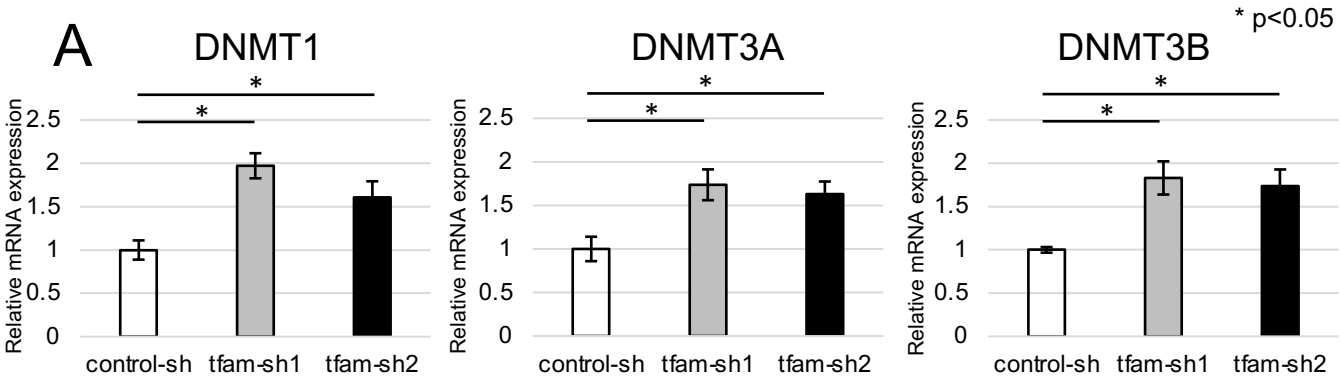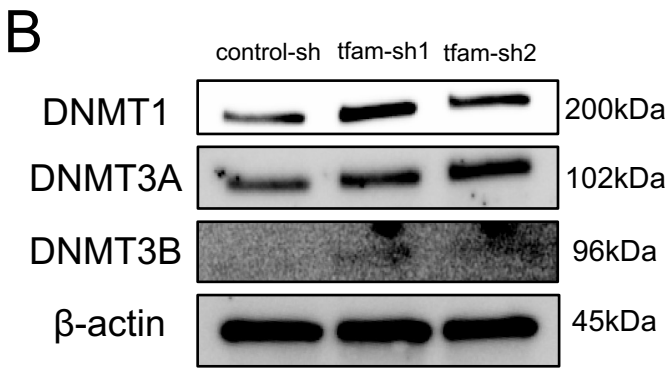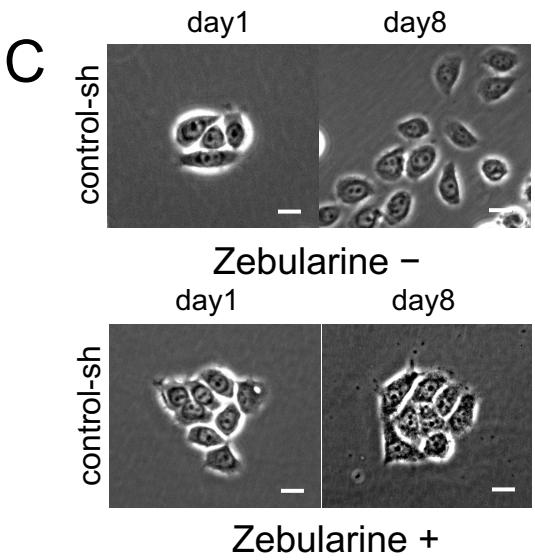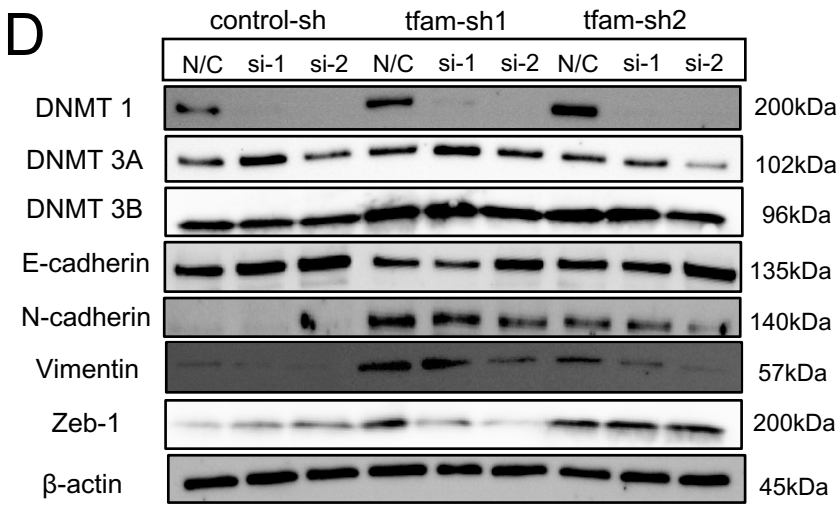Supplemental Figure. 3