

Scientists on the Spot: Re-awakening the heart's regenerative capacity

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Dr. Monika M Gladka from Amsterdam University Medical Center (The Netherlands), interviews Prof. Mauro Giacca, Professor of Cardiovascular Sciences at the School of Cardiovascular Medicine & Sciences at King's College London, London (UK).

Highlight: In this *OnLife* interview, Professor Giacca, one of the key opinion leaders in the cardiovascular field, talks about challenges and future perspectives in cardiac regeneration research.

Summary of interview

There is a tendency to consider the hope and promise of cardiac regeneration to be applicable solely to the realm of ischaemic heart disease, where over a billion cardiac muscle cells, or myocytes, can be lost in a few dramatic, life-altering minutes. In this interview, Professor Giacca quickly dispelled this notion. He highlighted that there is not a single cardiac disease that does not result in loss of cardiac myocytes, extending to the multitude of inherited disorders of cardiac muscle.

Even in ageing, longer life expectancies are intimately tied to the possibility of the heart to regenerate and maintain its function over more expansive time periods.

In terms of the practicality for inducing regeneration, Prof. Giacca believes stimulation of the endogenous proliferative capacities of

cardiomyocytes holds the biggest hope for clinical implementation.¹ The previous hope beginning around the turn of the 21st century was that stem cells could fulfil the regenerative dream for the heart. This, unfortunately, fell short of the weighty expectations. The distinctive feature of Prof. Giacca's research therefore is to re-awaken the regenerative capacity of the heart through the use of microRNAs, bearing in mind the heart's ability to recover and repair prior to birth (see *Figure 1*).

However, specific therapeutic delivery mechanisms for genes or nucleic acids to the heart are still a big challenge that is encountered. This has proven to be a general barrier to translatability with similar approaches to different diseases in different organs.

To end the interview with Prof. Giacca took the opportunity to share his wisdom and advice for young scientists:

- (1) **'Read, but not too much':** We are exposed to a huge amount of information and literature now at our fingertips. In an almost analogous way to a cardiomyocyte becoming overly specialized and losing its capacity to adapt and regenerative, if we become too absorbed in what is already known, and current ways of knowing, we can lose the capacity to think outside of the box—to adapt, reform. Try to look at raw data and interpret it yourself, instead of relying on other interpretations.
- (2) **'Mix up with intelligent people':** He advised surrounding yourself with intelligent and accomplished scientists, to learn from them all that you can in daily life. Prof. Giacca shared his experience with meeting Nobel laureates in his work with the United Nations and learning how they tackled biological problems, as well as problems in life more generally.

Conflict of interest: M.G. is a member of the Scientific Advisory Boards of Trizell Holding SA, Lausanne and DINAQR AG, Zurich-London and is founder, consultant and equity holder in Purespring Therapeutics and Forcefield Therapeutics, London, which operate in the field of gene therapy and cardioprotection.

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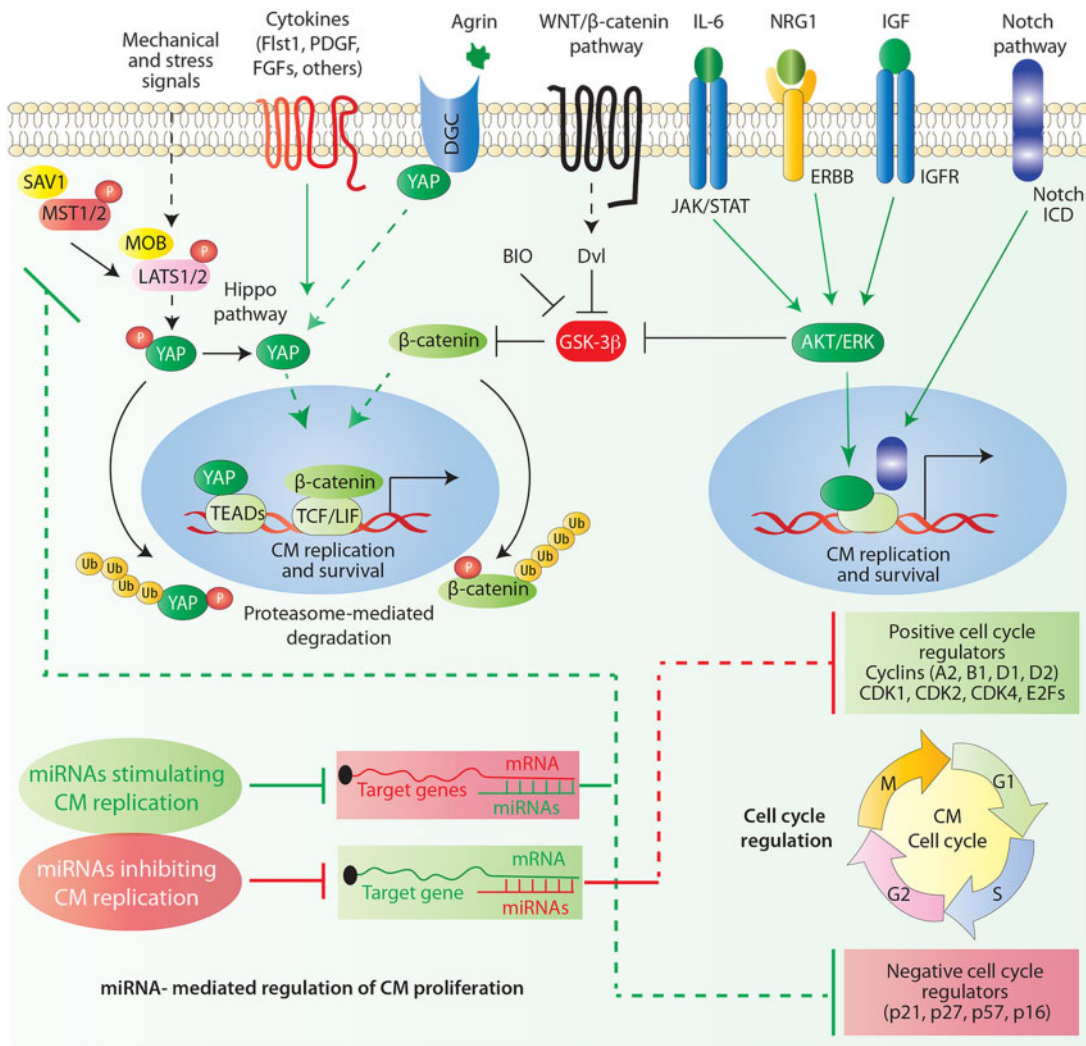


Figure 1 Extra-cellular and intra-cellular signalling regulating cardiomyocyte proliferation and cardiac regeneration. From: <https://academic.oup.com/cardiovascres/advance-article/doi/10.1093/cvr/cvaa071/5811760>.

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Reference

1. Braga L, Ali H, Secco I, Giacca M. Non-coding RNA therapeutics for cardiac regeneration. *Cardiovasc Res* 2021;**117**:674–693.

Authors



Biography: Dr Monika Gladka is an Assistant Professor at University Medical Center in Amsterdam. Until the beginning of 2021, she was a senior researcher at the Hubrecht Institute in Utrecht, which is a part of the Royal Netherlands Academy of Arts and Sciences (KNAW). Her current research focuses on understanding the molecular mechanisms that regulate cardiac repair, intending to identify new players to develop novel, improved gene therapies. She uses several state-of-the-art techniques such as single-cell sequencing, enabling an in-depth mechanistic understanding of the biological processes in injured cardiomyocytes. She is actively involved in several cardiac societies acting as a board member of Young@Heart from the Netherlands Heart Institute and nucleus member of the Scientists of Tomorrow from the European Society of Cardiology.



Biography: Mauro Giacca is Professor of Cardiovascular Sciences at the School of Cardiovascular Medicine & Sciences at King's College in London. Until 2019, he was the Director of the Italian Component of the International Center for Genetic Engineering and Biotechnology (ICGEB) and also a Professor of Molecular Biology at the Faculty of Medicine of the University of Trieste. His research interests focus on developing biotherapeutics for cardiovascular disorders, particularly on the identification of growth factors and microRNAs stimulating cardiac protection and regeneration after myocardial infarction. He is internationally recognized as an expert in the application of AAV vectors for gene therapy in cardiovascular diseases. He has published over 370 papers in peer-reviewed, international journals. He is also an Associate Editor of *Cardiovascular Research*.