Medical Xpress

New stem cell therapy for ischaemic heart disease

July 11 2014

An EU-funded project is looking into 'Cardiac stem cells' (CSCs) to tackle the problem of chronic heart failure in Europe. Whilst previous research has concentrated on cells from the patients themselves, the CARE-MI team focuses on cells from various donors. Clinical trials are expected as soon as summer 2014 in Spain and Belgium.

'Ischaemic heart disease' (IHD) was responsible for 12?% of all deaths in the OECD in 2011. The disease, which causes blood supplies to the heart to diminish, progressively damages heart tissue.

Whilst the introduction of angioplasty and stents has successfully helped reduce early mortality rates, the lack of solutions to repair the damaged tissue often leads to initial patient recovery being followed by cardiac remodelling and 'Chronic heart failure' (CHF). The only cure for CHF is heart transplantation, but few patients are lucky enough to find a compatible donor in time.

An alternative to heart transplantation may reside in endogenous CSCs, recently discovered pluripotent cells contained in adult myocardium (heart muscle). CSCs can potentially heal tissue through the production of new cardiac muscle cells (cardiomyocytes) or trigger molecular pathways of cardiac repair through growth factors.

This potential has only been tested recently by using autologous cell therapy for repairing damaged tissue. Put simply, the method consisted in using the patient's own cells to repair the myocardium. But although

promising, the autologous approach has so far proved very time-consuming, expensive and, most importantly, relatively ineffective.

Researchers from the CARE-MI (Cardio repair European multidisciplinary initiative) project have set out to tackle this issue with the help of FP7 funding, by shifting the view from autologous to allogeneic. Instead of taking cells from patients themselves, they developed a new methodology relying on cells from different donors.

Dr Antonio Bernad, coordinator of the project, believes this technique could be the basis of ready-to-use, affordable and user friendly therapies based on the in situ activation, multiplication and differentiation of endogenous CSCs.

What are the main objectives of the project?

Antonio Bernad: Our main goal is to develop widely available and clinically applicable treatments for IHD. CARE-MI exploits the biology of 'endogenous resident cardiac stem cells' (eCSCs) and the molecular mechanisms responsible for their activation and differentiation in situ. The proposed therapies may directly impact the resident eCSCs population, resulting in their activation, expansion and differentiation into cardiomyocytes - endothelial and smooth muscle vascular cells - to regenerate the contractile tissue and the microvasculature lost as a result of the ischaemic event.

These therapies have been validated in initial preclinical results in animals presenting a cardiac anatomy, physiology and pathology comparable to that of humans. Now, if we want to enable an effective and clinically-applicable myocardial regenerative therapy, we have to compare the relative merits of the two arms proposed, and see if combining them can result in any additional benefits.

What is new or innovative about the project?

CARE-MI relies on the use of allogeneic 'Cardiac stem cells' (CSCs) and/or a limited number of regenerative factors, known to be secreted by the eCSCs, for the activation/promotion in situ of the endogenous repair programme. These allogeneic CSCs, which survive only transiently in the recipient, set off a potent endogenous regenerative process by activating the endogenous eCSCs. The latter is capable of limiting progressive degeneration and partially restoring the anatomy and function of damaged myocardium.

The two proposed treatments and/or their combination will, for the first time, provide generic off-the-shelf regenerative therapies which will be ready to be applied at any time wherever the technical means and professional expertise needed to treat AMIs and perform PTCAs are available - that is, in most large medical centres.

Because of their generic nature, these therapies will be available to all candidate patients. An additional attractive feature of the proposed approach is the fact that despite their generic and off-the-shelf nature, these treatments will produce autologous regenerated myocardium. We believe that the transition from autologous cell therapy - as already clinically tested widely- to the use of allogeneic cells for their paracrine effect before moving to a cell-free therapy based on the subset of the paracrine factors is not only a logical conceptual progression, but also the safest route for making progress in this field.

What were the main difficulties you faced and how did you resolve them?

CARE-MI put an enormous effort into developing a solid background that demonstrates the feasibility of the use of allogeneic CSCs for the treatment of ischaemic cardiac disease. The logistics of the clinical trial

have been a major challenge for the consortium. For example, aspects related to large-scale cell production became especially painstaking as we were producing a medicinal product. The strict controls and the importance of robust results on the cell identity have consumed most of our efforts - under the leadership of CORETHERAPIX Ltd, partner and promoter of the clinical trial.

Moreover, the conditions associated with an allogeneic scheme (mainly CSC immunoregulation properties and putative CSC immunoresponse) have also involved many discussions, especially in defining the more solid and reliable methods for evaluating those properties. However, thanks to the collaboration of sound experts in the consortium, as well as external scientific advisors, CARE-MI has overcome most of these difficulties.

Are you satisfied with the project outcomes so far?

The project has produced very relevant results in this fourth year; CARE-MI has completed the GMP production of the cell therapy medicinal product to be used in the clinical trials, while the complete 'Clinical trial application' (CTA) has been submitted to Spanish and Belgian Regulatory Agencies (AEMPS and FAGG respectively).

The Spanish Regulatory Agency approved the CTA on 16 April 2014 - allowing CARE-MI to achieve one of the major milestones of the project - and we are awaiting the final decision from Belgium's Regulatory Agency (FAMHP). A clinical trial is expected to start shortly; currently we are in the recruiting phase and we expect to start treating our first patients this summer. This is a very exciting opportunity for us and we hope that we can produce more relevant results during the year.

What are the next steps for the project itself and after it ends?

Our next steps are devoted to speeding up the other relevant arm of our project, testing the growth factor therapy as a feasible alternative for the treatment of IHD. Our final goal is to produce enough data to generate the preclinical dossier taking into consideration our previous experience with regulatory agencies. Of course, we will also be involved in the development of the clinical trial and will try to produce relevant results regarding patient immune responses to the treatment, along with data regarding the safety and effectiveness of the proposed therapy.

Additionally, we have submitted a proposal (H2020) for the clinical evaluation of CSC (CARE-MI) in the chronic scenario. If we get funding, we would be ready to go into a clinical trial in two years.

When do you expect patients to start benefiting from your research?

When talking about innovative treatments we need to be very cautious to avoid giving false hope. We are in phase I/II of a clinical trial, which means that additional trials will be requested prior to the final release of the product.

However, we are confident of our results in the preclinical phase and expect positive outcomes with patients. It is difficult to predict the exact date on which this treatment will be available for the wider public, but we have set a five-year timeframe for our estimations. This is strictly dependent on the optimal development plan of our industrial partner, CORETHERAPIX, supporting Phase III.

Medical Xpress

Provided by CORDIS

Citation: New stem cell therapy for ischaemic heart disease (2014, July 11) retrieved 19 April 2024 from https://medicalxpress.com/news/2014-07-stem-cell-therapy-ischaemic-heart.html

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.