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The Let-7 microRNA precursor was identified from a study of developmental timing in C. elegans, and was later shown to be part of a much larger class of non-coding RNAs termed microRNAs. miR-98 microRNA precursor from human is a let-7 family member. Let-7 MicroRNAs have now been predicted or experimentally confirmed in a wide range of species (MIPF0000002). MicroRNAs are initially transcribed in long transcripts (up to several hundred nucleotides) called primary MicroRNAs (pri-MicroRNAs), which are processed in the nucleus by Drosha and Pasha to hairpin structures of about ~70 nucleotide. These precursors (pre-MicroRNAs) are exported to the cytoplasm by exportin5, where they are subsequently processed by the enzyme Dicer to a ~22 nucleotide mature MicroRNA. The involvement of Dicer in MicroRNA processing demonstrates a relationship with the phenomenon of RNA interference.

Let-7 family plays a key role in the progression of atherosclerosis and intracranial aneurysm (IA).

Sima et al. genotyped the 2 single nucleotide polymorphisms (SNPs) in 305 patients with IA and 401 healthy controls. The rs10877887 was analyzed using a polymerase chain reaction-restriction fragment length polymorphism assay, and the rs13293512 was analyzed using a TaqMan SNP genotyping method. The relative expression of let-7 family was measured in plasma of cases and controls using real-time PCR. We found that the rs13293512CT genotype was associated with a significantly increased risk of developing IA in a heterozygote comparison (adjusted OR = 1.43, 95% CI, 1.00-2.05, P=0.048) and dominant comparison (adjusted OR = 1.44, 95% CI, 1.02-2.03, P=0.04). Combined analysis showed that the rs10877887TT and rs13293512CC/CT genotypes had a significantly increased risk of IA (OR = 1.67, 95% CI, 1.04-2.68, P=0.03). Moreover, the levels of let-7a, let-7d, and let-7f were downregulated in IA patients, and patients with the rs13293512CC/CT genotypes had a lower level of let-7a than those with rs13293512TT genotype (P=0.03). These findings indicate that the rs13293512CC/CT is a risk factor for the development of IA, possibly because of the genotypes resulting in a lower level of let-7a ¹⁾.

Sima X, Sun H, Zhou P, You C. A Potential Polymorphism in the Promoter of Let-7 is Associated With an Increased Risk of Intracranial Aneurysm: A Case-Control Study. Medicine (Baltimore). 2015 Dec;94(51):e2267. doi: 10.1097/MD.0000000000002267. PubMed PMID: 26705209.

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