



Non-coding RNAs in cardiovascular health and disease



Cardiovascular disease is a worldwide epidemic. Even though new therapies are emerging, cardiac remodeling and subsequent heart failure remain critical issues after myocardial infarction with high rates of mortality. Because of the high death rate and the economic burden for society, researchers are exploring uncharted territory aiming to improve our understanding of the underlying processes of heart disease, with the ultimate goal to devise new strategies for therapeutic intervention. A previously unrecognized class of molecules, so called non-coding RNAs (ncRNA), is moving into the focus as valid therapeutic targets to tackle heart disease in (pre-)clinical settings [1].

With the advent of modern molecular biology techniques like next generation sequencing, it has become clear that the majority of the genome is transcribed into RNA, while only 2% of the transcribed genome encodes proteins. The transcribed portion of the genome that does not code for proteins is known as non-coding RNA. These non-coding RNAs include ribosomal RNAs, transfer RNAs, microRNAs (miRNAs) and long non-coding RNAs (lncRNAs). MiRNAs and lncRNAs are relatively recently discovered and play important roles in post-transcriptional and epigenetic gene expression regulation and are often expressed in a cell-type-specific manner [1].

In this special issue, several review papers cover recent advances in non-coding RNA research in the field of cardiovascular disease. Two publications provide an overview of current research on circular RNAs, a special class of RNAs that is formed by so-called backsplicing of exons [2,3]. These exciting molecules can modulate cell behavior and are particularly stable so that they are prime candidates for circulating biomarkers. Non-coding RNAs have also been implicated as inter-cellular messengers. In this regard, miRNAs have been most studied. A comprehensive overview of the latest developments in the cardiac field is provided by Ottaviani and colleagues [4]. Most current literature points towards a role in epigenetic regulations of gene expression by non-coding RNAs. This topic is covered in an excellent review paper by De Majo and colleagues [5].

lncRNAs are arguably the hottest non-coding RNA research topic of the moment. However, one of the biggest hurdles in coupling lncRNA sequences to function is determining the structure based on the primary sequence. Martens and colleagues review experimental and computational approaches to define lncRNA structures [6]. The roles of lncRNAs in the cardiovascular system are elaborately described in the review by Hermans-Beijnsberger and colleagues [7]. Finally, Di Mauro and colleagues provide a very timely overview of the possibilities and strategies to exploit non-coding RNAs for therapy of cardiovascular diseases, a critical step in translating non-coding RNA-based mechanisms into clinical practice [8].

Together, the articles published in this special issue of *Non-coding RNA Research* show the progress made in recent years in a fast developing field of studying non-coding RNAs in the cardiovascular system. Currently, therapies based on non-coding RNA are slowly entering the clinical arena. The microRNA-based Hepatitis C drug Miravirsen for example is one of the pioneers [9]. Undoubtedly, non-coding RNA-based therapies will also be developed for cardiovascular disease. The foundations for these novel strategies are being laid today by basic and applied research on circRNAs, microRNAs and lncRNAs, as described by the review articles in this special issue.

References

- [1] R.A. Boon, N. Jaé, L. Holdt, S. Dimmeler, Long noncoding RNAs: from clinical genetics to therapeutic targets? *J. Am. Coll. Cardiol.* 67 (2016) 1214–1226, <https://doi.org/10.1016/j.jacc.2015.12.051>.
- [2] C.P.C. Gomes, A. Salgado-Somoza, E.E. Creemers, C. Dieterich, M. Lustrek, Y. Devaux, Circular RNAs in the cardiovascular system, *Non-Coding RNA Res.* 3 (2018) 1–11, <https://doi.org/10.1016/J.NCRNA.2018.02.002>.
- [3] L.M. Holdt, A. Kohlmaier, D. Teupser, Molecular functions and specific roles of circRNAs in the cardiovascular system, *Non-Coding RNA Res.* 3 (2018) 75–98, <https://doi.org/10.1016/J.NCRNA.2018.05.002>.
- [4] L. Ottaviani, M. Sansonetti, P.A. da Costa Martins, Myocardial cell-to-cell communication via microRNAs, *Non-Coding RNA Res.* (2018), <https://doi.org/10.1016/J.NCRNA.2018.05.004>.
- [5] F. De Majo, M. Calore, Chromatin remodelling and epigenetic state regulation by non-coding RNAs in the diseased heart, *Non-Coding RNA Res.* 3 (2018) 20–28, <https://doi.org/10.1016/J.NCRNA.2018.02.003>.
- [6] L. Martens, F. Rühle, M. Stoll, lncRNA secondary structure in the cardiovascular system, *Non-Coding RNA Res.* 2 (2017) 137–142, <https://doi.org/10.1016/J.NCRNA.2017.12.001>.
- [7] S. Hermans-Beijnsberger, M. van Bilsen, B. Schroen, Long non-coding RNAs in the failing heart and vasculature, *Non-Coding RNA Res.* (2018), <https://doi.org/10.1016/J.NCRNA.2018.04.002>.
- [8] V. Di Mauro, M. Barandalla-Sobrados, D. Catalucci, The noncoding-RNA landscape in cardiovascular health and disease, *Non-Coding RNA Res.* 3 (2018) 12–19, <https://doi.org/10.1016/J.NCRNA.2018.02.001>.
- [9] H.L.A. Janssen, H.W. Reesink, E.J. Lawitz, S. Zeuzem, M. Rodriguez-Torres, K. Patel, A.J. van der Meer, A.K. Patick, A. Chen, Y. Zhou, R. Persson, B.D. King, S. Kauppinen, A.A. Levin, M.R. Hodges, Treatment of HCV infection by targeting microRNA, *N. Engl. J. Med.* 368 (2013) 1685–1694, <https://doi.org/10.1056/NEJMoa1209026>.

Reinier A. Boon*

*Institute for Cardiovascular Regeneration, Centre for Molecular Medicine,
Goethe University Frankfurt am Main, Germany
German Center for Cardiovascular Research (DZHK), Berlin, Germany
Department of Physiology, Amsterdam Cardiovascular Sciences, VU
University, Amsterdam UMC, Amsterdam, The Netherlands
E-mail address: r.boon@vumc.nl*

* Corresponding author. Department of Physiology, Amsterdam Cardiovascular Sciences, Amsterdam UMC, De Boelelaan 1117, 1081HV Amsterdam, The Netherlands.

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