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Targeting microRNA precursors as a new strategy for treatment of disease

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The mainstream pharmaceutical industry today considers RNA to be an undrugable target and RNA drugs to be too difficult to develop. To advance RNA as drugs and targets requires progress in three key areas: New classes of potent and selective ligands; new techniques to characterize RNA-ligand interactions so as to understand and improve their properties *in vivo*; and methods to identify RNAs that drive disease-associated pathways. MicroRNAs (miRNA) are small RNAs which bind to the 3'-UTRs of mRNAs and regulate gene expression. Their complex biosynthesis proceeds *via* a primary miRNA transcript and a shorter pre-miRNA precursor, both of which comprise stem-loop structures. As miRNA precursors are functional RNAs in their own right, so ligands which inhibit their biogenesis will be of value. Two high profile examples are the precursors of miR-122 and let-7. Using techniques developed to dissect the steps of miRNA processing, we show how ligands can be designed to bind pre-miRNAs and interfere with their processing. These ligands are being investigated for their value in the treatment of cancer and HCV.

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