Articles in this series


**MicroRNA Regulation of Cardiovascular Functions**

William C. Sessa

In the past decade, microRNAs (miRNA) have emerged as important regulators of posttranscriptional gene regulation, thereby “fine-tuning” the levels of gene expression during development and stress. miRNA are 22-nucleotide RNA molecules that are derived from intronic, exonic, or pseudogenic DNA. miRNA is processed by the enzymes Drosha and Dicer and can hybridize to the 3'-untranslated region of mRNA loaded onto the RNA-induced silencing complex. miRNA can then regulate mRNA and protein levels by promoting RNA decay or interfering with mRNA translation into protein. In the cardiovascular system, miRNA have been profiled in the heart, blood vessels, circulating cells, and plasma and in some cases are implicated in vascular diseases. In this *Arteriosclerosis, Thrombosis, and Vascular Biology* review series, several emerging areas of miRNA research will be explored with a specific emphasis on miRNA and vascular diseases.

In the article by Hata, the roles of miRNA regulating the differentiation and phenotypic state of vascular smooth muscle are discussed. Elucidating the mechanisms of smooth muscle specialization during development and understanding the balance between differentiation and proliferation of smooth muscle are important areas of vascular biology, and work highlighted in this review makes a compelling argument that miRNA control several aspects of these processes.

In the contribution by Fernández-Hernando and Moore, the authors focus on their discoveries of miRNA regulation of cholesterol metabolism. They delineate the synthesis of miRNA 33a and 33b, encoded by the *SREBP2* and *SREBP1* genes, respectively, resulting in reciprocal regulation of sterol-responsive genes. Early-stage in vivo experiments targeting these miRNA suggest a new promising approach in the treatment of dyslipidemias.

Finally, in the contribution by Dimmeler, the concept that circulating miRNA may serve as biomarkers of vascular disease processes is developed. There is growing evidence that specific molecular patterns of miRNA are associated with disease and that blood-borne miRNA may serve as paracrine mediators for long-range communication between different cell populations in the body. These exciting possibilities may allow the identification of unique disease biomarkers and potential new therapeutic avenues.

As illustrated in this series, miRNA are exciting new players in the field of biology and are here to stay as important regulators in the cardiovascular system. Deeper insights into the regulation/dysregulation of miRNA synthesis, metabolism, and actions will yield a greater appreciation of small RNA modulation of physiological processes.

**Key Words:** imaging agents ■ immune system ■ immunologic techniques

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