



Extended Data Figure 2 | A secondary screen identifies functionally diverse L1 regulators in K562 cells. a. Reproducibility between two independent secondary screens ($n = 2$) in K562 cells. R-squared value, linear regression model. b. The K562 secondary screen recovers more sgRNAs than the K562 genome-wide screen, suggesting a higher detection sensitivity in the secondary screen. c. Comparison of the secondary screen data (252 genes from $n = 2$ independent screens) with the genome-wide screen data ($n = 2$ independent screens) in K562 cells. R-squared

value, linear regression model. d. Volcano plot showing K562 secondary screen results (252 genes from two independent screens), with genes previously implicated in L1 biology colored in red. e. Classification diverse L1 activators and suppressors identified in K562 cells by their known biological process. f. The maximum effect size (center value) of indicated DNA repair genes, estimated by CastLE from two independent K562 secondary screens with 10 different sgRNAs per gene. Error bars, 95% credible intervals of the estimated effect size.