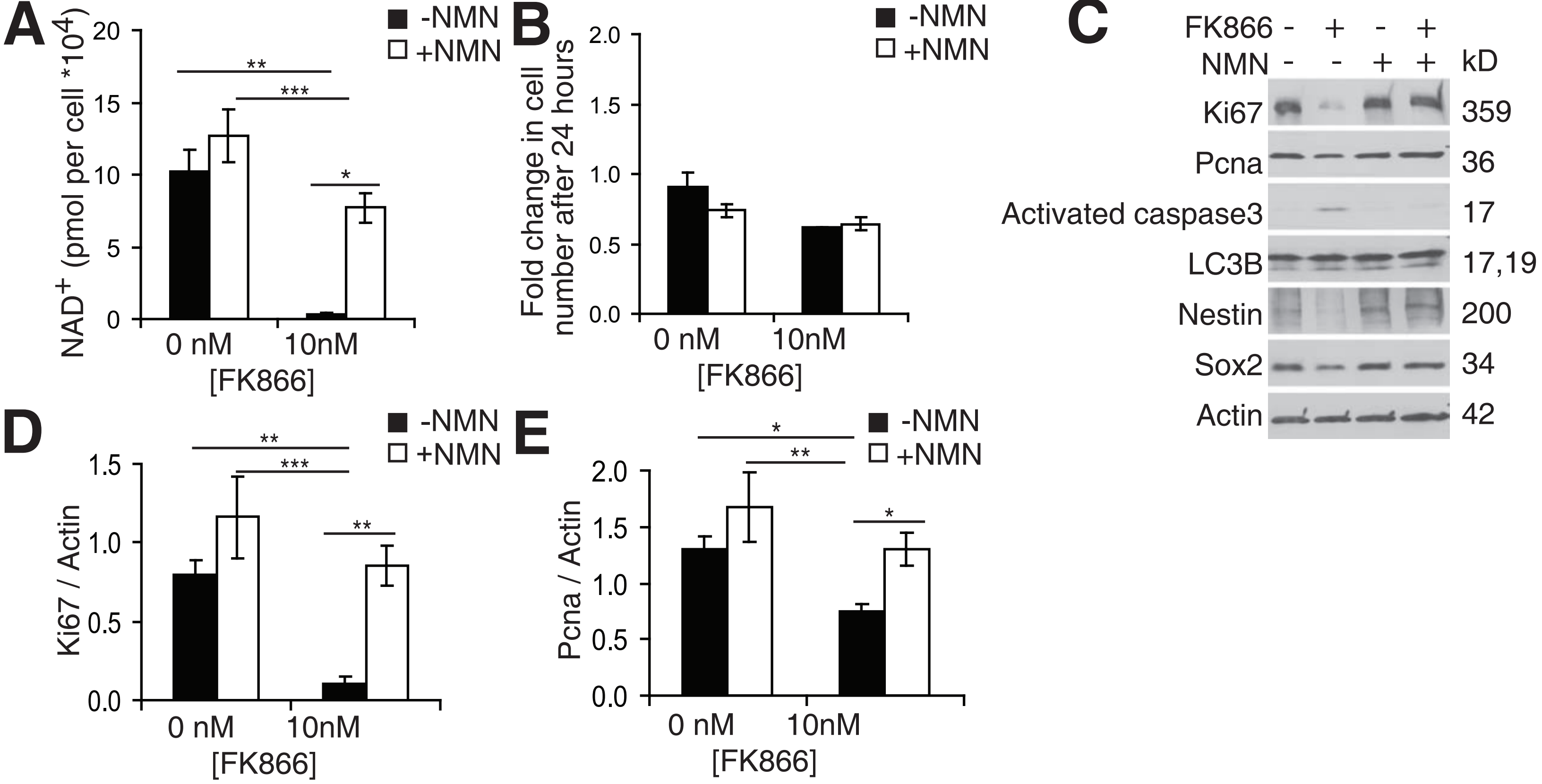

F Top 50 downregulated pathways

Pathway	Members	Changed	Z ratio	P value
NUCLEAR_PART	579	468	-7.07	0.000
DNA_METABOLIC_PROCESS	257	226	-6.49	0.000
DNA_REPLICATION	102	85	-6.20	0.000
DNA_DEPENDENT_DNA_REPLICATION	56	46	-6.07	0.000
DNA_REPAIR	125	111	-5.98	0.000
NUCLEUS	1433	1169	-5.95	0.000
INTRACELLULAR_ORGANELLE_PART	1192	988	-5.82	0.000
RESPONSE_TO_DNA_DAMAGE_STIMULUS	162	138	-5.80	0.000
ORGANELLE_PART	1197	992	-5.72	0.000
NUCLEOBASE__NUCLEOSIDE__NUCLEOTIDE_AND_NUCLEIC_AC	1246	1051	-5.34	0.000
ORGANELLE_LUMEN	458	372	-5.04	0.000
MEMBRANE_ENCLOSED_LUMEN	458	372	-5.04	0.000
CHROMOSOME	124	106	-4.75	0.000
CELL_CYCLE_PROCESS	193	167	-4.75	0.000
NUCLEAR_LUMEN	387	310	-4.74	0.000
CELL_CYCLE_GO_0007049	315	268	-4.63	0.000
RNA_PROCESSING	174	145	-4.32	0.000
BASE_EXCISION_REPAIR	17	15	-4.30	0.000
CELL_CYCLE_PHASE	170	147	-4.23	0.000
RESPONSE_TO_ENDOGENOUS_STIMULUS	200	168	-4.18	0.000
MACROMOLECULAR_COMPLEX	945	793	-4.14	0.000
NUCLEAR_CHROMOSOME	54	45	-4.11	0.000
STRUCTURE_SPECIFIC_DNA_BINDING	56	45	-4.08	0.000
DOUBLE_STRANDED_DNA_BINDING	32	26	-3.95	0.000
CELL_CYCLE_CHECKPOINT_GO_0000075	48	38	-3.92	0.000
TRNA_METABOLIC_PROCESS	19	18	-3.76	0.000
DNA_RECOMBINATION	47	45	-3.69	0.000
M_PHASE	114	100	-3.67	0.000
HYDROLASE_ACTIVITY__HYDROLYZING_N_GLYCOSYL_COMPOU	10	10	-3.63	0.000
NUCLEOPLASM	279	230	-3.62	0.000
REPLICATION_FORK	18	16	-3.60	0.000
CONDENSED_CHROMOSOME	34	27	-3.57	0.000
TRNA_PROCESSING	10	9	-3.51	0.000
RIBONUCLEOPROTEIN_COMPLEX	143	116	-3.49	0.000
MITOTIC_CELL_CYCLE	153	133	-3.48	0.001
CHROMOSOMAL_PART	96	83	-3.48	0.001
NUCLEOLUS	126	97	-3.47	0.001
NON_MEMBRANE_BOUND_ORGANELLE	632	513	-3.46	0.001
INTRACELLULAR_NON_MEMBRANE_BOUND_ORGANELLE	632	513	-3.46	0.001
RNA_BINDING	259	211	-3.44	0.001
TRANSFERASE_ACTIVITY__TRANSFERRING_ONE_CARBON_GRO	37	34	-3.37	0.001
CONDENSED_NUCLEAR_CHROMOSOME	18	15	-3.36	0.001
NUCLEOBASE__NUCLEOSIDE_AND_NUCLEOTIDE_METABOLIC_P	52	45	-3.35	0.001
METHYLTRANSFERASE_ACTIVITY	36	33	-3.30	0.001
INTERPHASE	68	57	-3.28	0.001
NUCLEOTIDE_METABOLIC_PROCESS	42	36	-3.21	0.001
DNA_INTEGRITY_CHECKPOINT	24	16	-3.20	0.001
SINGLE_STRANDED_DNA_BINDING	35	27	-3.17	0.002
PROTEIN_COMPLEX	816	689	-3.08	0.002
INTERPHASE_OF_MITOTIC_CELL_CYCLE	62	52	-3.07	0.002

G Top 50 upregulated pathways

Pathway	Members	Changed	Z ratio	P value
SYSTEM_DEVELOPMENT	863	759	4.69	0.000
MULTICELLULAR_ORGANISMAL_DEVELOPMENT	1051	910	4.64	0.000
SIALYLTRANSFERASE_ACTIVITY	10	10	4.59	0.000
PHOSPHOINOSITIDE_BINDING	20	13	4.49	0.000
ANATOMICAL_STRUCTURE_DEVELOPMENT	1017	891	4.47	0.000
ORGAN_DEVELOPMENT	572	499	4.28	0.000
RECEPTOR_BINDING	378	321	4.25	0.000
EXTRACELLULAR_REGION	448	374	4.10	0.000
ENZYME_LINKED_RECEPTOR_PROTEIN_SIGNALING_PA	140	126	4.05	0.000
GROWTH	77	63	3.85	0.000
NEGATIVE_REGULATION_OF_GROWTH	40	34	3.84	0.000
FOCAL_ADHESION_FORMATION	10	9	3.83	0.000
OLIGOSACCHARIDE_METABOLIC_PROCESS	11	11	3.82	0.000
EXTRACELLULAR_REGION_PART	339	283	3.82	0.000
REGULATION_OF_SIGNAL_TRANSDUCTION	223	189	3.77	0.000
SYSTEM_PROCESS	563	489	3.74	0.000
EXTRACELLULAR_SPACE	246	204	3.66	0.000
NEURON_PROJECTION	21	18	3.62	0.000
INTERMEDIATE_FILAMENT_CYTOSKELETON	24	22	3.61	0.000
INTERMEDIATE_FILAMENT	24	22	3.61	0.000
SENSORY_PERCEPTION	190	159	3.57	0.000
MEMBRANE	1998	1678	3.55	0.000
POSITIVE_REGULATION_OF_SECRETION	20	15	3.51	0.000
REGULATION_OF_CELL_GROWTH	46	38	3.49	0.000
REGULATION_OF_GROWTH	58	49	3.48	0.000
SIGNAL_TRANSDUCTION	1637	1394	3.47	0.001
PLASMA_MEMBRANE	1429	1199	3.46	0.001
MESODERM_DEVELOPMENT	22	17	3.45	0.001
CELL_DEVELOPMENT	579	512	3.44	0.001
FOCAL_ADHESION	13	10	3.44	0.001
ANATOMICAL_STRUCTURE_MORPHOGENESIS	379	335	3.39	0.001
NERVOUS_SYSTEM_DEVELOPMENT	386	342	3.39	0.001
EARLY_ENDOSOME	18	15	3.37	0.001
CYTOSKELETAL_PROTEIN_BINDING	159	137	3.36	0.001
TASTE_RECEPTOR_ACTIVITY	15	3	3.36	0.001
AXON_GUIDANCE	22	19	3.34	0.001
GENERATION_OF_NEURONS	83	76	3.34	0.001
CELL_JUNCTION	83	67	3.29	0.001
LIPID_HOMEOSTASIS	16	12	3.28	0.001
PDZ_DOMAIN_BINDING	14	13	3.26	0.001
LIGAND_DEPENDENT_NUCLEAR_RECEPTOR_ACTIVITY	25	23	3.26	0.001
NEUROGENESIS	93	84	3.21	0.001
CELL_MATRIX_JUNCTION	18	14	3.20	0.001
VACUOLE	69	56	3.19	0.001
IDENTICAL_PROTEIN_BINDING	305	253	3.19	0.001
CELL_MATRIX_ADHESION	38	34	3.18	0.001
TRANSMEMBRANE_RECEPTOR_PROTEIN_TYROSINE_KI	83	75	3.18	0.001
ACTIN_FILAMENT_BASED_PROCESS	116	96	3.18	0.001
CELL_SURFACE_RECEPTOR_LINKED_SIGNAL_TRANSDU	642	547	3.17	0.002
CELL_SUBSTRATE_ADHERENS_JUNCTION	16	13	3.17	0.002

SUPPLEMENTARY FIGURE 3

Supplementary Figure S3. Inhibition of Nampt in NSPCs impairs NAD^+ biosynthesis and proliferation *in vitro*.

Neurospheres were cultured with the Nampt-specific inhibitor FK866 (10 nM) with or without NMN (100 μM) for 24 **(A-B)** or 48 hours **(C-G)**. **A)** HPLC analysis of NAD^+ levels (n=6). **B)** Quantification of the fold increase of cell number in neurospheres under each condition indicated (n=5-11). **C)** A representative immunoblot of FK866-treated neurospheres. **D-E)** Quantification of immunoblots for Ki67 **(D)** and Pcna **(E)** normalized by actin in neurospheres (n=6). **F-G)** Top 50 biological pathways downregulated **(F)** or upregulated **(G)** by FK866. Parametric analysis of gene enrichment (PAGE) was conducted based on microarray analyses. See the Methods section. Data are presented as mean ± s.e.m. $*P < 0.05$. $**P < 0.01$. $***P < 0.001$.