MicroRNAs: Function in metabolism and therapeutic opportunities

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MicroRNAs (miRNAs) are an abundant class of short non-coding RNAs that have been identified in the genomes of a wide range of multi-cellular life forms as well as viruses. Like conventional mRNAs, miRNAs are transcribed by polymerase II as long primary transcripts that are capped, polyadenylated and spliced. Unlike mRNAs, miRNAs are processed into 19-22-nt duplexes by a two-step process involving nuclear and cytosolic RNase III-type endonucleases, known as Drosha and Dicer, to yield the 'mature' miRNA. In a final step this RNA duplex is loaded into the RNA silencing complex (RISC) where the functional strand engages in imperfect base pairing with specific sequences in a target mRNA, thereby inducing either degradation of its target transcript or translational repression. This mechanism resembles the process of RNA interference triggered by double-stranded RNA and utilizes similar molecular machinery. We have identified miRNAs that play essential roles in integrating metabolism by regulating the function of pancreatic b-cells, liver and adipocytes. I will discuss three microRNAs, miR-122, miR-375 and miR-103, which play essential roles in cholesterol synthesis, pancreatic b-cell growth and insulin sensitivity, respectively. Furthermore, the concept of pharmacologically targeting miRNAs to regulate protein networks that are involved in disease etiologies will be discussed.