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Ectopic expression of systemic RNA interference defective protein (SID-1) in embryonic stem cells: Implications for high-throughput gene screening

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RNA interference (RNAi), a post-transcriptional gene silencing mechanism originally described in C. elegans, involves sequence-specific mRNA degradation mediated by double-stranded RNAs (dsRNAs). Passive dsRNA uptake has been uniquely observed in *C. elegans* due to the expression of systemic RNA interference defective-1 (SID-1). Here we investigated the ability of ectopic SID-1 expression in pluripotent embryonic stem cells (ESCs) to enable passive cellular uptake of dsRNAs. Reporter firefly luciferase (luc^{Fir}) and either GFP or SID-1-GFP were co-expressed in ESCs, followed by simple soaking in control (non-silencing or *Renilla* luciferasespecific, luc^{Ren}) or luc^{Fir}-specific dsRNAs (100bp and 500bp). Soaking of SID-1-GFP- but not GFP-expressing ESCs in luc^{Fir}-dsRNAs suppressed luc^{Fir} activity. By contrast, suppression was not observed without lucFirdsRNAs, or when either GFP- or SID-1-GFP-expressing cells were soaked in control dsRNAs. These results may lead to high-throughput experimental strategies for studying ESC differentiation and novel approaches to genetically inhibit or eliminate the tumorigenicity of ESCs.

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