

## ESC News

# The ESC Working Group on cardiovascular regenerative and reparative medicine

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Cardiovascular disease (CVD) is a stealthy killer, for which several measures—including lifestyle changes, medications, percutaneous, and surgical interventions—can result in significant improvements by alleviating symptoms and reducing mortality rates. However, these can only typically slow down the progression of the disease. Several types of CVD ultimately lead to heart failure, which affects 1%–2% of the world's population and places a heavy burden on societies and economies. To overcome this grim prognosis, there is a compelling need to reverse the burden of CVD with novel approaches to effectively repair or regenerate injured cardiovascular tissues.

Biomedical and biotechnology research is exploring new approaches, gaining scientific insights into cardiovascular cell biology, and combining them with innovative technologies in an effort to repair or regenerate damaged tissues, by employing cells or cell-derived products in combination with tissue engineering technologies.<sup>1</sup> Regeneration of cardiovascular tissue is an appealing concept to overcome the progressive nature of CVD because it targets the root cause of the disease by replacing or repairing parts of damaged organs. Multiple applications of these concepts with different approaches in the cardiovascular field are envisaged (Figure 1), targeting the pathophysiology and mechanisms of cardiovascular conditions with different aetiologies, including end-stage ischaemic heart disease and heart failure.

Great expectations have been placed on the clinical potential of regenerative and reparative treatments for CVD, notably for heart failure. Initial excitement over encouraging preclinical data resulted in a rapid clinical translation. However, the neutral outcomes of early clinical trials suggest that preclinical testing may have been insufficient to predict clinical outcomes. Moreover, the failure to achieve clinical success has led to increasing scrutiny and scepticism among clinicians, industry stakeholders, and funding bodies as to the clinical readiness of stem cell

and gene therapy products. Similar to most drug development endeavours, there are phases of premature excitement followed by realistic expectations of the clinical potential. Cardiovascular regenerative and reparative medicine (CARE) has passed the phase of overly optimistic expectations and is building its foundations on solid scientific evidence more than eminent opinions. The current challenge to critically understand and decipher the accumulated knowledge and to translate it into realistic therapeutic trajectories remains the field's priority.

Against this background, the European Society of Cardiology (ESC) Working Group (WG) on CARE was established in 2017, with the aim to gather research groups and opinion leaders of complementary backgrounds to fostering scientific activities focused on emerging developments in CARE. The WG's first chair was Professor Francisco Fernández-Avilés, encouraged and supported by the then ESC President and the Chair of the Council on Basic Cardiovascular Science, professors Fausto Pinto and Lina Badimon, respectively. The original main interest was to provide a multidisciplinary platform to gain knowledge on novel mechanistic and therapeutic concepts related to cardiovascular regeneration and repair for basic, translational, and clinical scientists, with a special focus on young talented investigators and experts from different fields and other than cardiology, including biologists, biotechnologists, bioengineers, and advanced therapy developers. The current group includes a total of 12 nucleus voting members, including the chair, the chair-Elect, the immediate past-chair, the treasurer/secretary (Figure 2), as well as four ex-officio members.

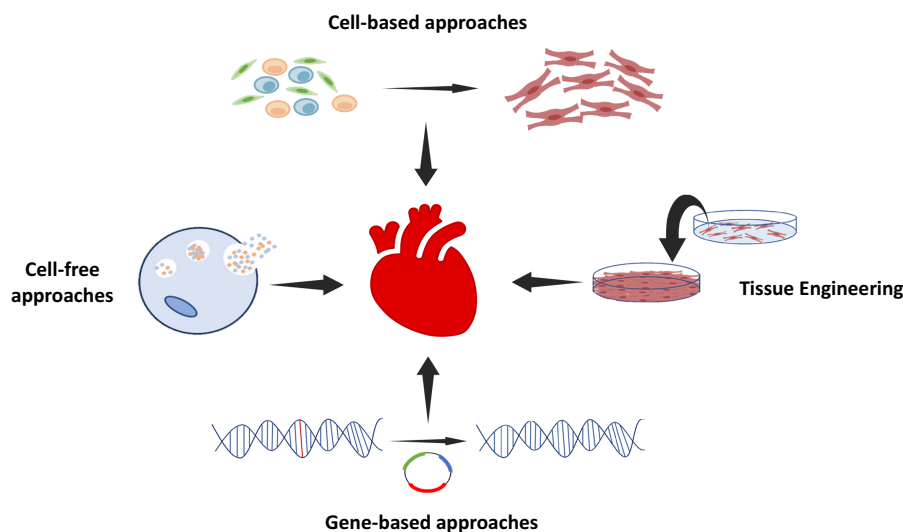
The main aims of the WG are:

- To enhance knowledge on cardiovascular regenerative medicine in clinical cardiology and basic science in Europe and across the globe, including disease mechanisms, and promising novel advanced therapy medicinal products.

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**Figure 1** Schematic representation of the most promising regenerative products tested at experimental and clinical level in the cardiovascular space.



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**Figure 2** Current leadership of the ESC Working Group on cardiovascular regenerative and reparative medicine.

- To stimulate and foster clinical research in regenerative therapies for unmet needs with special attention to subject the investigational products to the most rigorous standards of clinical evaluation
- To stimulate basic and preclinical research in cardiovascular regeneration and repair, to increase knowledge on the pathophysiology and mechanisms of action with a translational and personalized medicine perspective
- To create a collaborative network including all major stakeholders to overcome the obstacles that have hindered the successful translation of advanced therapy medicinal products in cardiovascular regenerative medicine
- To produce consensus documents, organize expert meetings and educational activities to support and help disseminate basic, preclinical, and clinical regenerative medicine practice in the cardiovascular arena.

The WG actively leads diverse educational initiatives, including scientific sessions at the annual ESC and *Frontiers in CardioVascular Biology* Congresses and in a series of webinars. The free webinar programme was particularly orientated towards training young practicing doctors, scientists, and clinical investigators. International experts in cardiovascular regenerative medicine provided updates on hot topics in basic and translational science and discussed current and future approaches and research technologies. The three webinars organized so far have focused on: (i) basic novel insights in cardiac regeneration based on extracellular vesicles, tissue engineering and cell-free approaches ([https://esc365.escardio.org/event/260?\\_ga=2.116695809.600534306.1673180724-1765751343.1665939185](https://esc365.escardio.org/event/260?_ga=2.116695809.600534306.1673180724-1765751343.1665939185)), (ii) on translational perspectives on growth-factors and cell therapeutics ([https://esc365.escardio.org/event/259?\\_ga=2.84748062.600534306.1673180724-1765751343.1665939185](https://esc365.escardio.org/event/259?_ga=2.84748062.600534306.1673180724-1765751343.1665939185)), and (iii) and finally on the promises of induced pluripotent stem cell technology for diagnostic and therapeutic purposes ([https://esc365.escardio.org/event/380?\\_ga=2.204604951.600534306.1673180724-1765751343.1665939185](https://esc365.escardio.org/event/380?_ga=2.204604951.600534306.1673180724-1765751343.1665939185)).

The educational task of the WG also includes the creation of consensus documents and position papers, focusing on specific themes of interest for the advancement of the field. We have published two position manuscripts so far; the former provided for the first time a much-needed global consensus document on cardiovascular regenerative medicine<sup>2</sup> and the latter focused on present and future insights into therapeutic products, preclinical research models, and clinical trials.<sup>3</sup>

The WG has successfully organized three consensus-generating Scientific Retreat Meetings at the ESC's Heart Agency in Brussels, gathering opinion leaders and experts from around the world to discuss and dissect specific themes of critical importance to advance the field. Questions prioritized during these meetings included (i) which products and preclinical and clinical development pipelines should be pursued to advance new therapeutics, (ii) the definition of current unmet needs in cardiology that may better benefit from advanced biologic therapies along with the roadmap to follow for the most promising products, and, finally, (iii) which technology platforms are envisaged to efficiently and safely deliver biologics to the heart. The output of the Retreats served as the scientific basis to generate opinion and position papers.

We welcome everybody interested in the exciting field of CARE to join us and become a member of our WG and engage in our activities. Membership is free and can be obtained through our website: <https://www.escardio.org/Working-groups/Working-Group-on-Cardiovascular-Regenerative-and-Reparative-Medicine/membership>. As a member, you will receive our bi-monthly newsletter, which provides a regular update on our activities as well as recommended readings relevant to our field. We are also open to new collaborations within the ESC family and joining in common activities with other ESC constituent bodies.

## Declaration

### Disclosure of Interest

S.J. participates in the Data Safety Monitoring Board of the University of Goettingen and is a mentor of the ESC WG CARE.

## References

1. Madonna R, Van Laake LW, Botker HE, Davidson SM, De Caterina R, Engel FB, et al. ESC Working Group on Cellular Biology of the Heart: position paper for Cardiovascular Research: tissue engineering strategies combined with cell therapies for cardiac repair in ischaemic heart disease and heart failure. *Cardiovasc Res* 2019;**117**:488–500. <https://doi.org/10.1093/cvr/cvz010>
2. Fernández-Avilés F, Sanz-Ruiz R, Climent AM, Badimon L, Bolli R, Charron D, et al. Global position paper on cardiovascular regenerative medicine. *Eur Heart J* 2017;**38**:2532–46. <https://doi.org/10.1093/eurheartj/ehx248>
3. Grigorian-Shamagian L, Sanz-Ruiz R, Climent A, Badimon L, Barile L, Bolli R, et al. Insights into therapeutic products, preclinical research models, and clinical trials in cardiac regenerative and reparative medicine: where are we now and the way ahead. Current opinion paper of the ESC Working Group on Cardiovascular Regenerative and Reparative Medicine. *Cardiovasc Res* 2021;**117**:1428–33. <https://doi.org/10.1093/cvr/cvaa337>