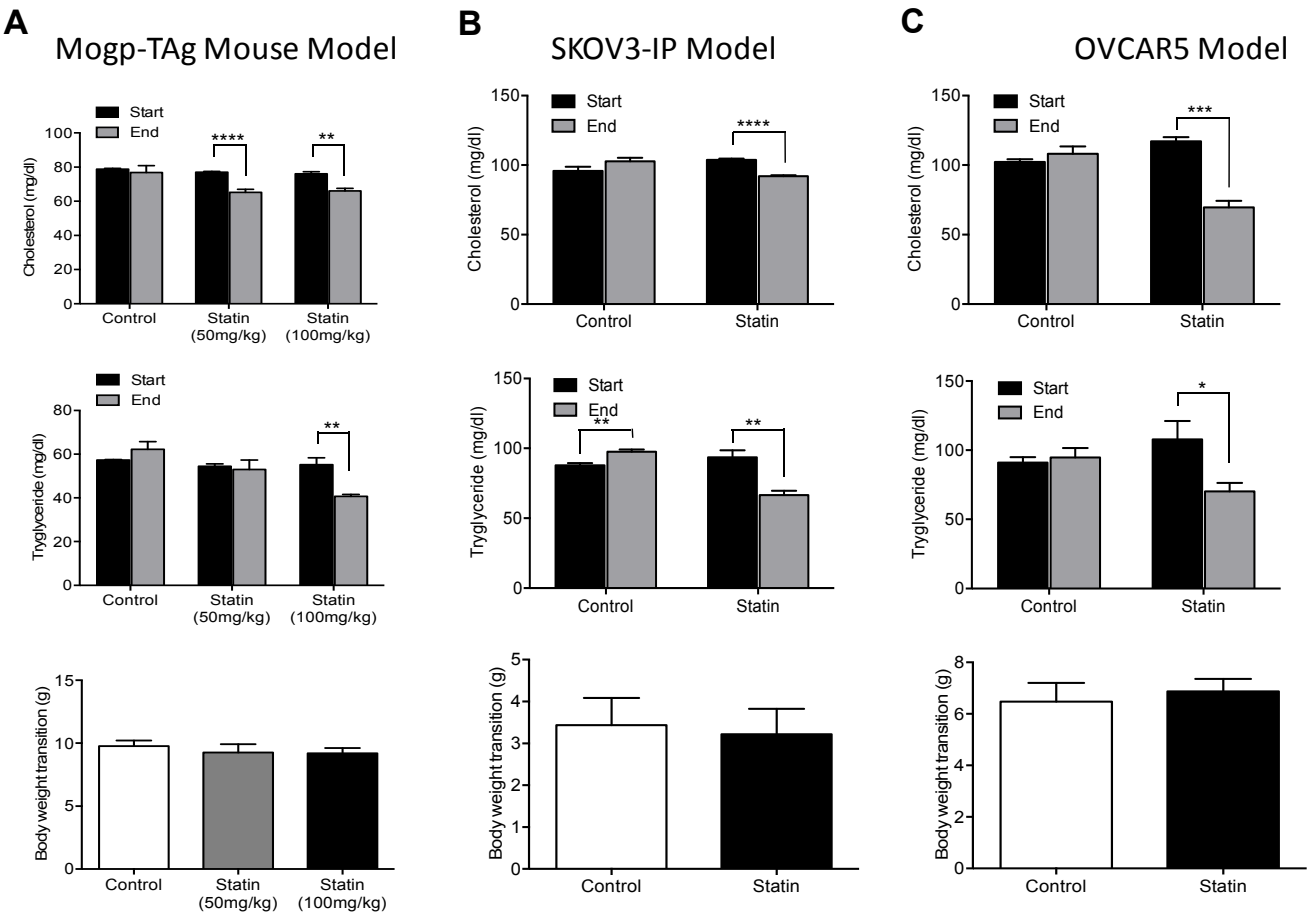
		OVCAR5		SKOV3		
ENTREZ_ID	Gene	logFoldChange	p.value	logFoldChange	p.value	response*
2026	ENO2	1.9267	0	1.4865	0	both
2027	ENO3	1.1383	0.0194	0.9641	0.0008	both
80201	HKDC1	1.7182	0.0001	1.6554	0	both
5091	PC	1.1696	0.0003	1.9366	0	both
226	ALDOA	0.6283	0.0048	0.2271	0.2522	one
330	ALDOC	0.4542	0.0339	0.3062	0.1835	one
3098	HK1	0.4674	0.0266	0.4603	0.0953	one
5211	PFKL	0.4437	0.0146	0.3666	0.1233	one
5223	PGAM1	0.1744	0.2073	-1.2398	0.0001	one
5315	PKM2	0.462	0.1192	0.5363	0.0444	one
441531	PGAM4	0.2375	0.1484	-0.9539	0.0006	one
5106	PCK2	0.2958	0.2338	2.7429	0	one
669	BPGM	-0.3534	0.1686	-0.0821	0.6739	none
2023	ENO1	0.1332	0.3068	0.1565	0.422	none
2597	GAPDH	0.1943	0.1922	0.1883	0.3414	none
2821	GPI	0.2281	0.1215	-0.1703	0.408	none
5213	PFKM	-0.4035	0.0799	-0.4633	0.0611	none
5214	PFKP	0.2286	0.1124	0.2107	0.2775	none
5230	PGK1	0.2514	0.0867	-0.1955	0.319	none
5313	PKLR	-0.2264	0.1972	-0.0693	0.7767	none
7167	TPI1	0.1554	0.2594	-0.3547	0.0871	none
83440	ADPGK	-0.2227	0.1529	-0.2949	0.1832	none
3099	HK2	-0.3752	0.0234	1.7229	0	other#

*Gene expression response in both, one, or none of the cell lines examined.
#Other indicates the response is different in each cell line.

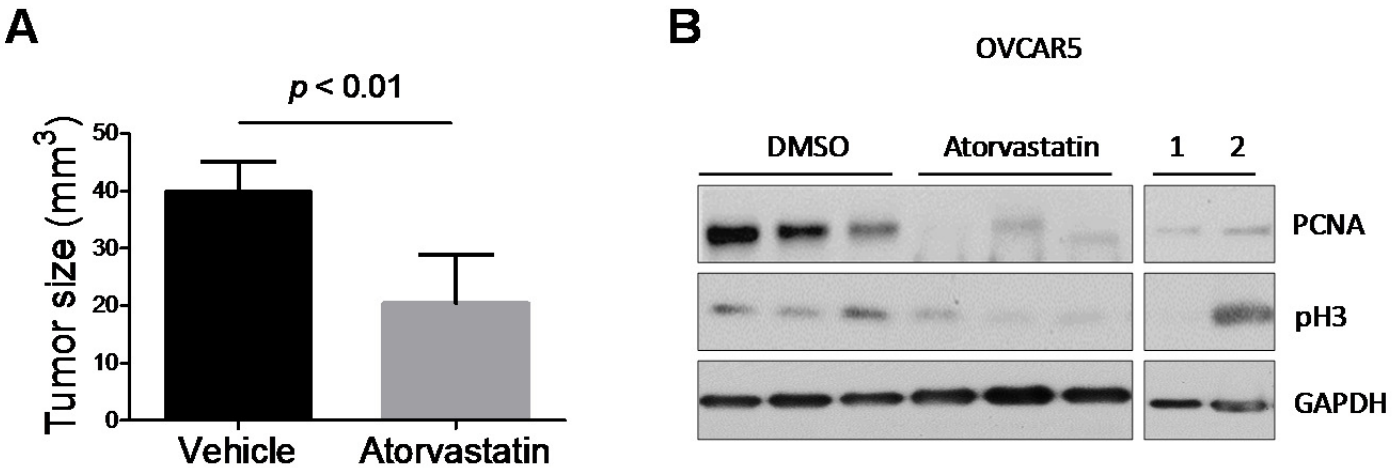


Supplemental Fig. 1. Daily administration of lovastatin prevents tumor growth in mogp-TAg transgenic mice.

A. Weight of gynecological tracts taken from mogp-TAg mice treated with lovastatin (50 mg/Kg, 100 mg/Kg) or vehicle (n=10 for each group; ***p< 0.001, two-tailed Mann-Whitney U test). B. Representative images of gynecological tracts from a mogp-TAg mouse treated daily with lovastatin (50 mg/Kg) and a mogp-TAg mouse treated daily with control vehicle.



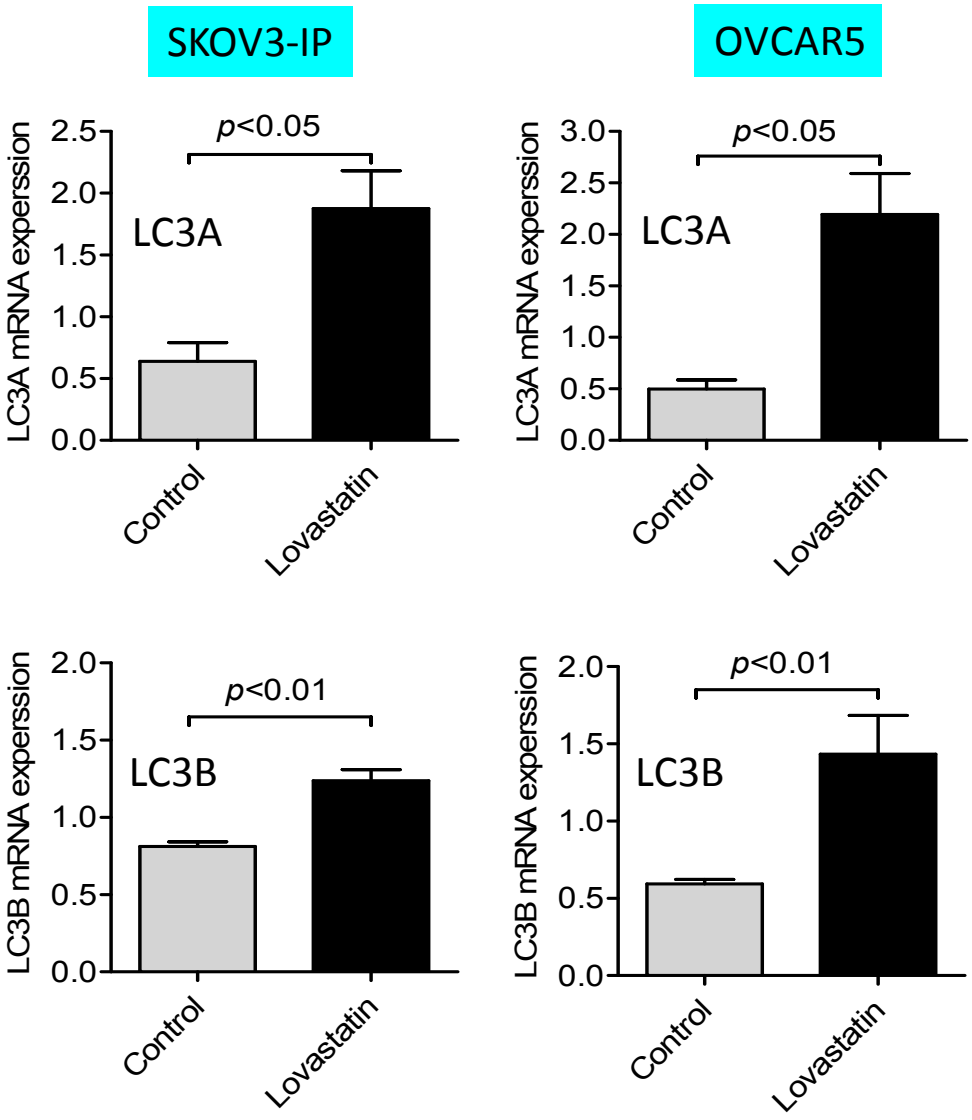
Supplemental Fig. 2. Body weight and serum levels of cholesterol and triglyceride in mogp-TAg, SKOV3-IP, and OVCAR5 mouse tumor models. (A) Oral administration of 50 or 100 mg/Kg lovastatin in the mogp-TAg mice reduced serum levels of cholesterol but did not affect body weight. High oral dose of lovastatin, 100 mg/Kg, affects triglycerides levels. (B) & (C) i.p. administration of lovastatin at 12.5 mg/Kg dose reduced cholesterol and triglyceride levels in the SKOV3-IP and OVCAR5 mouse models. Lovastatin did not affect mouse body weight at this dose. *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001, two-tailed Mann-Whitney U test.



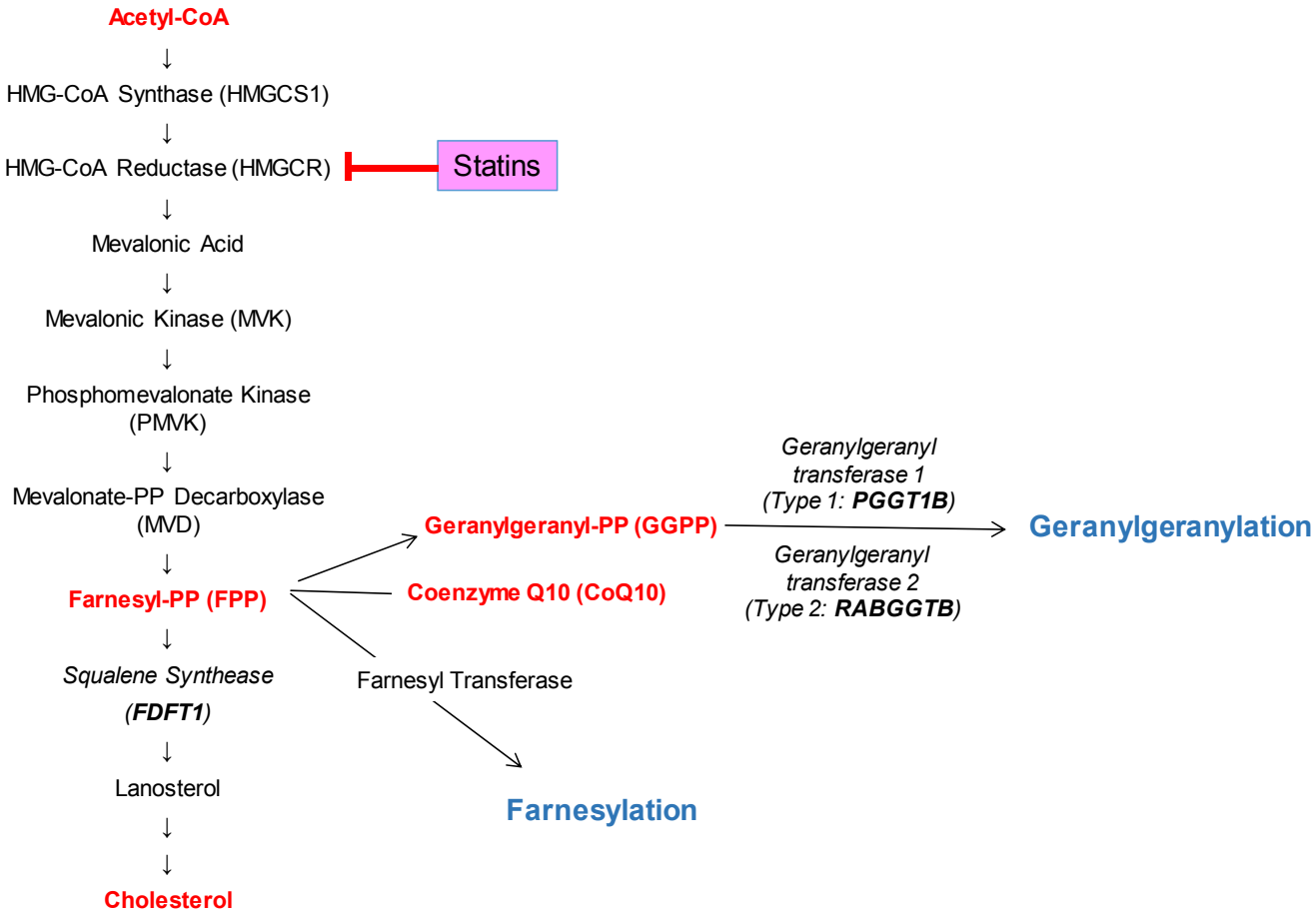
Supplemental Fig. 3. Atorvastatin treatment delays growth of ovarian tumor xenografts.

A. Tumor sizes in athymic nude mice inoculated with 5 million OVCAR5 ovarian cancer cells that received atorvastatin (daily 10 mg/Kg; i.p. administration) beginning at day 7. Mice were sacrificed at day 28 to measure tumor size. n=5 for each group; two-tailed Mann-Whitney U test.

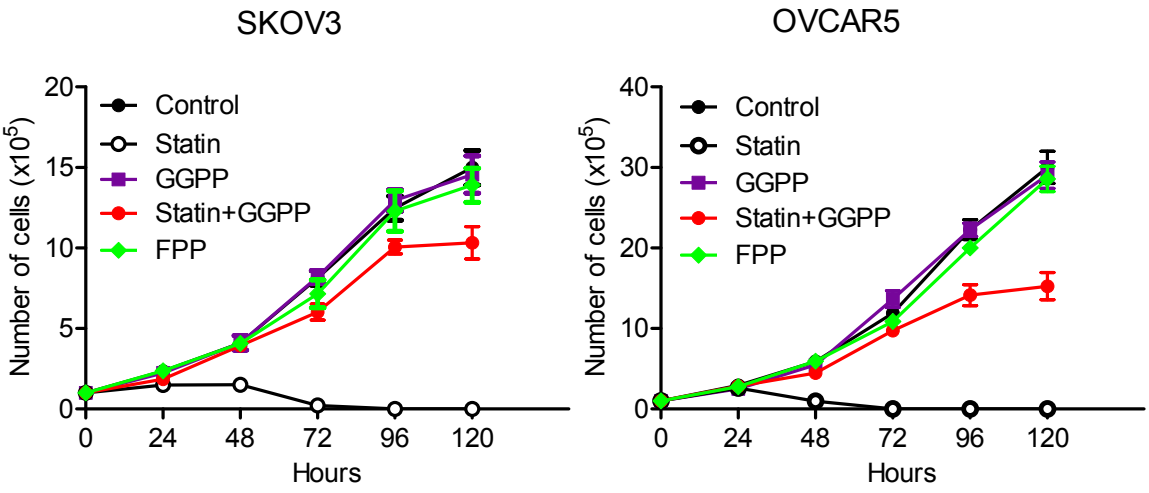
B. Western blot analyses show decreased expression of PCNA in three representative treated tumors as compared to control tumors. Similarly, expression of phospho-Histone H3 is reduced in the atorvastatin-treated group. GAPDH was used as the loading control. Each lane represents a different xenograft tumor sample. 1 and 2 represent OVCAR5 cell cultures treated with DMSO and nocodazole (1 μg/ml for 12 h), respectively, to serve as controls.



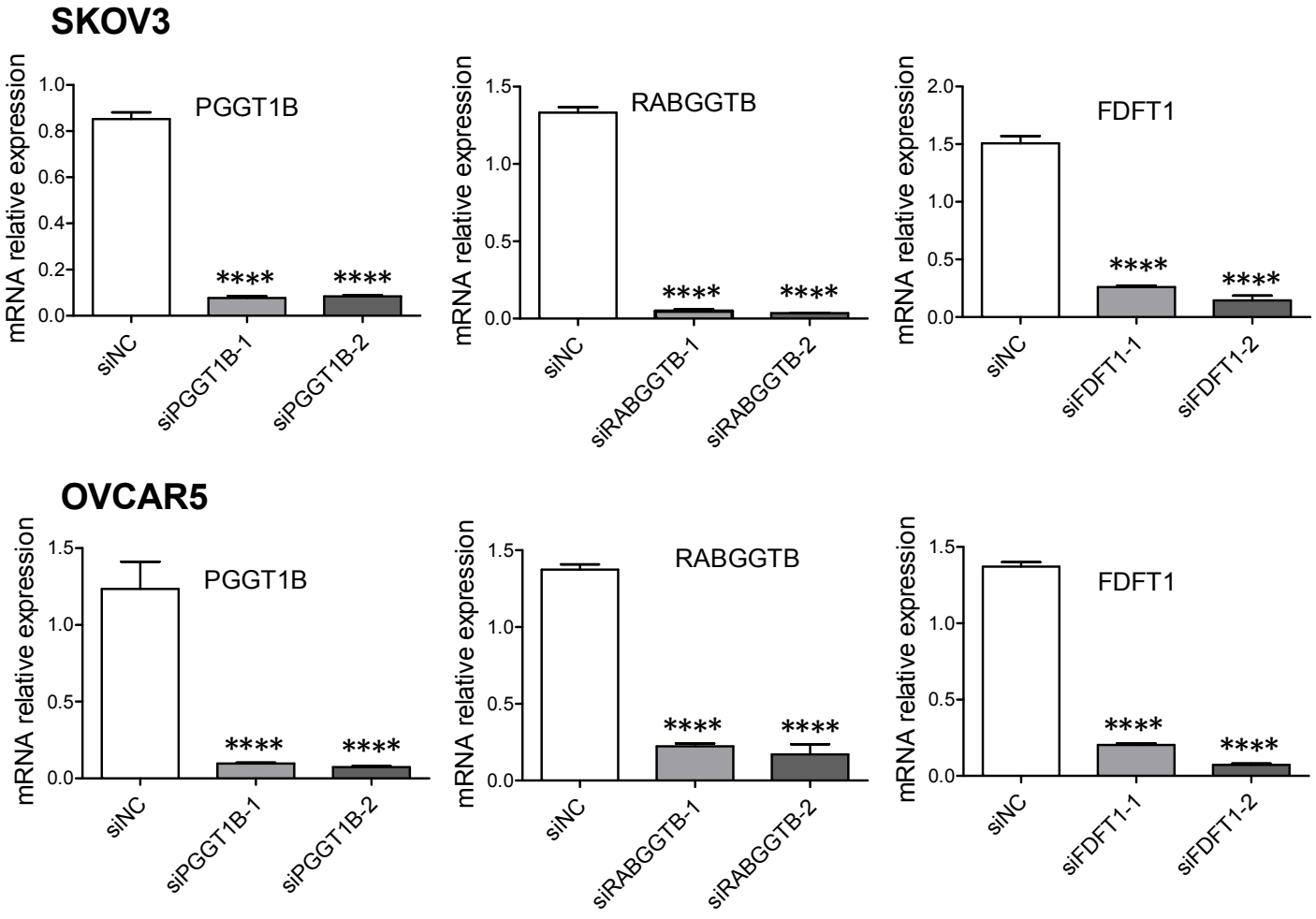
Supplemental Fig. 4. Statin treatment increases transcript levels of LC3A and LC3B. To determine transcript expression levels of LC3A and LC3B, qRT-PCR was performed on SKOV3-IP and OVCAR5 xenograft tumors obtained from lovastatin or vehicle-treated mice. n=5 for each group, two-tailed Mann-Whitney U test.



Supplemental Fig 5. Scheme of the mevalonate pathway. Intermediate metabolites are shown in red, enzymes in the pathway are shown in black, genes encoding enzymes targeted by RNAi in this study are shown in italics. The rate-limiting step of this pathway is catalyzed by HMG-CoA reductase, which can be inhibited by statins.



Supplemental Fig. 6. Applying GGPP or FPP as a single agent does not affect ovarian cancer cell proliferation. Cells were incubated with GGPP (25 μM), FPP (25 μM), lovastatin (10 μM), DMSO (vehicle control), or a combination of GGPP or FPP with lovastatin. Numbers of cells were measured every 24 h over a 120 h period. Data are presented as the mean ± SD (n=3).



Supplemental Fig. 7. Real-time qRT-PCR confirms knockdown efficiency of each siRNA.

The knockdown efficiency of each siRNA for the designated enzyme in the mevalonate pathway was analyzed by qRT-PCR. Non-targeting siRNA was used as a control. All values were normalized to expression of β-actin (ACTB), a housekeeping gene. **** $p<0.0001$