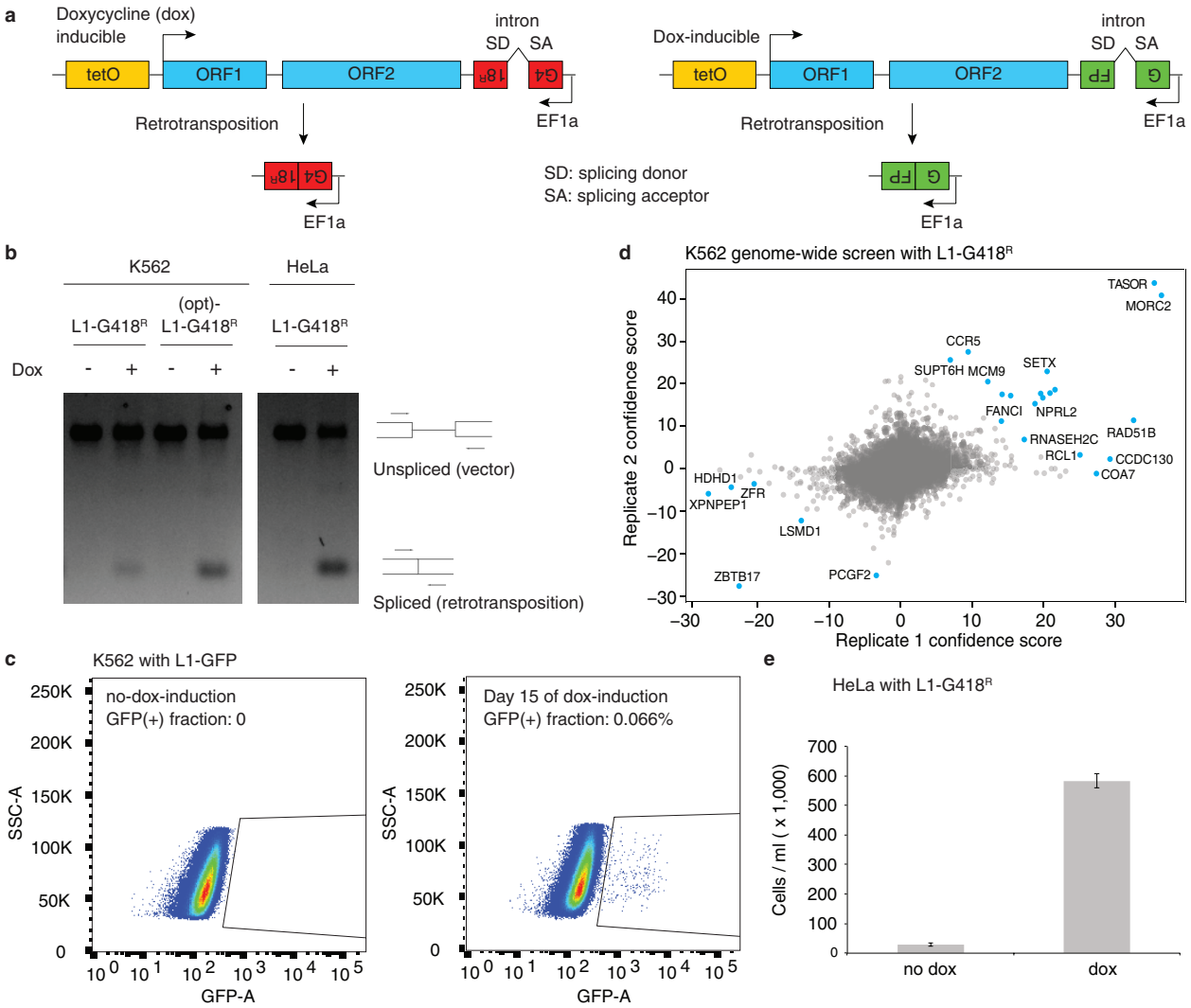

Extended Data Figure 1 | Genome-wide CRISPR/Cas9 screen for L1 regulators in K562 cells. a. Schematic representation of L1-G418^R and L1-GFP reporters used in this work. b. PCR assay on genomic DNA using primers that flank the engineered intron within the G418^R cassette. Two experiments repeated independently with similar results. The spliced PCR bands were not observed prior to dox induction in either K562 or HeLa cells, suggesting that the L1-G418^R reporter was not activated prior to the screening. However, there may exist extremely low level of reporter leakiness that is below the PCR assay detection limits. c. FACS results showing that the L1-GFP cells have no GFP signals without dox-induction (0 out of ~300,000 cells), and begin to produce GFP after dox-induction. Therefore, there is insignificant level of reporter leakiness without dox-induction. Two experiments repeated independently with similar results. d. CasTLE analysis of genome-wide screens in K562 cells, with 20,488 genes represented as individual points. Genes falling under 10% FDR colored in blue, CasTLE likelihood ratio test[11]. n = 2 biologically independent screens. e. HeLa with L1-G418^R are resistant to G418 after dox-induction. 7 days of dox-induction followed by 10 days of G418 selection. Live cells in equal volumes were counted in a single (n = 1) FACS experiment. Center value, total number of live cells. Error bar, square root of total events assuming Poisson distribution of counts.