Development of microRNA Cancer Therapeutics: miR-17 and miR-19 Inhibition in Myc-driven Hepatocellular Carcinoma

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MicroRNAs, an abundant class of small non-coding RNAs (ncRNAs) that regulate gene expression at the post-transcriptional level, have emerged as integral components of the oncogenic and tumor suppressor network and regulate nearly all cellular processes altered during tumorigenesis. The miR-17-92 gene cluster, a polycistron encoding six microRNAs (miRs), is frequently overexpressed in human cancers and has been shown to promote several aspects of oncogenic transformation, including evasion of apoptosis. Previously, it was been demonstrated that suppression of the Myc oncogene, which is also overexpressed in the majority of human cancers, can result in the restoration of intrinsic checkpoint mechanisms, including proliferative arrest, apoptosis and cellular senescence. This phenomenon, known as oncogene addiction, can be sufficient to induce sustained tumor regression. Myc is known to play a critical role in the regulation of the miR-17-92 cluster, leading us to have particular interest in identifying the molecular mechanism underlying this cooperation as well as the specific miRs involved. Here, the student researcher investigates how the inhibition of miRs in Myc driven tumor cells affects cancer progression. The student researcher conducted a comparative analysis between the inhibition of miR-17 and miR-19. The hypothesis was that inhibition of miR-17 and miR-19 in a Myc-driven hepatocellular carcinoma (HCC) cell line would result in proliferative arrest of the cells in vitro. HCC cells were isolated from Myc-driven mouse tumors and virally infected with miR-17 TuD, miR-19 TuD, or Non-coding TuD. Stable TuD expression was confirmed via qPCR. The proliferation rates of the cells was determined and compared. The hypothesis was partially supported by the final results.