Cardiac stem cell mechanosome and mechanosensitivity develop with differentiation

Citation for published version (APA):

Document license:
Unspecified

Document status and date:
Published: 22/03/2016

Please check the document version of this publication:

- A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher’s website.
- The final author version and the galley proof are versions of the publication after peer review.
- The final published version features the final layout of the paper including the volume, issue and page numbers.

Link to publication

General rights
Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal.

If the publication is distributed under the terms of Article 25fa of the Dutch Copyright Act, indicated by the “Taverne” license above, please follow below link for the End User Agreement:
www.tue.nl/taverne

Take down policy
If you believe that this document breaches copyright please contact us at:
openaccess@tue.nl
providing details and we will investigate your claim.

Download date: 21. Jul. 2019
Cardiac stem cell mechanosome and mechanosensitivity develop with differentiation

A. Mauretti1, N.A.M. Bax1, M.J. Goumans3, C. Sahlgren1, C.V.C Bouten1
1 Department of Biomedical Engineering, Eindhoven University of Technology
2 Departments of Molecular Cell Biology and Center for Biomedical Genetics, Leiden University Medical Center

Introduction
Stem cell mechanosensing and mechanoresponse is crucial for tissue regeneration in mechanically functional organs like the heart. However, very little is known about how cardiac resident stem cells, such as cardiomyocyte progenitor cells (CMPCs), sense and respond to the mechanical stimuli provided by the beating heart. Thus, the complex of cellular structures relevant for mechanosensing, made of focal adhesions (FAs) and actin stress fibers, the ‘mechanosome’, needs to be explored. Identifying the key players and the underlying mechanisms of cardiac stem cell mechanotransduction is essential to achieve optimal migration and integration of endogenous cardiac cells into the injured site. Here we demonstrate that the mechanosensitivity of CMPCs relies on the mechanosome, which develops with early cardiac differentiation.

Materials and methods
Cardiomyogenic differentiation of human L929 CMPCs was induced by biochemical stimulation for 14 days (predifferentiated CMPCs) [1]. Uniaxial cyclic strain (10% at 0.5Hz) was applied for 48h to undifferentiated (undiff) and predifferentiated (prediff) CMPCs seeded on collagen IV-coated Bioflex membranes. Unstrained samples were used as control.

CMPCs respond to mechanical cues upon differentiation

The CMPC mechanosome develops with differentiation and not with strain

Figure 2: CMPCs develop the mechanosome upon early cardiac differentiation. A) Immunofluorescence images show the expression of vinculin (VCL), integrin-linked kinase (ILK), and phosphorylated focal adhesion kinase (pFAK) in undifferentiated (undiff) and predifferentiated (prediff) CMPCs 24 hrs after seeding and before strain application (day0). Scale bar 100μm. B) Gene expression of cardiac troponin T (cTnT), VCL, ILK and FAK at day0. Results are expressed as mean ± SD (N=3).

Figure 3: The mechanosome development is not induced by external mechanical stimuli. Immunofluorescence stainings of vinculin (green) and F-actin (red) at day1 and day2 of straining, did not show differences between unstrained and strained samples in both undifferentiated (undiff) and predifferentiated (prediff) CMPCs. Results are expressed as mean ± SD (N=3).

Conclusions and outlook
In conclusion, we showed for the first time that the CMPC mechanosensing apparatus in direct contact with the ECM, the mechanosome, only develops upon differentiation, and allows differentiating CMPCs to align in response to uniaxial strain. This suggests that the lack of a developed mechanosome in undifferentiated CMPCs shields them from the mechanical environment of the beating heart, whereas differentiating cells can sense and respond to cyclic strain by aligning.

References: