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Mammalian gene 'knock-down'

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The use of RNAi (also known as double-stranded RNA-dependent post-transcriptional gene silencing) is revolutionizing genetic analysis in cellular systems. In the February 5 Proceedings of the National Academy of Sciences, Patrick Paddison and colleagues at the Cold Spring Harbor Laboratory describe a technique using long double-stranded RNA (dsRNA), of around 500 nt, to 'knock-down' gene expression in mammalian cell lines (*Proc Natl Acad Sci USA* 2002, **99**:1443-1448). They found that expression of GFP or luciferase reporter genes could be extinguished by dsRNA expression in P19 mouse embryonic carcinoma cells or embryonic stem cells. Paddison *et al.* developed a vector incorporating vaccinia virus K3L, which inhibits the normal defensive response of mammalian cells to exogenous dsRNA. Blocking non-specific responses to dsRNA enhanced specific RNAi effects in somatic cell lines. They also demonstrated that continuous expression of a hairpin dsRNA in P19 cell clones lead to stable, sequence-specific gene silencing, opening the possibility for phenotype-based genetic selection in mammalian cells.

References

1. Post-transcriptional gene silencing by double-stranded RNA.

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