

Biogenesis of liver-specific microRNA, miR-122.

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MicroRNAs (miRNAs) are small non-coding RNAs (18~24 nucleotides) that negatively regulate gene expression through interactions with 3' untranslated regions of their target mRNAs, which leads to mRNA cleavage or translational repression.

miR-122 is a liver-specific and highly abundant miRNA, constitutes 70% of the total hepatic miRNA, implicated in cholesterol and lipid metabolism and in replication of HCV RNA. Interestingly miR-122 is down-regulated in primary HCCs as well as hepatoma cell lines. It suggests that the downregulation of miR-122 is associated with hepatocarcinogenesis. Human miR-122 sequence is mapped in chromosome 18q21. But the structure of the gene is not understood until now. Therefore we study about the miR-122 gene and its expression.

We have determined the structure of human miR-122 gene by the sequence analysis of pri-miR-122 cDNAs, mapping of the transcription initiation site using 5' RACE method, and by the reporter assay for the promoter analysis. Human miR-122 gene is about 5kb and transcribed at least 4 alternatively spliced forms as non-coding and exonic pri-miR-122 RNA. Transcription of miR-122 gene is stimulated by three liver abundant transcriptional factors HNF3b, C/EBP β and unknown factor that interact at 200base upstream from transcription initiation site.

Expression of miR-122 gene was strongly stimulated by promoter-proxymal splicing event like many protein-coding genes. Transcription of miR-122 gene was also regulated epigenetically by the modification of histone3.

