pInducer lentiviral technology for inducible, in vivo RNAi

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Technology description

Publications:
The pINDUCER lentiviral toolkit for inducible RNA interference in vitro and in vivo. Meerbrey KL, Hu G, Kessler JD, Roarty K, Li MZ, Fang JE, Herschkowitz JI, Burrows AE, Ciccia A, Sun T, Schmitt EM, Bernardi RJ, Fu X, Bland CS, Cooper TA, Schiff R, Rosen JM, Westbrook TF, Elledge SJ. Proc Natl Acad Sci U S A. 2011 Mar 1;108(9):3665-70. Activation of multiple proto-oncogenic tyrosine kinases in breast cancer via loss of the PTPN12 phosphatase. Sun T, Aceto N, Meerbrey KL, Kessler JD, Zhou C, Migliaccio I, Nguyen DX, Pavlova NN, Botero M, Huang J, Bernardi RJ, Schmitt E, Hu G, Li MZ, Dephoure N, Gygi SP, Rao M, Creighton CJ, Hilsenbeck SG, Shaw CA, Muzny D, Gibbs RA, Wheeler DA, Osborne CK, Schiff R, Bentires-Alj M, Elledge SJ, Westbrook TF. Cell. 2011 Mar 4;144(5):703-18.

The developers have created a new lentiviral based system, pInducer, for in vitro and in vivo expression of shRNA or cDNA in mammalian cells in vivo. Eight versions of the vectors were initially generated which express either shRNA or cDNA. These provide for an inducible expression that is able to be traced via reporters all in one vector. The reporters also allow rapid isolation of the transduced cell populations, and substantially improve shRNA knockdown efficiency without the need for isolating mammalian clones. Several studies with these vectors have shown their utility in multiple human xenotransplantation models of cancer (efficient in vivo RNAi in 11 of 12 models tested thusfar). For example, Dr. Westbrook's lab utilized the pInducer system to inducibly-knockdown BIRC4, which is essential for some types of human breast cancer, in human breast cancer xenografts. These experiments showed: (a) imaging of in vivo shRNA expression, (b) depletion of the target gene (BIRC4), and (c) a significant decrease in tumor growth. Further studies used a vector library comprising shRNAs targeting human kinases and phosphatases to identify suppressors of cellular transformation. pInducer was used to validate anticancer targets in vivo in this study as well.

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