Figures S2  Schematic diagram of genetic screening to search for factors required for off-target silencing. *eri-1(mg366);dpy-13(e458)* animals were chemically mutagenized and searched for mutants that suppressed RNAi off-target effect but were dispensable for *pos-1* and *lir-1* RNAi. *pos-1* RNAi leads to unhatched F1 embryos; animals that are resistant to *pos-1* RNAi likely carry mutations in the core components of RNAi machinery. *lir-1/lin-26* genes are expressed in an operon; they are co-transcribed as a polycistronic pre-mRNA, which is spliced into distinct mRNAs in the nucleus before export to the cytoplasm. *lir-1(−)* mutant animals are viable. Loss of function alleles of *lin-26* are inviable. RNAi targeting *lir-1* induces a lethal phenotype by silencing the nuclear-localized *lir-1/lin-26* RNA. *nrde* mutant animals are viable following *lir-1* RNAi, because *nrde* genes are required to silence the nuclear-localized *lir-1/lin-26* RNA (Guang, 2008). Similarly, *nrde* genes are required to silence the nuclear-localized *lin-15b/lin-15a* polycistronic RNA. Nine mutants that were specifically defective in off-target silencing were isolated. Mutants were mapped by snp-SNP mapping and candidate genes are sequenced.