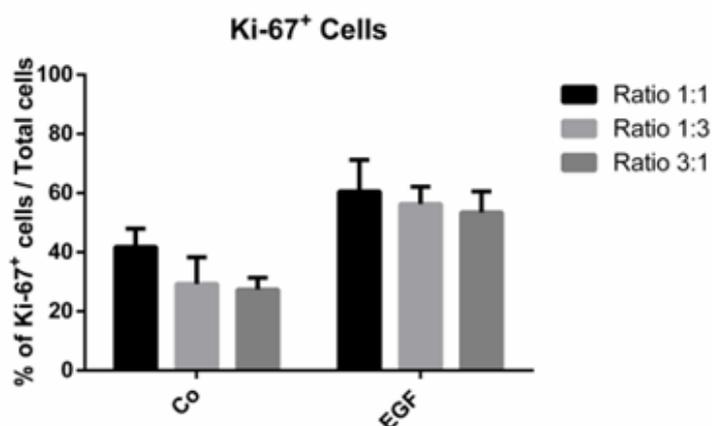
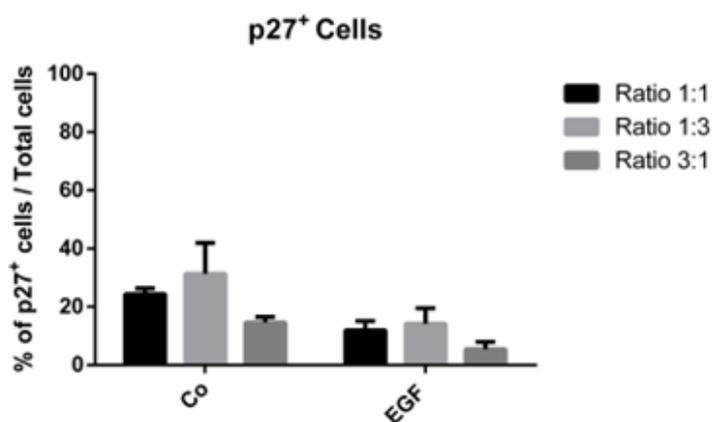


A)

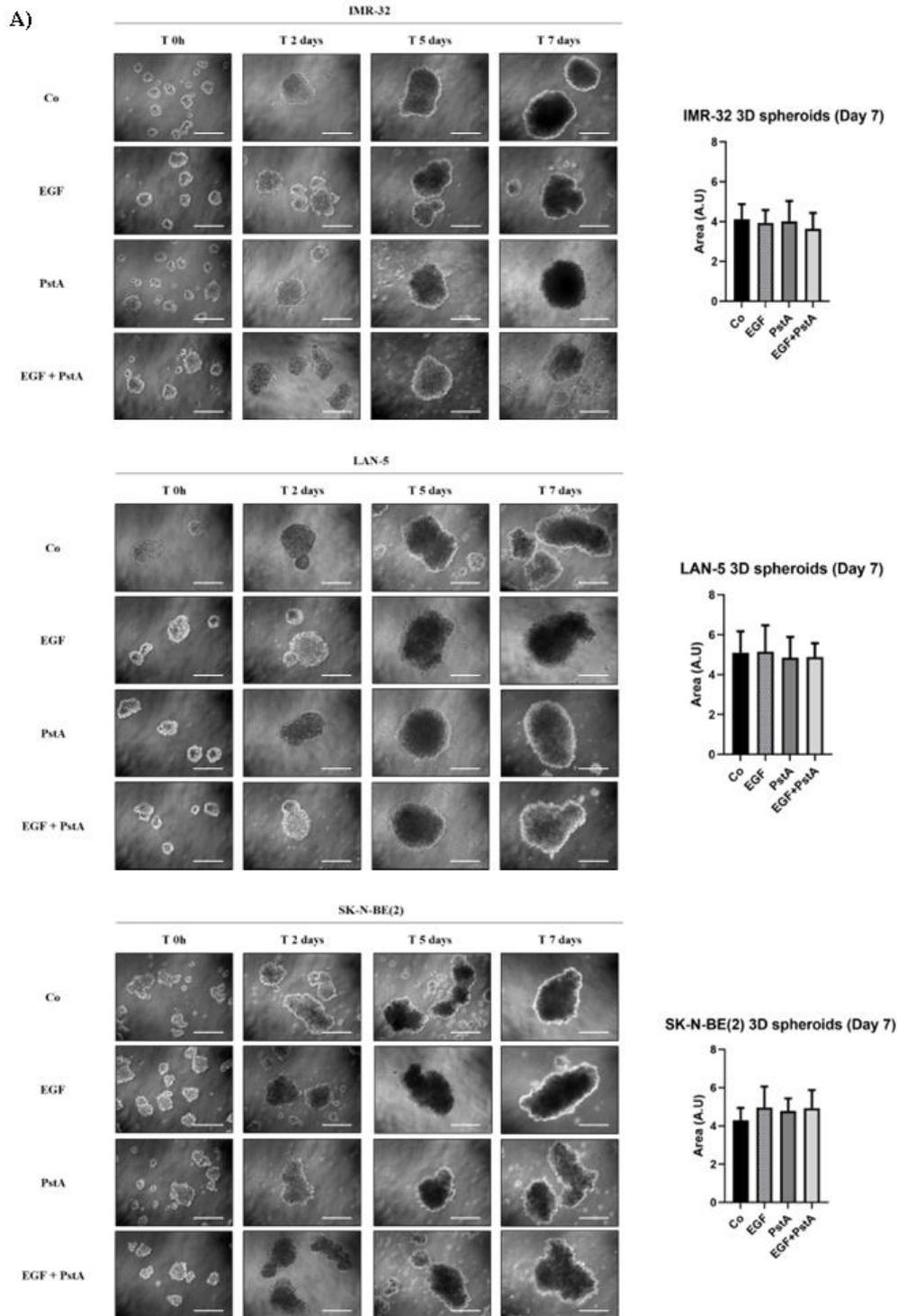


B)



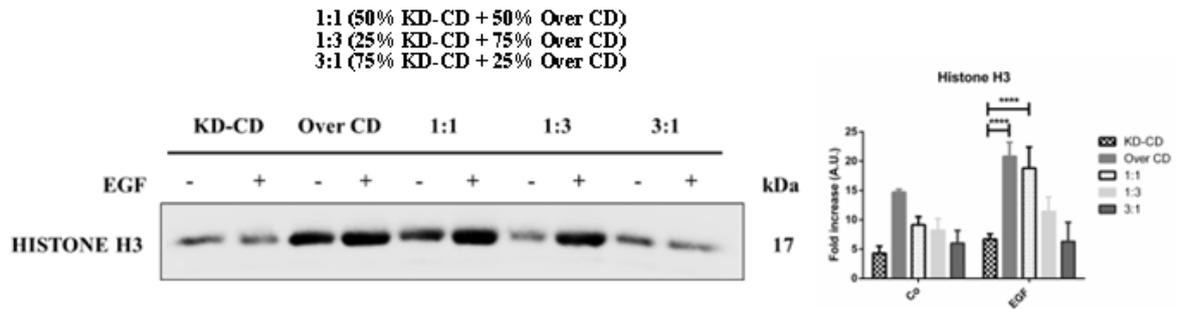
Supplementary Figure S1. CD knockdown clone expressing high levels of Ki-67 and reduced levels of p27 overtakes Over CD clone in EGF-stimulated growth of mixed cultures.

Immunofluorescence double staining of CD-Ki-67 or CD-p27 in SH-SY5Y KD-CD, Over CD and mixed cultures at different ratio: 50% KD-CD + 50% Over CD cells (1:1), 25% KD-CD + 75% Over CD (1:3) and 75% KD-CD + 25% Over CD cells (3:1). Fresh medium was replaced every day and EGF was added as indicated. After 72h of treatment, cells were fixed and stained for Ki-67 (green) / CD (red) and p27 (green) / CD (red). Quantification of Ki-67 and of p27 fluorescent signal was performed by ImageJ software. The percentages of Ki-67⁺ and p27⁺ cells relative to the total cell population in mixed cultures, calculated in random fields, are shown in the graphs.



Supplementary Figure S2. Monitoring of spheroid's formation in MYCN-amplified neuroblastoma cell lines IMR-32, LAN-5 and SK-N-BE(2) in the presence of EGF and/or PstA. IMR-32, LAN-5 and SK-N-BE(2) cells were plated on non-adherent Petri dishes and let grow for 48 hours to allow spheroid's formation. Cells were cultured for 7 days after the first treatment. At time 0h, cells were incubated with EGF and/or PstA and re-treated in fresh medium at day 2 and 5 until

the endpoint of 7 days. In the co-treatment condition, PstA was added before EGF administration to inhibit the enzymatic activity of CD. A) The 3D spheroid's growth was monitored at the phase-contrast microscope and images were acquired at different time points (time 0h, 2-, 5- and 7-days). Scale bar = 100 μm ; magnification = 20x. Quantification of spheroid's size was obtained through ImageJ software. The area is indicated as Arbitrary Unit (A.U.). Data represent the average \pm S.D. calculated for at least 5 to 10 spheroids for each condition in three separate experiments.



Supplementary Figure S3. Analysis of histone H3 expression in SH-SY5Y 3D spheroids of pure and mixed clones cocultured in the absence or presence of EGF. SH-SY5Y 3D spheroids of pure clones or clones mixed at the indicated ratio were cultured for 7 days in the absence or presence of EGF, samples were collected and then homogenates were assayed by western blotting for H3 protein. Densitometry of the bands is reported in the histograms. Significance was considered as follow: **** $p < 0.0001$.