Since they were first identified just over 20 years ago,1 microRNAs have emerged as major regulators of cellular physiology, as well as being identified as therapeutic targets for treating a number of cardiovascular diseases. MicroRNAs are small, noncoding RNA molecules that act as inhibitors of mRNA protein expression. MicroRNAs are highly conserved among species and have a critical role in regulating cellular physiology. Since the initial description of a microRNA in Caenorhabditis elegans,1 in excess of a thousand microRNAs have been identified, including numerous microRNAs involved in regulating the cardiovascular system. In addition, microRNAs have become a target for therapeutics in many types of cardiovascular diseases, with therapeutics aimed at modifying microRNA functions now entering clinical trials. This not only includes the use of microRNAs to inhibit protein expression, but also the use of inhibitors of microRNAs (such as antisense microRNAs) to overcome the inhibitory effects of microRNAs. Furthermore, microRNAs have become important biomarkers to identify cardiovascular disease. This issue of Heart and Metabolism consists of a number of key articles that address this exciting and emerging area of cardiovascular biology.

The article by Thomas Thum discusses the role of microRNAs in the cardiovascular system, including the role of microRNAs in fine-tuning and regulating proteins involved in many cardiovascular pathways, including cell signaling pathways, pathways involved in critical cellular functions, and developmental pathways. He also discusses the potential for long noncoding RNAs to regulate gene and protein expression. The article by John R. Ussher discusses how a number of microRNAs can undergo deregulated expression in response to numerous stresses including ischemia, heart failure, and pulmonary hypertension. This strengthens the concept of targeting microRNAs to treat cardiovascular disease.

The article by Eva van Rooij reviews the potential of regulating microRNAs in vivo for treating cardiovascular diseases and the therapeutic benefit of microRNA modulation. She also discusses the strategy of pharmacological modulation of individual microRNAs by modified antisense oligonucleotides (ie, anti-microRNAs) to inhibit a microRNA function, as well as the clinical status of this promising approach. Louise R. Rodino-Klapac’s article discusses potential strategies to modulate the activity of microRNA activity using several different approaches, which includes either upregulating or blocking microRNA function. The article by Philipp Jakob and Ulf Landmesser also demonstrates the potential of microRNA targeting to regulate cardiac developmental processes and cardiomyocyte proliferation. They demonstrate the importance of microRNAs in cardiac repair, cardiac lineage commitment, and regulation of cardiomyocyte proliferation. The authors also discuss the potential of targeting microRNAs to reprogram cells to induce pluripotency and conversion of cells into cardiomyocytes.
that can be used to treat myocardial injury. The paper by Anna Zampetaki et al discusses the potential use of microRNAs to design novel therapeutic approaches to cardiovascular disease, as well as the potential to use circulating microRNA signatures as disease biomarkers and as diagnostic and prognostic tools.

As microRNAs emerge as important regulators of the cardiovascular system, it becomes important to develop new molecular imaging tools to evaluate microRNAs. The article by Wanda Kloos et al describes the state-of-the-art approaches being developed to assess microRNA expression, including sensitive and dynamic in vivo imaging capabilities. This includes the use of fluorescent proteins, bioluminescent enzymes, molecular beacons, and nanoparticles to monitor microRNA function.

While microRNAs have emerged as critical regulators of gene expression in cardiovascular disease, it is by no means the only way to alter gene expression in cardiovascular disease. This point is stressed in the article by Pericle Di Napoli who describes the nonmetabolic effects of trimetazidine in regulating gene expression and preventing adverse remodeling in ischemic heart disease.

In a very short period of time, microRNAs have emerged as a promising target for therapeutic intervention in treating many types of cardiovascular diseases. This has occurred despite only a decade having passed since the identification of the first human microRNA. The next decade should solidify microRNA biology as a major therapeutic approach to treat cardiovascular disease.

REFERENCES