

# Presidential Symposium — Small RNAs Make Big News

By Richard Schwab, MD, and Paul Cheng, MD, PhD

RNA interference by micro-RNAs is a hot topic. In October 2006, Drs. Andrew Fire and Craig Mello were awarded the Nobel Prize in Medicine for their discovery of gene regulation by RNA interference. Echoing the interest in this research, this year's ASH Presidential Symposium will focus on RNA interference by microRNAs. The Presidential Symposium promises to elaborate on a complex discovery that has correctly been given the highest scientific recognition.

MicroRNAs (MiRs) are naturally occurring double-stranded RNAs that regulate gene expression. When expressed, a MiR causes the degradation of its "complementary" mRNA. Given that there may be up to 1,000 MiRs in the human genome and that individual MiRs can regulate multiple genes, this mechanism of gene regulation is likely to be biologically important. The small size of MiRs, on the order of 20 nucleotides, makes them difficult to study. Also adding to this challenge is the fact that about one-fourth of MiRs actually come from introns. This "unused" RNA, spliced out of pre-RNA, turns out to have an important function in the regulation of gene expression. The work of today's three Presidential Symposium speakers has solidified the biologic and clinical significance of this discovery.

Dr. Carlo Croce will be discussing the role of MiR genes in leukemogenesis. In 2004, he published work identifying that the majority of MiR genes are in cancer-associated genomic regions or in chromosome-fragile sites. The following year, in the *New England Journal of Medicine*, a group he led published the identification of a signature of 13 MiR genes associated with prognosis in chronic lymphocytic leukemia. His work in this area continues. At one of yesterday's scientific sessions, his group presented data associating upregulation of certain MiRs with specific FAB classifications and cytogenetic subtypes of acute myelogenous leukemia (AML) and with poor-prognosis AML. He should provide symposium attendees with insight into the importance of MiR in leukemia and the clinical implications of these discoveries.

Dr. James Dahlberg will present on the molecular biology of MiRs and the role they play in lymphoma. His group's work on the regulation of MiR expression has been critical in advancing this area. This work is also highly clinically relevant given that these quantitative differences are seen in poor prognosis lymphomas.

Lastly Dr. Chang-Zheng Chen will discuss how MiRs regulate differentiation and signaling. In 2004, he published work in the journal *Science* identifying three MiRs involved in the regulation of hematopoietic lineage differentiation. His insight into the critical normal functions of MiR will be of great interest to research and clinical hematologists alike.

Hematology has always been at the leading edge of molecular medicine, and this year's Presidential Symposium is continued evidence of this. MiRs are a newly-recognized yet critically important component of gene regulation. Yet again, hematology researchers have been the first to translate a gigantic basic molecular discovery into clinically relevant findings that will improve the lives of patients. Today's outstanding presenters will make for a memorable symposium.