

Prof. Stefanie Dimmeler: long non-coding RNAs—why it is important in cardiovascular disease

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Introduction

During 2016 Shanghai University International Forum on Biomedicine (Cardiovascular Disease): from basic research to clinic study, *Annals of Translational Medicine (ATM)* has the honor to interview Prof. Stefanie Dimmeler.

Prof. Dimmeler (*Figure 1*) received her under-graduate, graduate, and Ph.D. degree from the University of Konstanz (Germany). She then completed a fellowship in Experimental Surgery at the University of Cologne and in Molecular Cardiology at the University of Frankfurt (Germany). She is Professor of Experimental Medicine (since 2001) and Director of the Institute of Cardiovascular Regeneration, Center for Molecular Medicine at the University of Frankfurt since 2008.

Her group elucidates the basic mechanisms underlying cardiovascular disease and vessel growth with the aim to develop new cellular and pharmacological therapies for improving the treatment of cardiovascular disease. Ongoing research focuses on epigenetic mechanisms that control cardiovascular repair, specifically the function of histone modifying enzymes and non-coding RNAs.

Interview

ATM: *You just gave an excellent speech on the identification of new long non-coding RNAs, and could you please briefly introduce it to our audiences?*

Prof. Dimmeler: Thank you very much. I'm happy to introduce long non-coding RNAs to you. Actually, it is well known that the human genome is encoding many RNAs which are not dedicated to form proteins. Thus, 97% of human genome comprises non-coding information. These so-called non-coding RNAs have important functions. Long non-coding RNAs are longer than 200 nucleotides while small non-coding RNAs, for example including micro-RNAs, are about 22 nucleotides in length and control gene expression by binding to mRNAs. Long non-coding RNAs have many functions:



Figure 1 Prof. Stefanie Dimmeler.

they can act as epigenetic regulators, they can also control transcription factor binding sites, and also they can control mRNA processing and splicing as well as acting as micro-RNAs sponge to give you some examples.

ATM: *What is the status of micro-RNA or long non-coding RNA therapeutics for cardiovascular diseases?*

Prof. Dimmeler: I think micro-RNA therapeutics is a very interesting option, because it is feasible to inhibit micro-RNAs by small antisense molecules. These antimiRs can be delivered quite safely and efficiently, and we and others are developing antimiR therapeutics for targeting micro-RNA functions for example in heart failure, and this may be promising. With respect to long non-coding RNAs less is known, but one can also block them by so-called GapmeRs, which is a different type of inhibitor but also based on the antisense principle. A recent study by Thomas Thum showed that blocking a long non-coding RNA called Chart can improve cardiac function in heart failure models.

ATM: *What about the application of microRNA-based therapeutics for cardiovascular diseases in clinic?*

Prof. Dimmeler: We are currently developing programs

for blocking a micro-RNA called miR-RNA-92a with anti-miRs. We have performed several proof studies in small and large animals to document that cardiovascular protective function of these anti-miRs. We are now having almost completed the required toxicology program hopefully allowing us to test this substance first in man soon. The first human patient study then could be starting in about 2 years. We hope that we can treat patients with acute coronary syndromes to improve the vascular and cardiac function.

ATM: Could you share your view on the prospect of long non-coding RNAs applied to cardiovascular disease?

Prof. Dimmeler: As I mentioned before, quite little is known regarding the function of long non-coding RNAs and only very first publications reported about their role in the cardiovascular system. Examples include MALAT1, which controls neovascularization and diabetic retinopathy, or Chart, which controls cardiac function and Mhrt which regulates chromatin remodeling in the heart. But in general, this field is less well explored compared to micro-RNAs.

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ATM: What interests you most in the research of vascular biology and molecular cardiology?

Prof. Dimmeler: Of course, cardiovascular diseases are still the main cause of death in the abroad, and developing therapeutics particular for heart failure is a major need. This is my motivation actually. I also think that heart is a very important and interesting organ to study, particularly because of the different cell types that interact with each other: besides cardiomyocytes, endothelial cells and fibroblasts are critical players. To understand the molecular processes that drive cardiac disease in these cell types is fascinating.

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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