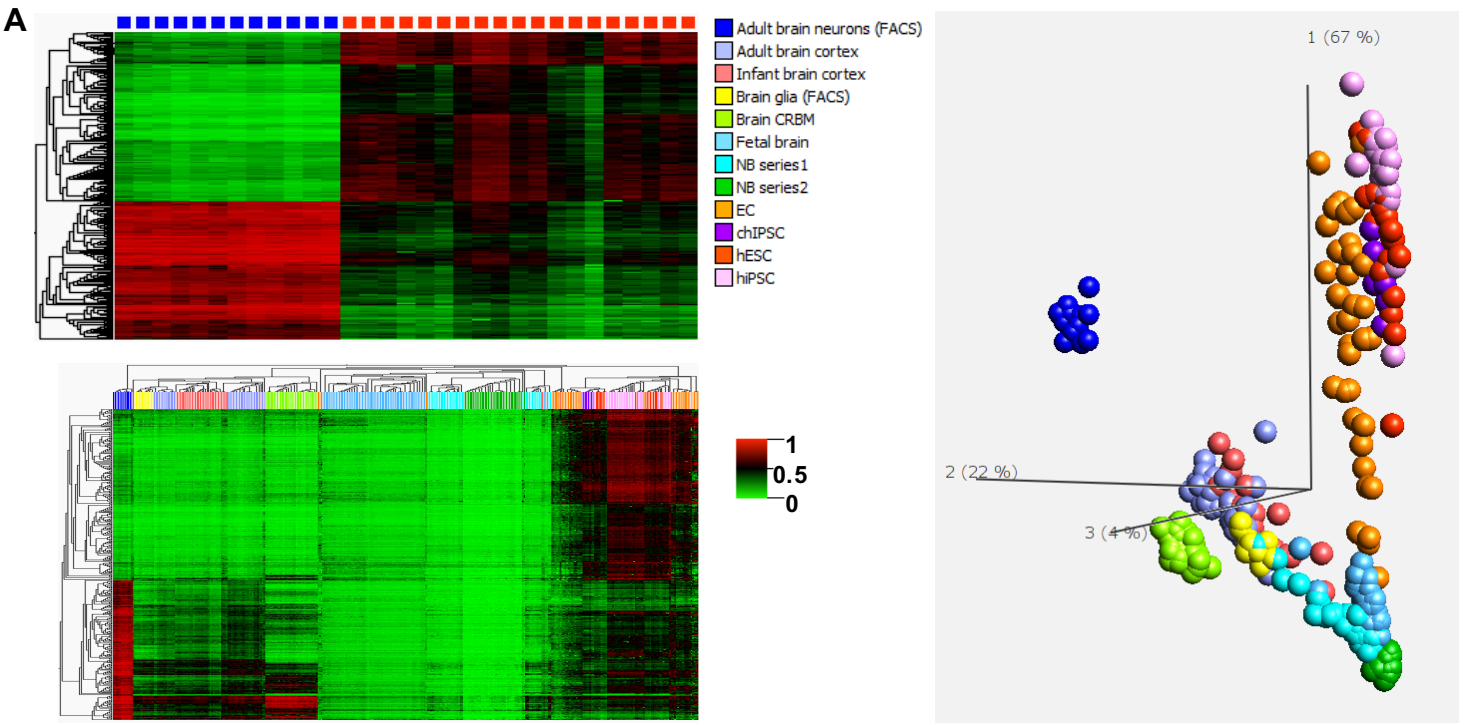
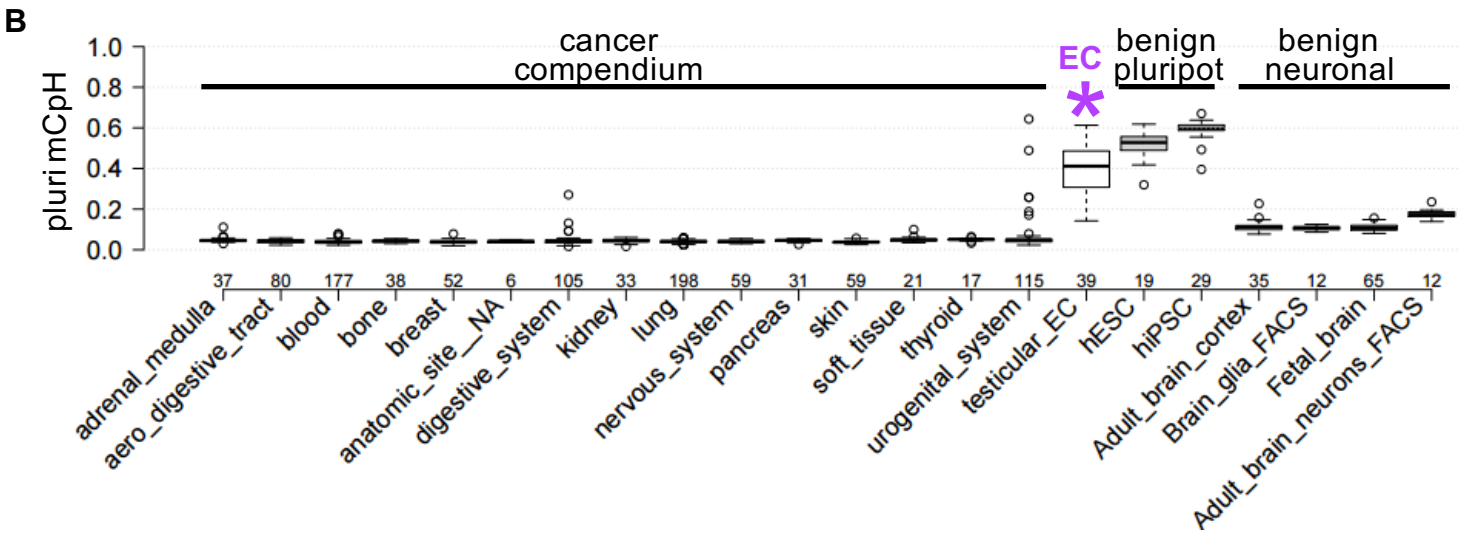
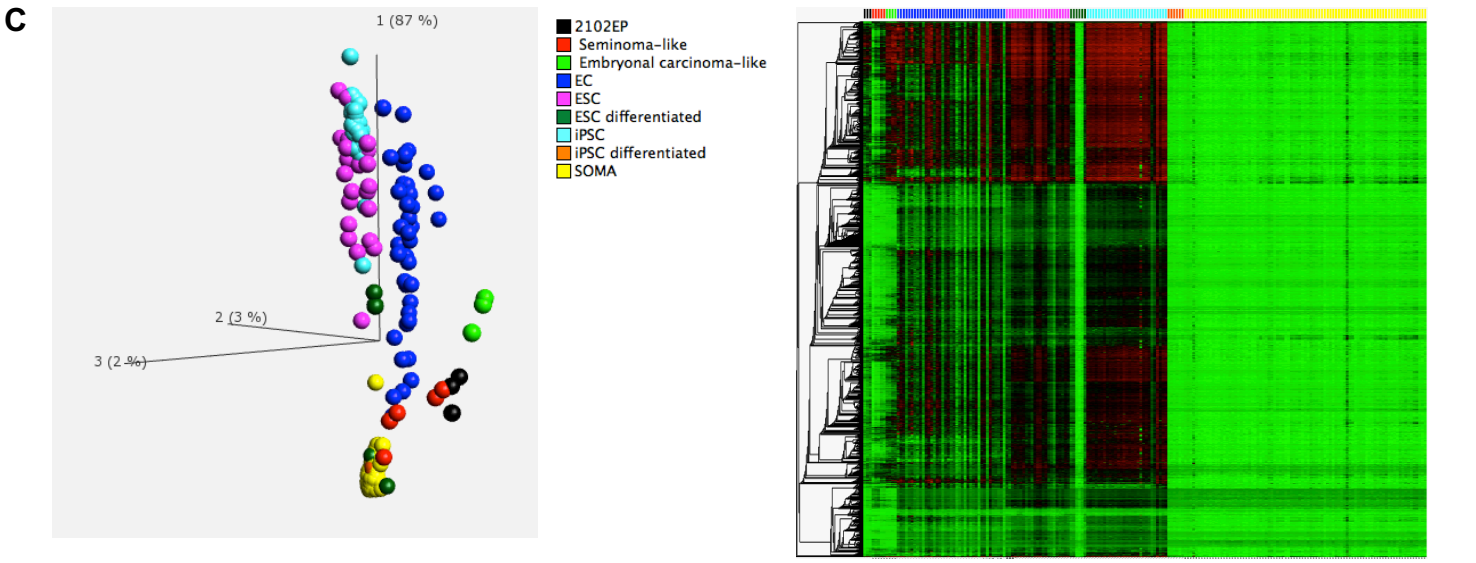

A
Adult brain neurons (FACS)
Adult brain cortex
Infant brain cortex
Brain glia (FACS)
Brain CRBM
Fetal brain
NB series1
NB series2
EC
chIPSC
hESC
hiPSC
1
0.5
0
1 (67 %)
2 (22 %)
3 (4 %)


B
pluri mCpH
1.0
0.8
0.6
0.4
0.2
0.0
cancer compendium
EC
benign pluripot
benign neuronal
37 80 177 38 52 6 105 33 198 59 31 59 21 17 115 39 19 29 35 12 65 12
adrenal_medulla
aero_digestive_tract
blood
bone
breast
anatomic_site__NA
digestive_system
kidney
lung
nervous_system
pancreas
skin
soft_tissue
thyroid
urogenital_system
testicular_EC
hESC
hiPSC
Adult_brain_cortex
Brain_glia_FACS
Fetal_brain
Adult_brain_neurons_FACS


C
1 (87 %)
2 (3 %)
3 (2 %)
2102EP
Seminoma-like
Embryonal carcinoma-like
EC
ESC
ESC differentiated
iPSC
iPSC differentiated
SOMA

Supplemental Fig. S9. **A**. Pluripotency- vs. neuron-signifying CpH methylation. Top left: 1-D clustered heatmap of adult neuron and hESC cells and identified 473 high-contrast CpH DMT between these two groups. Bottom left: 2-D cluster using same 473 CpH target module, now including EC and multiple different test groups indicated in color legend. EC, hiPSC, and chimp iPSC (chiPSC) cluster with ESC, while postnatal cortex and cerebellum cluster with FACS-sorted neurons. Neuroblastoma and fetal brain are practically unmethylated for these DMT. Top right: PCA of same groups shows orthogonality of neuronal versus pluripotency methyl-CpH axes: EC, hiPSC, and chiPSC track along the ESC/pluripotency axis, while postnatal cortex and cerebellum lay on the neuronal axis. **B**. Measurement of mCpH-pluri levels in the cancer compendium, EC, and benign pluripotent and neuronal references. Sample numbers and anatomic site for each group are shown on the x-axis. Y-axis is the average methylation level of the mCpH-pluri 256 targets. Note: the three outlier samples in the urogenital system group are embryonal carcinoma cell lines. **C**. CpH methylation in experimental reversion to pluripotency of SE cultivars. Xenograft-generated EC phenotypes from the seminoma-like TCam-2 cell line (this and other seminoma-like samples labeled in red; this and other sample annotations provided in sample color legend) (GSE60787) (Nettersheim et al. 2015) induces CpH methylation. The PCA and heatmap demonstrate greater convergence of EC with ESC/iPSC, and relative loss of CpH-me in TCam-2 and 2102EP, which are nullipotent. Induced gain of potency in xenografted TCam-2 is coupled to CpH-me elevation.