INTEGRATED DNA TECHNOLOGIES, INC.

IDT's Unified RNAi Parameters

The rational selection of effective RNAi molecules for gene knockdown involves including features that enhance the success and avoiding features that increase the failure of the resulting RNAi molecule. Software for the design of effective RNAi molecules should select candidate RNAi sequences based upon their ability to conform to effectiveness criteria. IDT's default unified RNAi design parameters incorporate the following criteria for RNAi selection and ranking from the target sequence of interest.

Unified RNAi design parameters:

1) General Nucleotide Patterns

Target: AA-N19 (Elbashir *et al*. 2001)

Avoid: GGGG, AAAA, CCCC, TTTT, SSSS (Hseih *et al*. 2004; Ui-Tei *et al*. 2004)

2) Position Specific Nucleotide Patterns

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	ref
+	S																		W	[1]
+	S					A							U						H	[2]
+											S		A			G			T	[3]
+			A							U									A	[4]
-	U									U									G	[2]
-						C					W								G	[3]
-													G						S	[4]

[1] (Ui-Tei *et al*. 2004), [2] (Amarzguioui and Prydz 2004), [3] (Hseih *et al*. 2004), [4] (Reynolds *et al*. 2004)

3) Asymmetric thermodynamics of 5’ and 3’ ends of the RNAi duplex

The 5’ end of antisense strand should be less thermodynamically stable than the 5’ end of the sense strand, possibly influencing the bias of strand incorporation into the RISC. (Khorova *et al*. 2003; Schwarz *et al*. 2003).

References

Amarzguioui, M., and H. Prydz. 2004. An algorithm for selection of functional siRNA sequences. Biochemical and Biophysical Research Communications 316:1050-1058.

Elbashir, S. M., J. Harborth, W. Lendeckel, A. Yalcin, K. Weber, and T. Tuschul. 2001. Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells. Nature 411:494-498.

Hseih, A. C., R. Bo, J. Manola, F. Vazquez, O. Bare, A. Khorova, S. Scaringe, and W. R. Sellers. 2004. A library of siRNA duplexes targeting the phosphoinositide 3-kinase pathway: determinants of gene silencing for use in cell-based screens. Nucleic Acids Res. 32:893-901.

Khorova, A., A. Reynolds, and S. D. Jayasena. 2003. Functional siRNAs and miRNAs Exhibit Strand Bias. Cell 115:209-216.

Reynolds, A., D. Leake, Q. Boese, S. Scaringe, W. S. Marshall, and A. Khorova. 2004. Rational siRNA design for RNA interference. Nature Biotechnology 22:326-330.

Schwarz, D. S., G. Hutvagner, T. Du, Z. Xu, N. Aronin, and P. D. Zamore. 2003. Asymmetry in the Assembly of the RNAi Enzyme Complex. Cell 115:199-208.

Ui-Tei, K., Y. Naito, F. Takahashi, T. Haraguchi, H. Ohki-Hamazaki, A. Juni, R. Ueda, and K. Saigo. 2004. Guidelines for the selection of highly effective siRNA sequences for mammalian and chick RNA interference. Nucleic Acids Res. 32:936-948.

© 2004 INTEGRATED DNA TECHNOLOGIES, INC.

version updated 2004/06/08