Geminin deficiency enhances survival in a murine medulloblastoma model by inducing apoptosis of preneoplastic granule neuron precursors – Sankar etal

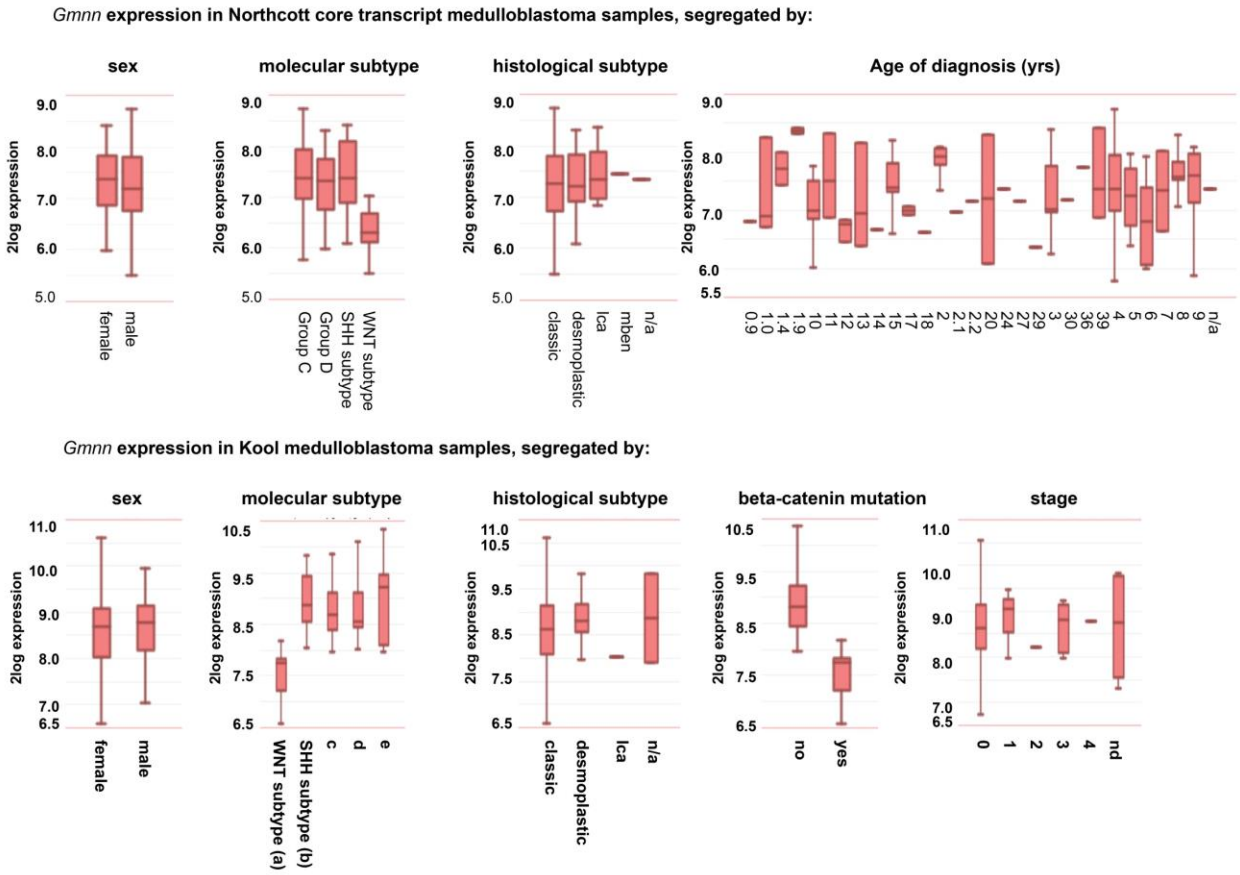

Figure S1: **Geminin expression levels in medulloblastomas do not correlate with tumor molecular or histological subtypes, staging, age of diagnosis, or sex.** Geminin expression levels were analyzed in two human medulloblastoma datasets by using the R2 Megasampler tool (see Methods; datasets used were Northcott core transcript, n=103, GSE21140 and Kool, n=62, GSE10327) and did not segregate based upon sex, molecular or histological subtype, age of diagnosis, or stage. *Gmnn* is on human chr6 and expression levels are lower in the Wnt and β-catenin mutated subtypes, congruent with monosomy 6 in the Wnt tumor subclass.

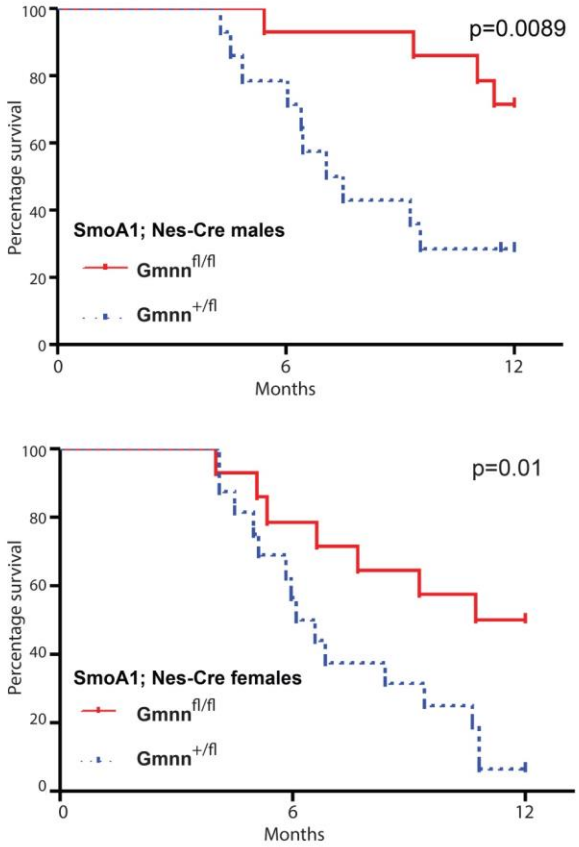

Figure S2: Geminin loss of function enhances survival in the SmoA1 medulloblastoma model. Kaplan-Meier survival plot is shown for cohorts of male or female mice hemizygous for both the Nes-Cre and SmoA1 transgenes and either heterozygous or homozygous for the floxed Gem allele. Animals were euthanized by transcardial perfusion when they exhibited neurologic impairment or morbidity or at the end of the study and presence or absence of tumors assessed by sectioning and histology.

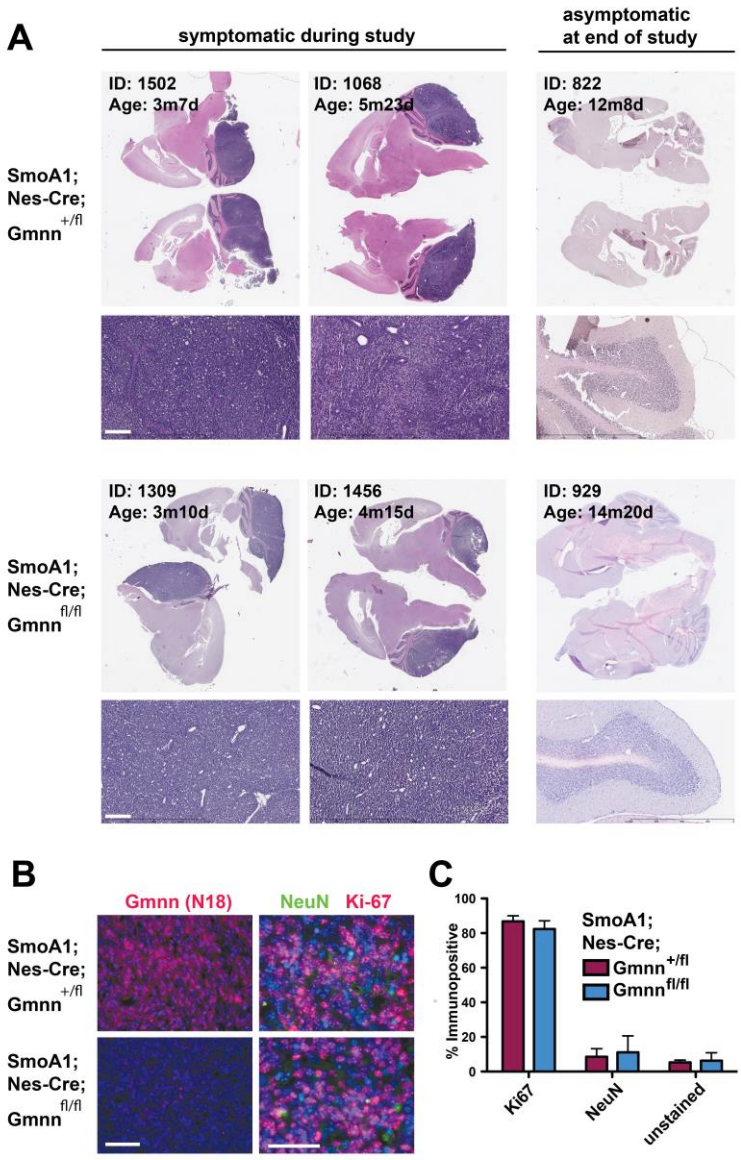

Figure S3: Histology and molecular marker expression in SmoA1 tumors. (**A**) Cohorts of mice with the SmoA1; Nes-Cre; Gmnn$^{+/fl}$ and SmoA1; Nes-Cre; Gmnn$^{fl/fl}$ genotypes were generated and tracked for one year. Mice that developed clinical symptoms of medulloblastoma (enlarged posterior fossa, tilted head, hunched posture, ataxia) and animals that remained asymptomatic through the end of the study were euthanized and histological sectioning of the brain was performed. Examples are shown, with identification number and age at the time euthanized indicated. Parasaggital sections of all symptomatic animals revealed large, bilateral tumor masses, while very few animals that remained asymptomatic

through the end of the study exhibited a visible tumor mass. Lower panels: higher magnification views through the tumor or cerebellum. Tumor size and histology appeared similar between the two genotypes. Scale bar=200µm. (**B**) For each genotype, three tumors were also analyzed by frozen sectioning and immunofluorescence for Gmnn, Ki67, and NeuN, with DAPI (blue) counterstaining of all nuclei. Scale bars=50µm, with (**C**) numbers of Ki67 or NeuN immunopositive cells scored for three sections through each tumor and expressed as a percentage +/- stdev. Gmnn protein levels were strongly diminished in the SmoA1; Nes-Cre; $Gmnn^{fl/fl}$ tumors, while similar fractions of cells expressing Ki67 or NeuN were seen for both genotypes.

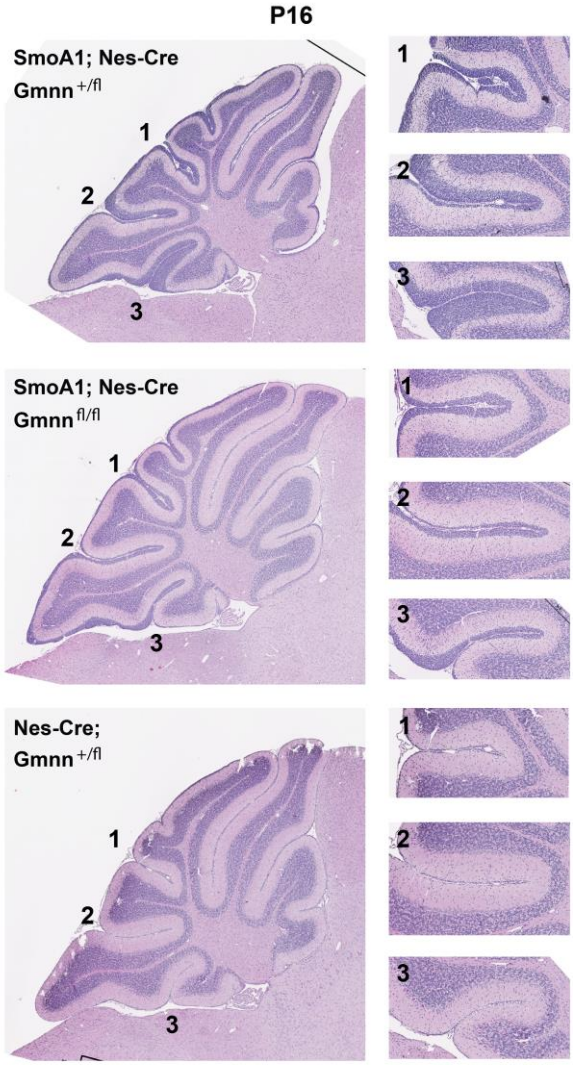

Figure S4: Geminin loss reduces numbers of persisting preneoplastic GNPs in SmoA1 mice. Animals hemizygous for the SmoA1 and Nes-Cre transgenes and heterozygous for the Gmnn floxed allele (SmoA1; Nes-Cre; Gmnn$^{+/fl}$) retained much thicker EGL regions in P16 cerebellar sections than those seen in SmoA1; Nes-Cre; Gmnn$^{fl/fl}$ homozygous animals, with animals lacking the SmoA1 transgene shown as an additional control.

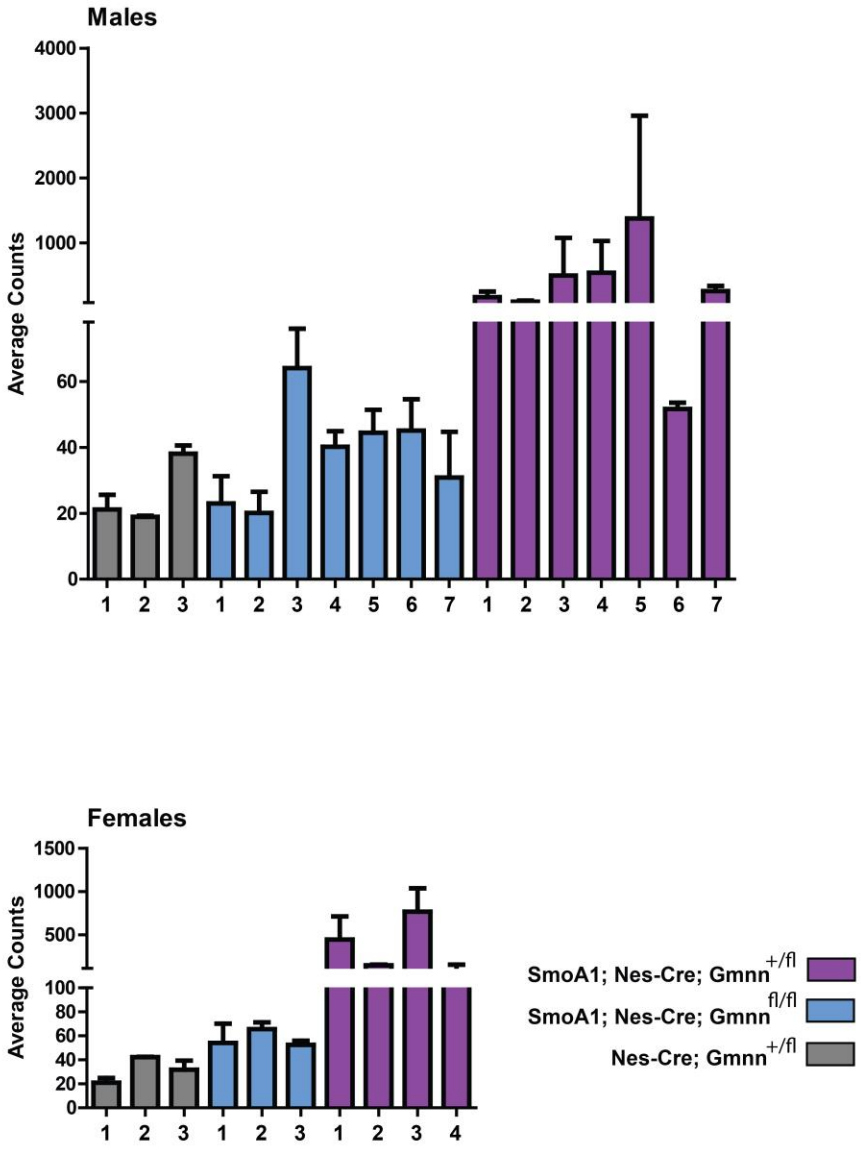

Figure S5: Quantitation of GNPs at the cerebellar surface in individual P28 animals, comparing animals hemizygous for the SmoA1 and Nes-Cre transgenes and heterozygous versus homozygous for the Gmnn floxed allele, with animals lacking the SmoA1 transgene as an additional control. Quantitative data (summarized for all animals in **Fig. 3D**) was obtained as averaged counts/section from 4 matched serial sections per brain, and is shown as averaged counts for each animal assayed. SmoA1; Nes-Cre; Gmnn$^{fl/fl}$ homozygous P28 animals had six-fold fewer pGNPs than SmoA1; Nes-Cre; Gmnn$^{+/fl}$ heterozygotes.

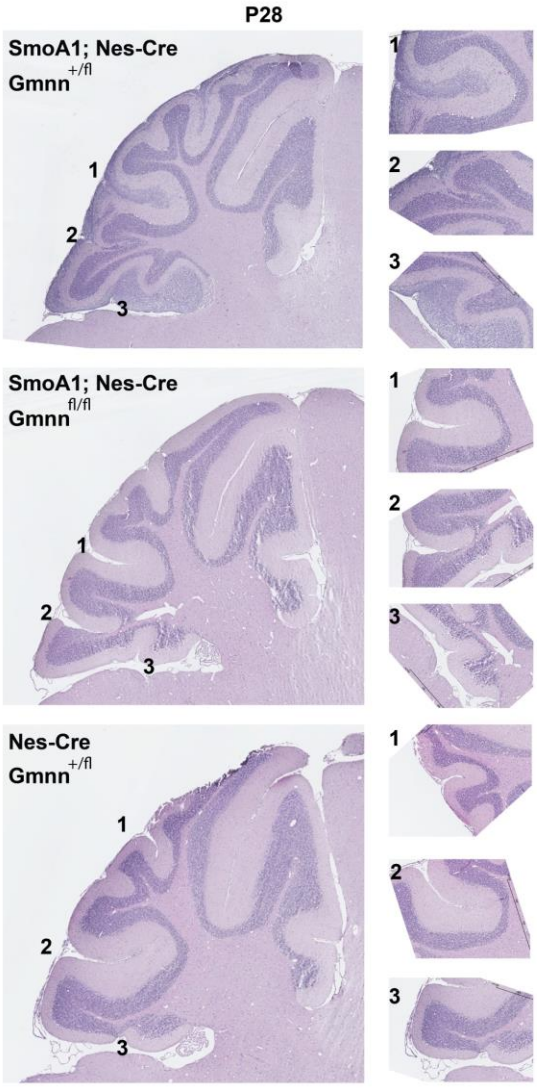

Figure S6: Example of severe dysplasia seen in some P28 animals hemizygous for the Nes-Cre and SmoA1 transgenes and heterozygous for the floxed Gmnn allele. This was not observed in any of the Nes-Cre; SmoA1 animals homozygous for the floxed Gmnn allele. Example of one representative animal for each genotype is shown.

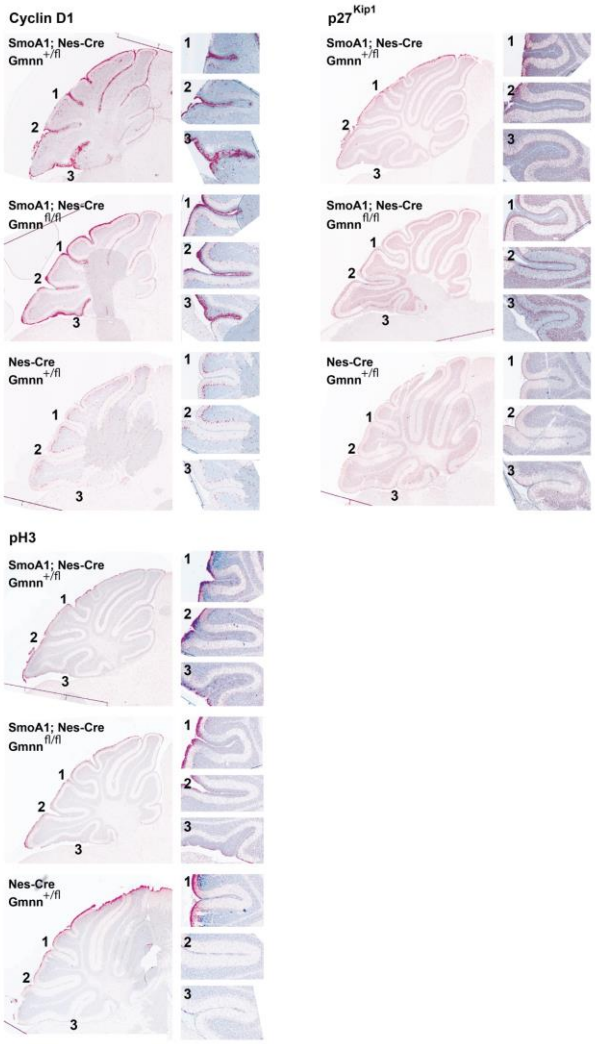

Figure S7: Immunohistochemistry for Cyclin D1, p27^{Kip1}, and pH3 on P14 cerebellar sections from animals hemizygous for the Nes-Cre and SmoA1 transgenes and either heterozygous or homozygous for the Gmnn floxed allele. No significant differences in the relative frequency of GNPs immunopositive for these antibodies was observed between animals heterozygous versus homozygous for the Gmnn floxed allele.

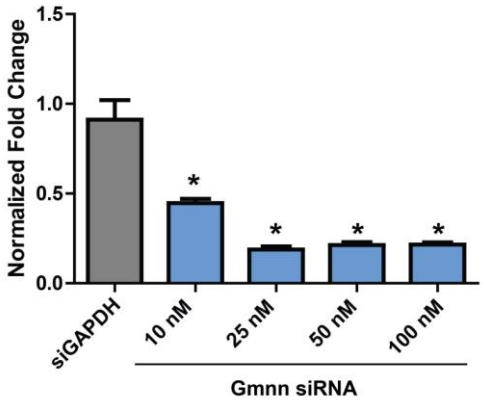

Figure S8: Gmnn siRNA dose response in Daoy cells. Daoy cells were transfected with increasing concentrations of a Gmnn siRNA (#2) as shown. After 72 hrs., Gmnn mRNA levels were analyzed by qRTPCR, represented as normalized fold change relative to the control (siGAPDH). Subsequent experiments used the lowest dose of Gmnn siRNA #2 that provided effective knockdown (25 nM). *<0.05 was defined by two-tailed student's t-test.

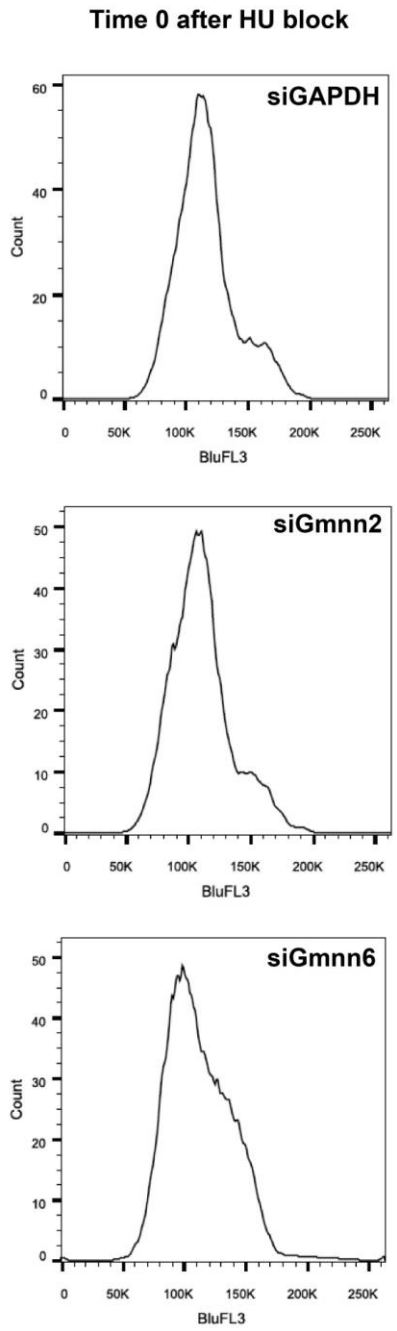

Figure S9: Cell cycle synchronization of Daoy cells. Synchronization with 100 nM hydroxyurea (HU) was performed for 14 hrs as described (see Methods). Time 0 after release from HU was analyzed by flow cytometry analysis with PI stained cells. In all three knockdown conditions, cells are predominantly synchronized in G1/S of cell cycle.

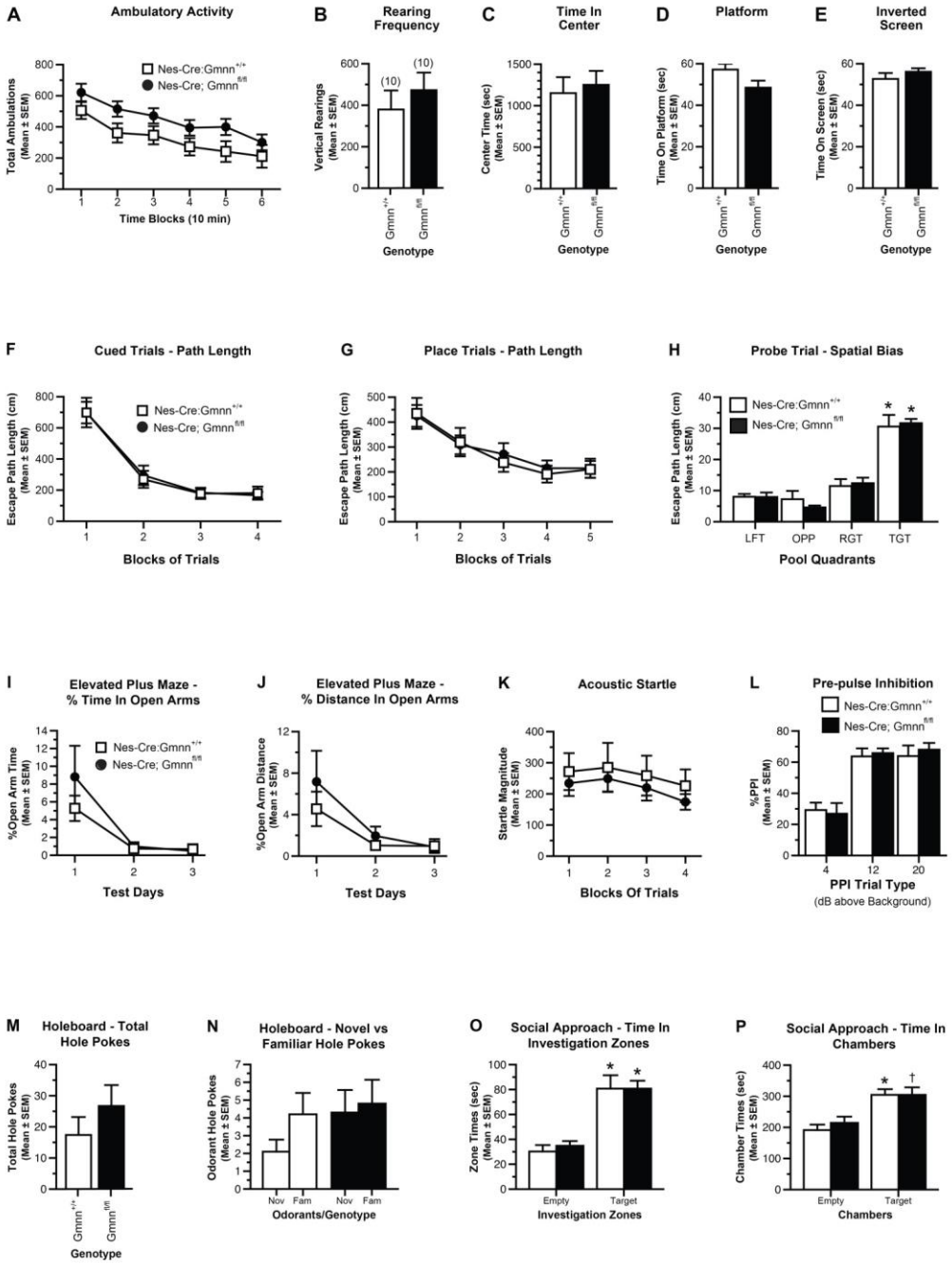

Figure S10: Behavioral testing failed to reveal a definitive phenotype in Nes-Cre; Gmnn conditional loss of function mice. To characterize any behavioral phenotypes resulting from Nes-Cre-mediated Geminin conditional loss of function, we generated cohorts of 3-4 month old mice that were hemizygous for the Nes-Cre transgene and either wild-type for Gmnn (Nes-Cre; Gmnn$^{+/+}$; n=10;

males=5/females=5) or homozygous for the floxed Gmnn allele (Nes-Cre; $Gmnn^{fl/fl}$)(n=10; males=5/females=5). These were evaluated utilizing a range of behavioral analyses, as described in the Supplemental Methods and Results. **(A-C)** Results from a 1-h locomotor activity test showed that the $Gmnn^{+/+}$ and $Gmnn^{fl/fl}$ groups did not differ in terms of ambulatory activity **(A)**, vertical rearing frequency **(B)** or in time spent in the center of the test field **(C)**. **(D-E)** The $Gmnn^{+/+}$ and $Gmnn^{fl/fl}$ mice also did not differ significantly on the platform **(D)** or inverted screen **(E)** tests, which were part of the battery of sensorimotor measures. **(F-H)** Testing in the Morris water maze did not reveal any cognitive deficits in the $Gmnn^{+/+}$ and $Gmnn^{fl/fl}$ mice in terms of acquisition performance during the cued **(F)** or place (spatial) learning **(G)** trials. Likewise, the groups both showed intact retention during the probe trial by exhibiting a spatial bias for the target quadrant that had contained the submerged platform **(H)**. This was documented by each group spending significantly more time in the target quadrant versus the times spent in each of the other quadrants (*$p<0.008$). (**I-J**) Elevated plus maze test assessed time spent and distance travelled in the open arms relative to total time/distance in all of the arms and did not detect significant differences. **(K-L)** Analysis of the acoustic startle/PPI data indicated that the groups did not differ in terms of the magnitude of the ASR **(K)**, nor in %PPI levels **(L)**, suggesting that sensorimotor reactivity and gating did not differ in the $Gmnn^{+/+}$ and $Gmnn^{fl/fl}$ mice. **(M-N)** Analysis of the data from the holeboard exploration/olfactory preference test showed that the $Gmnn^{+/+}$ and $Gmnn^{fl/fl}$ groups did not differ in terms of total exploratory hole pokes **(M)** or in terms of poke frequencies for corner holes that contained a novel versus a familiar odorant **(N)**. **(O-P)** The results from the social approach test did not provide evidence of abnormal behaviors on the part of the $Gmnn^{fl/fl}$ mice. Specifically, the $Gmnn^{+/+}$ and $Gmnn^{fl/fl}$ groups showed similar degrees of sociability by exhibiting significantly increased investigation zone times surrounding the stimulus mouse (**O**) relative to the times in the zones around the empty withholding cage (*$p<0.00005$), and each group spent more time in the chamber containing the stimulus mouse (**P**) compared to the empty chamber (*$p=0.003$; †$p=0.035$).

Tables S1-S3: Genes whose expression is most strongly correlated with that of Geminin in 103 medulloblastoma samples were defined for the Northcott core transcript dataset (GSE21140) using the R2 Megasampler (http://hgserver1.amc.nl/cgi-bin/r2/main.cgi). GO terms for genes with Gmnn co-correlated (**Table S1**) and anti-correlated (**Table S2**) expression and genes with Gmnn co-correlated expression (**Table S3**) are shown.

Geminin expression co-correlated GO terms

Enrichment by Process Networks

#	Networks	p-value	FDR
1	Cell cycle_Core	1.37E-15	5.60E-14
2	Cell cycle_Mitosis	1.08E-12	2.21E-11
3	Cytoskeleton_Spindle microtubules	1.07E-11	1.47E-10
4	Cell cycle_S phase	2.65E-11	2.72E-10
5	Cell cycle_G2-M	1.81E-08	1.48E-07
6	DNA damage_MMR repair	6.26E-05	4.28E-04
7	Transcription_mRNA processing	1.00E-03	5.86E-03
8	DNA damage_DBS repair	1.47E-03	7.52E-03
9	Cell cycle_Meiosis	7.19E-03	3.28E-02
10	Transcription_Chromatin modification	1.37E-02	5.15E-02

Enrichment by GO Molecular Functions

#	Molecular functions	p-value	FDR
1	nucleotide binding	2.47E-07	1.57E-05
2	protein binding	3.31E-07	1.57E-05
3	ATP binding	3.32E-07	1.57E-05
4	protein serine/threonine kinase activity	6.09E-07	2.16E-05
5	damaged DNA binding	2.01E-06	5.70E-05
6	transferase activity, transferring phosphorus-containing groups	4.94E-05	1.17E-03
7	DNA binding	7.62E-05	1.54E-03
8	kinetochore binding	8.73E-05	1.55E-03
9	kinase activity	1.05E-04	1.66E-03
10	single-stranded DNA binding	2.32E-04	3.30E-03

Enrichment by GO Processes

#	Processes	p-value	FDR
1	cell cycle	1.20E-29	5.48E-27
2	mitotic cell cycle	9.85E-25	2.26E-22
3	cell division	3.02E-18	4.61E-16
4	mitosis	1.29E-17	1.48E-15
5	chromosome segregation	6.43E-11	5.89E-09
6	nucleosome assembly	1.59E-09	1.22E-07
7	response to DNA damage stimulus	4.78E-09	3.13E-07
8	DNA repair	1.19E-08	6.80E-07
9	G1/S transition of mitotic cell cycle	2.03E-08	1.03E-06
10	attachment of spindle microtubules to kinetochore	2.66E-08	1.22E-06

Enrichment by Pathway Maps

#	Maps	p-value	FDR
1	Cell cycle_Role of APC in cell cycle regulation	2.59E-11	1.14E-09
2	Cell cycle_The metaphase checkpoint	6.36E-11	1.40E-09
3	Cell cycle_Start of DNA replication in early S phase	1.38E-07	2.02E-06
4	Cell cycle_Chromosome condensation in prometaphase	1.20E-06	1.32E-05
5	Cell cycle_Role of Nek in cell cycle regulation	6.98E-06	5.81E-05
6	Cell cycle_Spindle assembly and chromosome separation	7.92E-06	5.81E-05
7	DNA damage_Mismatch repair	6.29E-05	3.95E-04
8	Reproduction_Progesterone-mediated oocyte maturation	5.16E-04	2.84E-03
9	Cell cycle_Initiation of mitosis	4.37E-03	2.08E-02
10	DNA damage_ATM / ATR regulation of G2 / M checkpoint	4.72E-03	2.08E-02

Enrichment by GO Localizations

#	Localizations	p-value	FDR
1	nucleus	9.71E-22	1.02E-19
2	condensed chromosome kinetochore	2.27E-16	1.19E-14
3	nucleoplasm	4.78E-15	1.67E-13
4	chromosome, centromeric region	6.69E-14	1.69E-12
5	chromosome	8.06E-14	1.69E-12
6	kinetochore	1.65E-13	2.89E-12
7	cytosol	5.19E-08	7.78E-07
8	spindle	1.72E-07	2.26E-06
9	condensed chromosome, centromeric region	4.72E-07	5.50E-06
10	centrosome	1.36E-06	1.43E-05

Geminin expression anti-correlated GO terms

#	Networks	p-value	FDR
1	Transport_Calcium transport	2.363E-02	6.633E-01
2	Neurophysiological process_Transmission of nerve impulse	3.247E-02	6.633E-01
3	Transport_Sodium transport	4.133E-02	6.633E-01
4	Reproduction_Male sex differentiation	5.145E-02	6.633E-01
5	Signal transduction_Neuropeptide signaling pathways	5.871E-02	6.633E-01
6	Muscle contraction	7.628E-02	6.633E-01
7	Inflammation_Innate inflammatory response	8.476E-02	6.633E-01
8	Cell adhesion_Synaptic contact	8.804E-02	6.633E-01
9	Neurophysiological process_Olfactory transduction	1.038E-01	6.633E-01
10	Reproduction_Gonadotropin regulation	1.052E-01	6.633E-01

Enrichment by GO Molecular Functions

#	Molecular functions	p-value	FDR
1	enzyme activator activity	2.048E-10	3.626E-08
2	lipid binding	2.676E-05	2.368E-03
3	ion channel activity	2.752E-04	1.623E-02
4	voltage-gated calcium channel activity	4.805E-04	2.111E-02
5	high voltage-gated calcium channel activity	6.702E-04	2.111E-02
6	calcium channel activity	7.156E-04	2.111E-02
7	protein-hormone receptor activity	8.353E-04	2.112E-02
8	5-hydroxy-6E,8Z,11Z,14Z-icosatetraenoic acid binding	4.385E-03	4.085E-02
9	somatostatin receptor binding	4.385E-03	4.085E-02
10	fucokinase activity	4.385E-03	4.085E-02

Enrichment by GO Processes

#	Processes	p-value	FDR
1	positive regulation of peptide secretion	2.740E-07	1.982E-04
2	negative regulation of heart rate	3.621E-07	1.982E-04
3	cytoskeletal anchoring at plasma membrane	8.041E-07	2.201E-04
4	negative regulation of hormone secretion	8.041E-07	2.201E-04
5	smooth muscle contraction involved in micturition	2.376E-06	5.203E-04
6	regulation of vasodilation	3.251E-06	5.490E-04
7	adult walking behavior	3.510E-06	5.490E-04
8	transmission of nerve impulse	5.213E-06	6.601E-04
9	negative regulation of renal sodium excretion	5.668E-06	6.601E-04
10	calcium ion import	6.028E-06	6.601E-04

Enrichment by Pathway Maps

#	Maps	p-value	FDR
1	Neurophysiological process_ACM regulation of nerve impulse	3.104E-04	2.917E-02
2	Neurophysiological process_Kappa-type opioid receptor in transmission of ner	3.409E-03	1.242E-01
3	Nicotine signaling in glutamatergic neurons	4.116E-03	1.242E-01
4	Keratan sulfate metabolism p.2	5.715E-03	1.242E-01
5	Apoptosis and survival_Apoptotic TNF-family pathways	6.604E-03	1.242E-01
6	Ascorbate metabolism	5.149E-02	1.867E-01
7	Cytoskeleton remodeling_Alpha-1A adrenergic receptor-dependent inhibition c	5.428E-02	1.867E-01
8	Neurophysiological process_Olfactory transduction	5.706E-02	1.867E-01
9	Role of ZNF202 in regulation of expression of genes involved in atherosclerosi	5.982E-02	1.867E-01
10	Taurine and hypotaurine metabolism	6.259E-02	1.867E-01

Enrichment by GO Localizations

#	Localizations	p-value	FDR
1	plasma membrane	7.270E-08	9.160E-06
2	integral to membrane	3.243E-06	2.043E-04
3	membrane	2.516E-05	1.057E-03
4	collagen	6.476E-05	2.040E-03
5	integral to plasma membrane	1.394E-04	3.514E-03
6	voltage-gated calcium channel complex	2.292E-04	4.813E-03
7	dendrite terminus	5.940E-04	1.069E-02
8	proteinaceous extracellular matrix	2.719E-03	4.283E-02
9	postsynaptic density	3.718E-03	4.329E-02
10	collagen type XIII	4.123E-03	4.329E-02

Geminin expression co-correlated genes in medulloblastoma

probeset	HUGO	R-value	R-pvalue	probeset	HUGO	R-value	R-pvalue	probeset	HUGO	R-value	R-pvalue	probeset	HUGO	R-value	R-pvalue	probeset	HUGO	R-value	R-pvalue
2898597	GMNN	1	0	2427074	PSMA5	0.638	5.01E-11	3042421	HNRNPA2B1	0.586	4.95E-09	2540578	E2F6	0.548	8.72E-08	3592366	SPATA5L1	0.52	5.64E-07
2914777	TTK	0.829	1.38E-23	3080283	XRCC2	0.638	5.01E-11	3236395	HSPA14	0.586	4.85E-09	2407439	SF3A3	0.547	9.17E-08	2539765	ITGB1BP1	0.519	5.87E-07
2980241	FBXO5	0.829	1.87E-23	2858668	ERCC8	0.637	5.70E-11	2396480	EXOSC10	0.585	5.53E-09	2464499	HNRNPU	0.547	9.05E-08	2808612	MRPS30	0.519	5.86E-07
2894663	PAK1IP1	0.79	1.22E-19	2679796	THOC7	0.636	6.36E-11	2616018	CNOT10	0.584	5.83E-09	2967650	RTN4IP1	0.547	9.04E-08	2961816	PHIP	0.519	5.81E-07
2451200	UBE2T	0.779	8.74E-19	2805786	TARS	0.636	6.08E-11	3129149	PBK	0.584	5.62E-09	3011977	GTPBP10	0.547	9.58E-08	2964200	UBE2J1	0.519	5.91E-07
2813442	CENPH	0.77	4.40E-18	2811745	IPO11	0.636	6.04E-11	3290210	ZWINT	0.584	5.78E-09	3020804	NAA38	0.547	9.41E-08	3176999	RMI1	0.519	5.99E-07
3776139	NDC80	0.761	2.20E-17	3003143	MRPS17	0.636	6.16E-11	2940987	SLC35B3	0.583	6.12E-09	2750594	MSMO1	0.546	9.63E-08	3452622	RPAP3	0.519	5.85E-07
2793951	HMGB2	0.758	3.08E-17	2746269	LSM6	0.635	6.52E-11	3458133	PRIM1	0.581	7.21E-09	3421177	NUP107	0.546	9.91E-08	2517549	RBM45	0.518	6.24E-07
2411228	STIL	0.755	4.56E-17	3291435	RTKN2	0.635	6.60E-11	2469252	RRM2	0.58	8.18E-09	3781429	RBBP8	0.546	9.82E-08	2812273	PPWD1	0.518	6.24E-07
2494484	NCAPH	0.755	4.87E-17	2380554	RRP15	0.634	7.33E-11	2689208	NAA50	0.58	7.77E-09	2434490	ENSA	0.545	1.03E-07	2892979	CDYL	0.518	6.25E-07
2416218	ITGB3BP	0.752	6.37E-17	2740005	LARP7	0.634	7.61E-11	2709062	TRA2B	0.58	7.79E-09	2512601	TANK	0.545	1.08E-07	2998404	RALA	0.518	6.36E-07
2973168	ECHDC1	0.751	7.08E-17	2491935	PTCD3	0.632	9.30E-11	2745220	ZNF330	0.579	8.80E-09	2609560	THUMPD3	0.545	1.03E-07	3262165	TAF5	0.518	6.33E-07
2929036	LTV1	0.75	8.40E-17	3881443	TPX2	0.632	9.09E-11	2860666	TAF9	0.579	8.57E-09	2773907	SDAD1	0.545	1.05E-07	3482888	GTF3A	0.518	6.24E-07
2780172	CENPE	0.747	1.37E-16	2553970	PNPT1	0.631	9.90E-11	3269662	BCCIP	0.579	8.60E-09	2902736	C6orf48	0.545	1.04E-07	3799542	CEP76	0.518	6.23E-07
2364438	NUF2	0.741	3.27E-16	2934089	WTAP	0.63	1.13E-10	2401275	HNRNPR	0.578	9.80E-09	3312490	MKI67	0.545	1.03E-07	2386397	GGPS1	0.517	6.67E-07
2388219	EXO1	0.734	1.03E-15	3342426	C11orf82	0.629	1.22E-10	3591704	WDR76	0.577	1.02E-08	2549455	THUMPD2	0.544	1.12E-07	3388914	DCUN1D5	0.517	6.69E-07
2748163	MND1	0.731	1.44E-15	4012142	ERCC6L	0.627	1.57E-10	2333136	CDC20	0.576	1.16E-08	2495782	LIPT1	0.543	1.21E-07	3567469	TRMT5	0.517	6.57E-07
2783715	MAD2L1	0.73	1.52E-15	2818454	XRCC4	0.626	1.58E-10	3082181	NCAPG2	0.576	1.09E-08	2519756	WDR75	0.543	1.26E-07	3804000	INO80C	0.517	6.74E-07
2813414	CCNB1	0.729	1.84E-15	3936913	CDC45	0.626	1.62E-10	2363902	DUSP12	0.575	1.20E-08	2491702	USP39	0.542	1.28E-07	3884892	FAM83D	0.517	6.62E-07
2921374	RPF2	0.728	1.91E-15	2730531	UTP3	0.625	1.83E-10	2523144	NOP58	0.575	1.24E-08	2920962	FIG4	0.542	1.36E-07	3956433	CHEK2	0.517	6.66E-07
2577896	MCM6	0.726	2.65E-15	2815455	UTP15	0.623	2.12E-10	2610241	FANCD2	0.575	1.19E-08	3412008	PPHLN1	0.542	1.31E-07	2353881	MAN1A2	0.516	7.17E-07
2468920	CPSF3	0.722	5.01E-15	2353773	TTF2	0.622	2.31E-10	3235789	MCM10	0.575	1.20E-08	3511189	MTRF1	0.542	1.31E-07	2422885	GLMN	0.516	6.98E-07
2742985	PLK4	0.721	5.17E-15	2443518	METTL18	0.622	2.45E-10	3779684	PSMG2	0.575	1.19E-08	3840142	ZNF480	0.542	1.35E-07	2478017	MORN2	0.515	7.75E-07
2652675	ECT2	0.72	5.86E-15	2858592	DEPDC1B	0.622	2.32E-10	2547716	FAM98A	0.574	1.29E-08	2385197	GNPAT	0.541	1.44E-07	2517408	AGPS	0.515	7.47E-07
2951300	TAF11	0.72	5.49E-15	2948564	MDC1	0.622	2.33E-10	2548871	HNRPLL	0.574	1.33E-08	2892738	PRPF4B	0.541	1.43E-07	2845274	CCDC127	0.515	7.77E-07
3728964	PRR11	0.719	5.85E-15	2957126	MCM3	0.622	2.34E-10	2862716	GFM2	0.574	1.32E-08	2984573	SFT2D1	0.541	1.38E-07	2856484	MOCS2	0.515	7.47E-07
2908572	CDC5L	0.717	8.61E-15	2954678	XPO5	0.621	2.58E-10	2915491	CYB5R4	0.574	1.26E-08	2465519	ZNF669	0.54	1.53E-07	3004768	ZNF273	0.515	7.42E-07
2425447	DPH5	0.716	8.77E-15	3005069	ZNF92	0.621	2.68E-10	2841528	BNIP1	0.573	1.38E-08	2483016	CCDC104	0.54	1.48E-07	3197528	PLGRKT	0.515	7.52E-07
3595979	CCNB2	0.715	1.06E-14	3539147	SNAPC1	0.62	2.97E-10	2902559	CSNK2B	0.573	1.38E-08	2485176	MDH1	0.54	1.53E-07	3624362	LEO1	0.515	7.43E-07
2604254	HJURP	0.713	1.35E-14	2746024	ABCE1	0.619	3.03E-10	3090697	CDCA2	0.573	1.35E-08	2869275	GIN1	0.54	1.51E-07	4002809	APOO	0.515	7.63E-07
2522212	SGOL2	0.711	1.72E-14	2971378	GOPC	0.619	3.03E-10	3788049	SKA1	0.573	1.40E-08	2967321	PREP	0.54	1.47E-07	2452319	RBBP5	0.514	8.37E-07
2570616	BUB1	0.711	1.78E-14	2980812	TFB1M	0.619	3.04E-10	2728224	SRP72	0.572	1.50E-08	2773655	RCHY1	0.539	1.55E-07	2486520	ETAA1	0.514	7.86E-07
3011454	DBF4	0.709	2.03E-14	2916390	ORC3	0.618	3.21E-10	2738723	HADH	0.572	1.46E-08	2972759	HDDC2	0.539	1.59E-07	2679864	PSMD6	0.514	8.31E-07
2665572	SGOL1	0.707	2.68E-14	2954005	MRPS10	0.618	3.26E-10	2823820	WDR36	0.572	1.55E-08	2374956	TIMM17A	0.538	1.75E-07	3345593	CEP57	0.514	7.95E-07
2752725	NEIL3	0.704	3.97E-14	3019401	ZNF277	0.618	3.23E-10	2339414	USP1	0.571	1.64E-08	2454532	INTS7	0.538	1.79E-07	2529782	MRPL44	0.513	8.72E-07
2966232	COQ3	0.703	4.75E-14	3200611	HAUS6	0.618	3.24E-10	2412988	SELRC1	0.571	1.63E-08	2871717	CCDC112	0.538	1.78E-07	2834093	TCERG1	0.513	8.68E-07
2919873	QRSL1	0.7	7.25E-14	3433747	RFC5	0.618	3.21E-10	3097152	MCM4	0.571	1.55E-08	2913983	SENP6	0.538	1.69E-07	2975287	HBS1L	0.513	8.42E-07
3658925	ORC6	0.7	6.74E-14	2593352	GTF3C3	0.617	3.65E-10	2917767	MANEA	0.57	1.77E-08	2766359	RFC1	0.537	1.89E-07	2991103	BZW2	0.513	8.89E-07
2908100	POLH	0.699	7.79E-14	2923359	ASF1A	0.617	3.73E-10	2574884	IWS1	0.569	1.94E-08	2962998	KIAA1009	0.537	1.86E-07	3839142	ZNF473	0.513	8.50E-07
2893721	RIOK1	0.696	1.19E-13	3257338	KIF20B	0.615	4.44E-10	2653902	ZNF639	0.569	1.86E-08	3396736	PUS3	0.537	1.92E-07	3392840	BUD13	0.512	8.97E-07
2417528	DEPDC1	0.695	1.28E-13	2838201	PTTG1	0.614	4.84E-10	3004628	ZNF107	0.569	1.95E-08	3726992	UTP18	0.537	1.80E-07	4012949	ABCB7	0.512	9.11E-07
2951674	SRPK1	0.695	1.27E-13	3367338	KIF18A	0.614	4.84E-10	3716893	ATAD5	0.569	1.83E-08	2339682	ALG6	0.536	2.02E-07	2406766	MRPS15	0.511	9.91E-07
3331903	FAM111B	0.694	1.34E-13	3590388	NUSAP1	0.612	6.06E-10	2402068	SYF2	0.568	1.97E-08	2594535	PPIL3	0.536	1.94E-07	2544164	C2orf44	0.511	9.77E-07
2481142	MSH6	0.693	1.54E-13	3775842	TYMS	0.611	6.26E-10	2522439	BZW1	0.568	2.08E-08	2712906	RNF168	0.536	2.03E-07	2978876	PPIL4	0.511	9.51E-07
2958670	RAB23	0.691	1.90E-13	2639874	UMPS	0.61	6.78E-10	2853768	NUP155	0.568	2.03E-08	2839671	RARS	0.536	2.00E-07	3343008	TMEM126A	0.511	9.66E-07
2450345	KIF14	0.69	2.26E-13	2847710	FASTKD3	0.61	6.74E-10	3073597	CHCHD3	0.568	1.97E-08	2916246	SMIM8	0.536	2.03E-07	3869461	ZNF616	0.511	9.86E-07
2458742	LIN9	0.689	2.32E-13	2714955	TACC3	0.609	7.52E-10	2406420	CLSPN	0.567	2.17E-08	2940551	SSR1	0.536	2.00E-07	4021508	ZNF280C	0.511	9.66E-07
3603408	PSMA4	0.688	2.62E-13	3793588	TIMM21	0.609	7.58E-10	3474495	TRIAP1	0.567	2.13E-08	3821908	RNASEH2A	0.536	1.96E-07	2412529	NRD1	0.51	1.03E-06
2346399	CDC7	0.686	3.70E-13	2704188	PDCD10	0.608	7.97E-10	2407191	GNL2	0.566	2.37E-08	2404377	SNRNP40	0.535	2.10E-07	2476411	TTC27	0.51	1.03E-06
2412799	ORC1	0.685	4.11E-13	3468261	NUP37	0.608	7.96E-10	2775858	LIN54	0.566	2.43E-08	2406245	PSMB2	0.535	2.15E-07	2828856	HSPA4	0.51	1.05E-06
2334098	KIF2C	0.684	4.34E-13	2788143	ANAPC10	0.607	9.13E-10	2920716	CEP57L1	0.566	2.39E-08	2502300	DDX18	0.535	2.08E-07	2866543	CETN3	0.51	1.01E-06
2620256	KIF15	0.684	4.58E-13	3367036	CCDC34	0.606	9.88E-10	3888133	CSE1L	0.566	2.34E-08	2806256	DNAJC21	0.535	2.15E-07	3019519	IFRD1	0.51	1.03E-06
3354799	CHEK1	0.683	4.95E-13	3619945	OIP5	0.606	9.47E-10	2413423	TMEM48	0.565	2.55E-08	2757319	SLBP	0.534	2.28E-07	3026599	TRIM24	0.51	1.06E-06
2553730	MTIF2	0.68	6.97E-13	2417737	LRRC40	0.603	1.34E-09	2594569	ORC2	0.565	2.52E-08	2413180	MAGOH	0.533	2.40E-07	3105467	E2F5	0.51	1.01E-06
2859667	CENPK	0.68	6.92E-13	3258444	CEP55	0.603	1.29E-09	2913594	MTO1	0.565	2.56E-08	2651671	MYNN	0.533	2.35E-07	3166718	DNAJA1	0.51	1.06E-06
2908052	POLR1C	0.68	6.92E-13	2331974	ZNF684	0.601	1.52E-09	2691798	IQCB1	0.564	2.70E-08	2675936	POC1A	0.533	2.38E-07	3202171	PLAA	0.51	1.04E-06
3044753	LSM5	0.68	7.04E-13	2662020	RAD18	0.601	1.52E-09	3529156	NGDN	0.564	2.74E-08	2961317	TMEM30A	0.533	2.36E-07	3482977	POLR1D	0.51	1.03E-06
2548970	SRSF7	0.679	7.38E-13	2863049	POC5	0.601	1.56E-09	3736290	BIRC5	0.564	2.69E-08	2672467	CCDC12	0.532	2.60E-07	2476176	YIPF4	0.509	1.07E-06
2905118	SRSF3	0.679	7.27E-13	2950668	DAXX	0.601	1.56E-09	3766861	POLG2	0.564	2.66E-08	2903343	BRD2	0.532	2.51E-07	2946232	HIST1H1C	0.509	1.12E-06
2905469	RNF8	0.679	7.08E-13	2986546	PDCD2	0.601	1.51E-09	2955025	MRPL14	0.563	2.86E-08	2326410	CEP85	0.531	2.79E-07	2422517	ZNF644	0.508	1.15E-06
2971139	ZUFSP	0.677	9.08E-13	3523855	TEX30	0.601	1.52E-09	2963929	RNGTT	0.563	2.89E-08	2348854	RTCA	0.531	2.73E-07	2458017	NVL	0.508	1.19E-06
3910785	AURKA	0.677	8.72E-13	2937984	TBP	0.6	1.69E-09	3258168	KIF11	0.563	2.84E-08	2370991	DHX9	0.531	2.70E-07	2562115	LSM3	0.508	1.13E-06
2916952	CASP8AP2	0.676	1.05E-12	3013952	ACN9	0.6	1.60E-09	3318009	RRM1	0.562	3.23E-08	2419235	FUBP1	0.531	2.71E-07	2640855	MCM2	0.508	1.14E-06
2519140	ZC3H15	0.675	1.08E-12	3854218	HAUS8	0.6	1.60E-09	3831260	ZNF146	0.562	3.10E-08	2936564	FGFR1OP	0.531	2.82E-07	2849960	ZNF622	0.508	1.20E-06
2965739	MMS22L	0.675	1.17E-12	2393816	C1orf174	0.599	1.77E-09	3831514	ZNF567	0.562	3.22E-08	2964771	MAP3K7	0.531	2.74E-07	3421630	CCT2	0.508	1.19E-06
2923819	HSF2	0.674	1.29E-12	2566740	TXNDC9	0.598	1.93E-09	2499234	CCDC138	0.561	3.27E-08	2971724	FAM184A	0.531	2.81E-07	2429277	CSDE1	0.507	1.25E-06
2347023	CCDC18	0.672	1.57E-12	2673085	CDC25A	0.598	1.99E-09	2875634	ZCCHC10	0.56	3.62E-08	3021123	ING3	0.531	2.78E-07	2521997	C2orf69	0.507	1.25E-06
2893847	SNRNP48	0.671	1.82E-12	3485074	RFC3	0.598	1.94E-09	3151534	ATAD2	0.56	3.63E-08	3649811	NDE1	0.531	2.81E-07	3527418	PARP2	0.507	1.25E-06
3484641	BRCA2	0.671	1.65E-12	2521278	CCDC150	0.597	2.14E-09	2412082	FAF1	0.559	3.91E-08	2389130	EFCAB2	0.53	2.88E-07	3630099	TIPIN	0.507	1.24E-06
2926476	TBPL1	0.67	1.79E-12	2636272	GTPBP8	0.597	2.13E-09	2713950	ZNF141	0.559	4.04E-08	2775562	HNRPDL	0.53	2.86E-07	3325680	EIF3M	0.506	1.37E-06
2931683	C6orf211	0.67	1.81E-12	2939814	RPP40	0.597	2.11E-09	2731417	MTHFD2L	0.559	3.99E-08	2930863	PCMT1	0.53	2.97E-07	2403470	DNAJC8	0.505	1.41E-06
2978957	KATNA1	0.67	1.81E-12	2969289	WASF1	0.597	2.17E-09	2977471	ADAT2	0.559	4.09E-08	2938636	GMDS	0.53	2.97E-07	2707359	DNAJC19	0.505	1.37E-06
2779486	H2AFZ	0.669	2.03E-12	3784670	C18orf21	0.597	2.07E-09	2350840	GNAI3	0.558	4.28E-08	3435362	KNTC1	0.53	2.95E-07	2750227	TMA16	0.505	1.42E-06
3168508	MELK	0.668	2.24E-12	3991109	MST4	0.597	2.17E-09	2877314	CDC23	0.558	4.11E-08	3758317	BRCA1	0.53	2.99E-07	2787005	CLGN	0.505	1.46E-06
3428845	PARPBP	0.668	2.27E-12	2727976	CEP135	0.596	2.36E-09	3017123	PMPCB	0.558	4.37E-08	2695941	TOPBP1	0.529	3.15E-07	3467315	IKBIP	0.505	1.39E-06
2840002	SPDL1	0.667	2.52E-12	2945645	TDP2	0.596	2.34E-09	3448428	ASUN	0.558	4.20E-08	3163728	CNTLN	0.529	3.08E-07	2586227	FASTKD1	0.504	1.49E-06
2975655	MTFR2	0.667	2.44E-12	2489806	MRPL19	0.595	2.46E-09	3629103	KIAA0101	0.558	4.37E-08	2649609	MLF1	0.528	3.33E-07	2843619	HNRNPAB	0.504	1.54E-06
2826064	SRFBP1	0.666	2.67E-12	2902178	TCF19	0.595	2.50E-09	3809324	TXNL1	0.558	4.37E-08	2930592	TAB2	0.528	3.24E-07	2922840	KPNA5	0.504	1.47E-06
2970532	HDAC2	0.665	3.17E-12	3045047	RP9	0.595	2.55E-09	2405364	AIK2	0.557	4.59E-08	2949431	LSM2	0.528	3.27E-07	3365249	SAAL1	0.504	1.54E-06
2515369	HAT1	0.664	3.33E-12	3653072	PLK1	0.595	2.43E-09	2948485	DHX16	0.557	4.47E-08	2965674	NDUFAF4	0.528	3.33E-07	2332144	CTPS1	0.503	1.55E-06
3599811	KIF23	0.662	4.47E-12	2901913	TUBB	0.594	2.64E-09	3720896	CDC6	0.557	4.67E-08	3340269	POLD3	0.528	3.27E-07	2498046	C2orf49	0.503	1.65E-06
3590086	RAD51	0.661	4.94E-12	2643157	CDV3	0.593	2.86E-09	3829768	UBA2	0.557	4.69E-08	3506936	MTIF3	0.528	3.26E-07	2678526	C3orf67	0.503	1.64E-06
2963407	SYNCRIP	0.66	5.20E-12	2900059	HIST1H2BM	0.593	2.98E-09	2421753	GTF2B	0.556	5.00E-08	3682135	FOPNL	0.528	3.37E-07	3432138	MAPKAPK5	0.503	1.60E-06
2454444	NEK2	0.659	5.86E-12	2904248	SNRPC	0.593	2.88E-09	2775965	COQ2	0.556	4.70E-08	2608156	TRNT1	0.527	3.45E-07	3719112	ZNHIT3	0.503	1.60E-06
2966371	CCNC	0.659	5.83E-12	3047963	PSMA2	0.593	2.89E-09	2907596	RRP36	0.556	4.85E-08	3003193	CCT6A	0.527	3.59E-07	2618702	ZNF620	0.502	1.66E-06
2516023	CDCA7	0.658	6.55E-12	2497892	MRPS9	0.592	3.04E-09	2482211	CHAC2	0.555	5.27E-08	2401448	E2F2	0.526	3.85E-07	2633587	TBC1D23	0.502	1.67E-06
2801526	CCT5	0.658	6.60E-12	2559696	TPRKB	0.592	3.13E-09	2580304	ORC4	0.555	5.37E-08	2587747	CIR1	0.526	3.77E-07	2784131	BBS7	0.502	1.73E-06
2334404	NASP	0.657	7.07E-12	2564599	MRPS5	0.592	3.21E-09	2633917	TRMT10C	0.555	5.20E-08	2674808	TRAIP	0.526	3.70E-07	2868523	CHD1	0.502	1.70E-06
2330899	UTP11L	0.655	9.62E-12	2733928	COPS4	0.592	3.22E-09	3490655	CKAP2	0.555	5.10E-08	2802739	FAM105B	0.526	3.82E-07	2894689	TMEM14C	0.502	1.72E-06
2952679	GLO1	0.655	9.68E-12	3065963	ORC5	0.592	3.14E-09	2448971	UCHL5	0.554	5.74E-08	2855501	HMGCS1	0.526	3.87E-07	2952781	SAYSD1	0.502	1.74E-06
2518743	NUP35	0.654	9.86E-12	3400190	CCDC77	0.592	3.23E-09	2807000	WDR70	0.554	5.60E-08	2997952	STARD3NL	0.526	3.69E-07	2962767	PGM3	0.502	1.66E-06
3248289	CDK1	0.654	9.94E-12	2924619	TRMT11	0.591	3.38E-09	2979704	RMND1	0.554	5.74E-08	3050367	FIGNL1	0.526	3.74E-07	3638048	MRPL46	0.502	1.71E-06
2947073	HIST1H1B	0.652	1.26E-11	3608298	BLM	0.591	3.31E-09	3817501	CHAF1A	0.554	5.67E-08	3764002	MRPS23	0.526	3.78E-07	2413519	HSPB11	0.501	1.81E-06
2997376	ANLN	0.649	1.69E-11	2424148	ALG14	0.59	3.55E-09	3728776	RAD51C	0.553	5.81E-08	2434319	ANP32E	0.525	3.98E-07	2633631	NIT2	0.501	1.76E-06
2488078	MPHOSPH1	0.648	1.97E-11	2693149	SNX4	0.59	3.55E-09	2928392	VTA1	0.552	6.79E-08	2908144	MAD2L1BP	0.525	4.05E-07	2384956	COG2	0.5	1.93E-06
3765580	BRIP1	0.648	1.90E-11	2733767	ENOPH1	0.59	3.56E-09	2633460	CMSS1	0.551	7.09E-08	3560711	BAZ1A	0.525	3.99E-07	2555490	XPO1	0.5	1.90E-06
2732611	MRPL1	0.647	2.22E-11	2855614	C5orf34	0.59	3.60E-09	2836886	MRPL22	0.551	7.08E-08	2477980	GEMIN6	0.524	4.24E-07	2824986	COMMD10	0.5	1.95E-06
2967550	ATG5	0.647	2.15E-11	2897576	E2F3	0.59	3.56E-09	2901660	PRR3	0.551	6.82E-08	2519981	PMS1	0.524	4.33E-07	2859494	SREK1IP1	0.5	1.91E-06
2423597	DNTTIP2	0.646	2.27E-11	3044129	GGCT	0.59	3.54E-09	3066436	PUS7	0.551	7.18E-08	2580635	MMADHC	0.524	4.25E-07	3187577	CNTRL	0.5	1.93E-06
3515965	DIAPH3	0.646	2.35E-11	3984655	CENPI	0.59	3.64E-09	2330773	CDCA8	0.55	7.67E-08	3040454	TWISTNB	0.524	4.19E-07	3573261	SNW1	0.5	1.86E-06
3590014	CASC5	0.646	2.30E-11	2768145	COMMD8	0.588	4.19E-09	2469094	TAF1B	0.55	7.38E-08	3683806	ERI2	0.524	4.37E-07				
2963707	RARS2	0.645	2.47E-11	2815965	HMGCR	0.588	4.22E-09	2473571	RAB10	0.55	7.35E-08	2861952	MRPS27	0.523	4.53E-07				
3607510	FANCI	0.645	2.46E-11	2868283	RIOK2	0.588	4.21E-09	2510485	RIF1	0.55	7.28E-08	3374856	MRPL16	0.523	4.54E-07				
2773997	NUP54	0.643	3.00E-11	3056414	RFC2	0.588	4.05E-09	2900372	ZNF193	0.55	7.54E-08	2701595	DHX36	0.522	4.80E-07				
3401804	RAD51AP1	0.643	3.05E-11	3536336	CDKN3	0.588	4.12E-09	2695393	MRPL3	0.549	7.98E-08	3887049	UBE2C	0.522	5.06E-07				
3563395	POLE2	0.642	3.56E-11	3639031	PRC1	0.588	4.06E-09	2763805	DHX15	0.549	8.03E-08	2379280	FLVCR1	0.521	5.19E-07				
2378937	DTL	0.641	4.02E-11	3505937	CENPJ	0.587	4.35E-09	2878246	PFDN1	0.549	8.02E-08	2420521	SSX2IP	0.521	5.36E-07				
2812120	CWC27	0.639	4.68E-11	2555630	CCT4	0.586	4.78E-09	2466141	ACP1	0.548	8.33E-08	2407128	MEAF6	0.52	5.55E-07				