



Supplementary Figure S2. Adult NSPC-specific deletion of *Nampt* impairs NSPC proliferation and self-renewal *in vivo*.

A-F) iNSPC-Nampt-KO and littermate control (iNSPC-GFP) mice were injected with tamoxifen (TAM) or vehicle (5 total injections, 1 injection per day). **A-B)** Representative images of immunofluorescence for Dapi (blue), activated caspase 3 (red), and NestinGFP (green) in the indicated brain regions at 28 (**A**) or 3 (**B**) days post TAM injection. Arrows highlight the rare activated caspase 3+ cells observed. Scale bars denote 50 μ m. SGZ, subgranular zone; SVZ, subventricular zone; CC, corpus callosum. **A)** Control iNSPC-GFP mice were treated with oil or TAM to ensure that there was no leaky NestinGFP reporter expression. **B)** iNSPC-Nampt-KO or iNSPC-GFP mice were treated with TAM. **C)** Recombination-confirmatory PCR performed on hippocampal DNA from TAM treated iNSPC-Nampt-KO (KO) and control mice (n=7-8). The ~350 base pair band confirms the deletion of exons 5 and 6. The 1,800 base pair band corresponds to a *Nampt* gene with a full-length exon 5 to 6 sequence. **D)** Quantification of the percentages of NestinGFP-positive cells in the SGZ that also express NSPC (Sox2: n=190 cells from 7 mice; Gfap: n=208 cells from 7 mice) or neuronal (Dcx, NeuN, n=473 cells from 7 mice) markers in 3 to 6 month old iNSPC-GFP mice 7 days post initial TAM injection. Separate from these SGZ-localized cell populations, $3 \pm 1\%$ of NestinGFP+ cells had extremely strong GFP expression, were localized to the granule layer, and expressed NeuN, likely due to residual CreERT2 protein left in the progeny of previously differentiated NSPCs. **E)** Quantification of the percentages of NestinGFP-positive cells that also express *Nampt* in iNSPC-Nampt-KO and iNSPC-GFP mice in the DG at the indicated days post initial TAM injection (n= more than 350 cells from 7 mice). **F)** Newborn neurons (Dcx+, n=12-16) were categorized by the length of their projection per unit area of the dentate gyrus (DG). Immature cells had no or horizontal

projections. Mature cells had vertical projections spanning the granule cell layer. **G)** Mice were injected with NMN (500 mg/kg body weight, IP), and hippocampal NAD⁺ levels were measured by HPLC at the indicated time points post injection (n=3-9). **H-I)** Mice were administered NMN (100 or 300 mg/kg body weight) in their drinking water from 6 to 18 months of age. Quantification of Ki67⁺ (**H**) and Dcx⁺ (**I**) cells in the DG per unit area of the DG (n=5). Data are presented as mean \pm s.e.m. *P < 0.05. **P < 0.01. ***P < 0.001.