MicroRNA controls expression of oncogenes

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A new study demonstrates that microRNAs can modulate the expression of well known tumor-specific oncogenic translocation proteins and may play a significant role in some human cancers. The research, published by Cell Press in the June issue of the journal *Cancer Cell*, is likely to lead to new strategies for treating some specific lymphomas and leukemias.

MicroRNAs (miRNAs) are small noncoding pieces of RNA that can modulate the expression of specific target genes. Recent studies have suggested that increases or decreases in miRNA expression may be linked with regulation of oncogenes or tumor suppressors and are therefore likely to play an important role in human cancers.

Dr. Marcos Malumbres from the Spanish National Cancer Research Center (CNIO) in Madrid, Spain and colleagues identified a miRNA-rich chromosomal region in mice that is frequently lost in T cell malignancies. This particular region encodes about 12% of all genomic miRNAs. The researchers used miRNA expression profiling to reveal that one particular miRNA, miR-203, is silenced by both genetic and epigenetic mechanisms in several mouse and human blood cell malignancies, including chronic myelogenous leukemias and some acute lymphoblastic leukemias.

The researchers went on to show that transcriptional silencing of miR-203 lead to upregulation of the oncogene ABL1 and the BCR-ABL1 oncogenic fusion protein in various mouse and human hematopoietic malignancies. Further, restoration of miR-203 resulted in a subsequent reduction of ABL1 and BCR-ABL1 and in decreased

proliferation of tumor cells.

"Our results suggest that miR-203 functions as a tumor suppressor and re-expression of this microRNA might have therapeutic benefits in specific hematopoietic malignancies, including some acute or chronic leukemias," concludes Dr. Malumbres. "This may be particularly beneficial for patients who are resistant to small molecule kinase inhibitors like Gleevec as resistant isoforms of ABL and BCR-ABL should contain the target site for miR-203 and are likely to respond to restored miR-203 function."

Source: Cell Press