

siPOOLS: highly complex but accurately defined siRNA pools eliminate off-target effects

Abstract: Short interfering RNAs (siRNA) are widely used as tool for gene inactivation in basic research and therapeutic applications. One of the major shortcomings of siRNA experiments are sequence-specific off-target effects. Such effects are largely unpredictable because siRNAs can affect partially complementary sequences and function like microRNAs (miRNAs), which inhibit gene expression on mRNA stability or translational levels. Here we demonstrate that novel, complex siRNA pools - referred to as siPOOLS -

containing up to 60 selected siRNAs eliminate off-target effects while maintaining highly efficient and reliable target gene silencing. This is achieved by the low concentration of each individual siRNA diluting sequence-specific off-target effects below detection limits. In fact, whole transcriptome analysis reveal that single siRNA transfections can severely affect global gene expression. However, when complex siRNA pools are transfected, almost no transcriptome alterations are observed.

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