X-ray Crystallographic Studies of pri-miR-21

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Micro RNA (miRNA) are noncoding RNAs that are involved in gene silencing and transcriptional regulation. microRNAs are transcribed as long stem-loop structures (pri-miRNA). These molecules undergo double-stranded cleavage by the enzyme drosha in the nucleus to form a shorter stem-loop called pre-miRNA. After export from the nucleus to the cytoplasm, pre-miRNA undergoes another double-stranded cleavage by the enzyme dicer to eventually form mature miRNA of 20-22 nucleotide residues in length. miR-21 is considered an "onco-miR" because it is one of a family of micro RNAs that are upregulated in some cancers. To understand the structure of miR-21, we performed X-ray crystallography utilizing a general toolkit of RNA binding proteins. Here we describe the structure of nearly full-length pri-miR-21 in complex with an RNA-binding Fab solved at 1.8 Å resolution. All 55 nucleotides of the miR-21 double helical region are visible in the structure including the drosha and dicer cleavage sites. A ligand-bound ternary complex was also captured at 2.0 Å resolution using the tool compound neomycin. Neomycin binds near the dicer cleavage site and distorts the conformation of the RNA backbone near the A29 bulge region.