Exploiting conformation and structural analysis of endogenous miRNAs to refine gene targeting evaluation

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Mature microRNAs (miRNAs) are a class of evolutionally conserved, single-stranded, small (approximately 19−23 nucleotides), endogenously expressed, and non-protein-coding RNAs that act as post-transcriptional regulators of gene expression in a broad range of animals, plants, and viruses.(1,2) The biogenesis of miRNAs is a multiple step process, which complete with the incorporation of the mature miRNA into RNA-induced silencing complex.(3) The RISC complex functions by perfectly or imperfectly matching with its complementary target mRNA, and induces target mRNA degradation or translational inhibition. Thus, alterative expression of miRNAs has been associated with a number of diseases, genetic disorders and tumors progression.(3)
We think that the knowledge of the miRNA structure may give a new insight into miRNA-dependent gene regulation mechanism and be a step forward in the understanding their function and involvement in cancerogenesis. With this aim we characterized the conformation and structures adopted by several endogenous miRNA in physiological conditions. Preliminary data obtained by CD melting experiments, using synthetic miRNA,(4) highlighted the important role played by the structures adopted by miRNA. Indeed the sequences showed a sigmoidal CD melting curves induced a significant inhibition of the luciferase activity for two of the most prominent genes associated to lung cancer, c-MET and Epidermal Growth Factor Receptor (EGFR).

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