

Cell-matrix interactions in cardiomyocyte progenitor cells upon cyclic strain

Citation for published version (APA):

Mauretti, A., Sahlgren, C. M., Baaijens, F. P. T., & Bouten, C. V. C. (2015). *Cell-matrix interactions in cardiomyocyte progenitor cells upon cyclic strain*. Poster session presented at CellMech 2015, Barcelona, Spain.

Document status and date:

Published: 01/05/2015

Document Version:

Publisher's PDF, also known as Version of Record (includes final page, issue and volume numbers)

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:

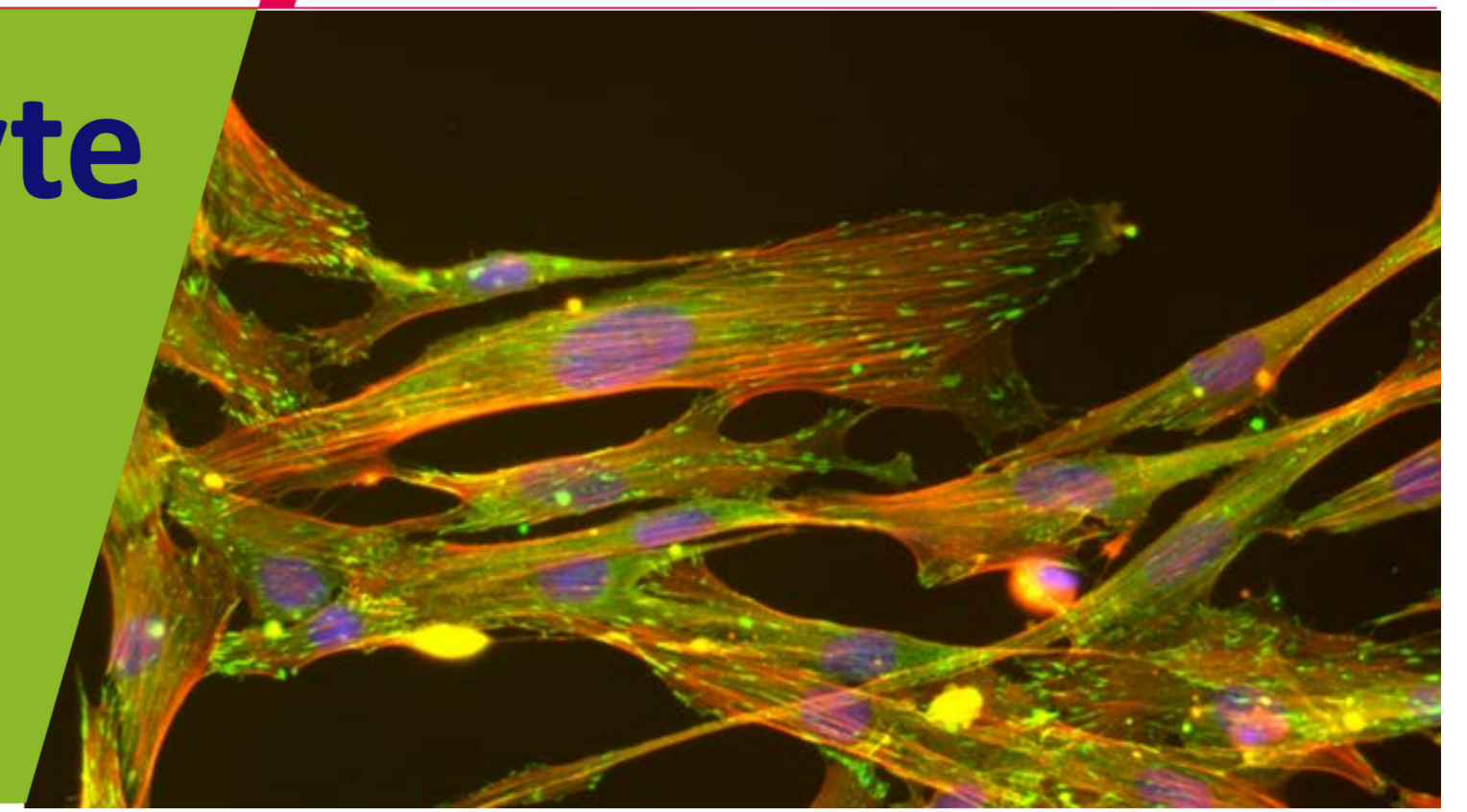
openaccess@tue.nl

providing details and we will investigate your claim.

Cell-matrix interactions in cardiomyocyte progenitor cells upon cyclic strain

A. Mauretti, C. Sahlgren, F. Baaijens, C. Bouten

Eindhoven University of Technology, Eindhoven, The Netherlands



Introduction

After myocardial infarction (MI), the contractility of the heart is severely compromised, and scar tissue is formed. Human cardiomyocyte progenitor cells (CMPCs) injected in the injured myocardium have potential to replace death cardiomyocytes and repair the damaged heart [1;3]. Integration of the transplanted cells in the host tissue and their response to the biomechanical stimuli provided by the heart are crucial for a good outcome of the therapy. The development of focal adhesions (FAs) and actomyosin stress fibers (the **mechanosome**) allows cells to respond upon mechanical stimulation [1;2]. The key to transplanted CMPC integration and functioning in the heart might reside in mechanosome development and CMPC ability to respond to mechanical cues. Here we study the mechanosome of undifferentiated and predifferentiated CMPCs, and their response upon cyclic strain.

Methods

Cardiomyogenic differentiation of human L9TB CMPCs was induced by biochemical stimulation for 14 days (predifferentiated CMPCs) [3;4]. Uniaxial cyclic strain with 10% strain and 0.5Hz was applied to undifferentiated (undiff) and predifferentiated (prediff) CMPCs seeded on collagen IV-coated Bioflex membranes for 48h (Figure 1). Static samples were used as control.

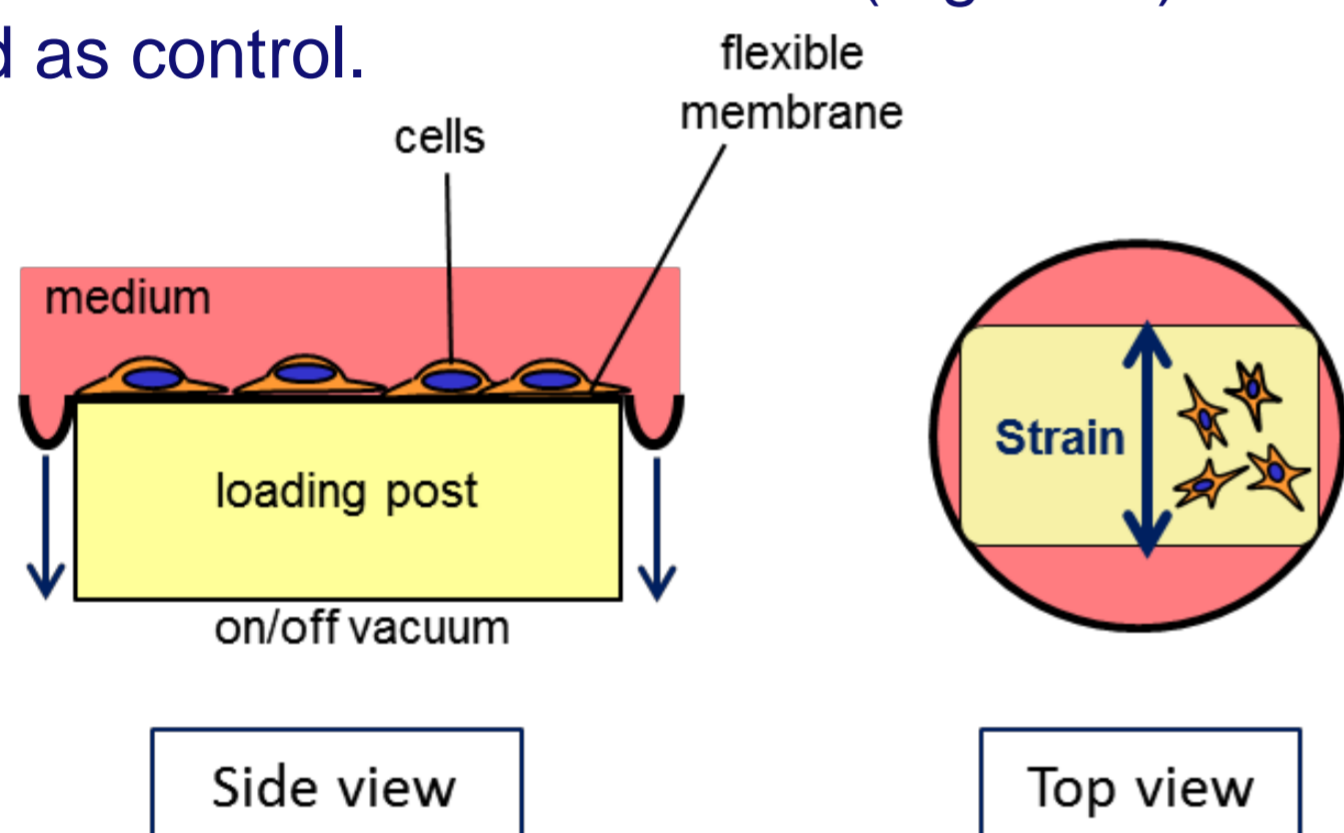


Figure 1: Experimental setup. Cyclic strain was applied with the FlexCell system.

Differentiation and the mechanosome

Prediff CMPCs developed mature FAs and actin stress fibers (the mechanosome) 24h after seeding. Undiff cells showed immature FAs, and no stress fibers were present (Figure 2). Cardiomyogenic differentiation is thus needed for the mechanosome development in CMPCs.

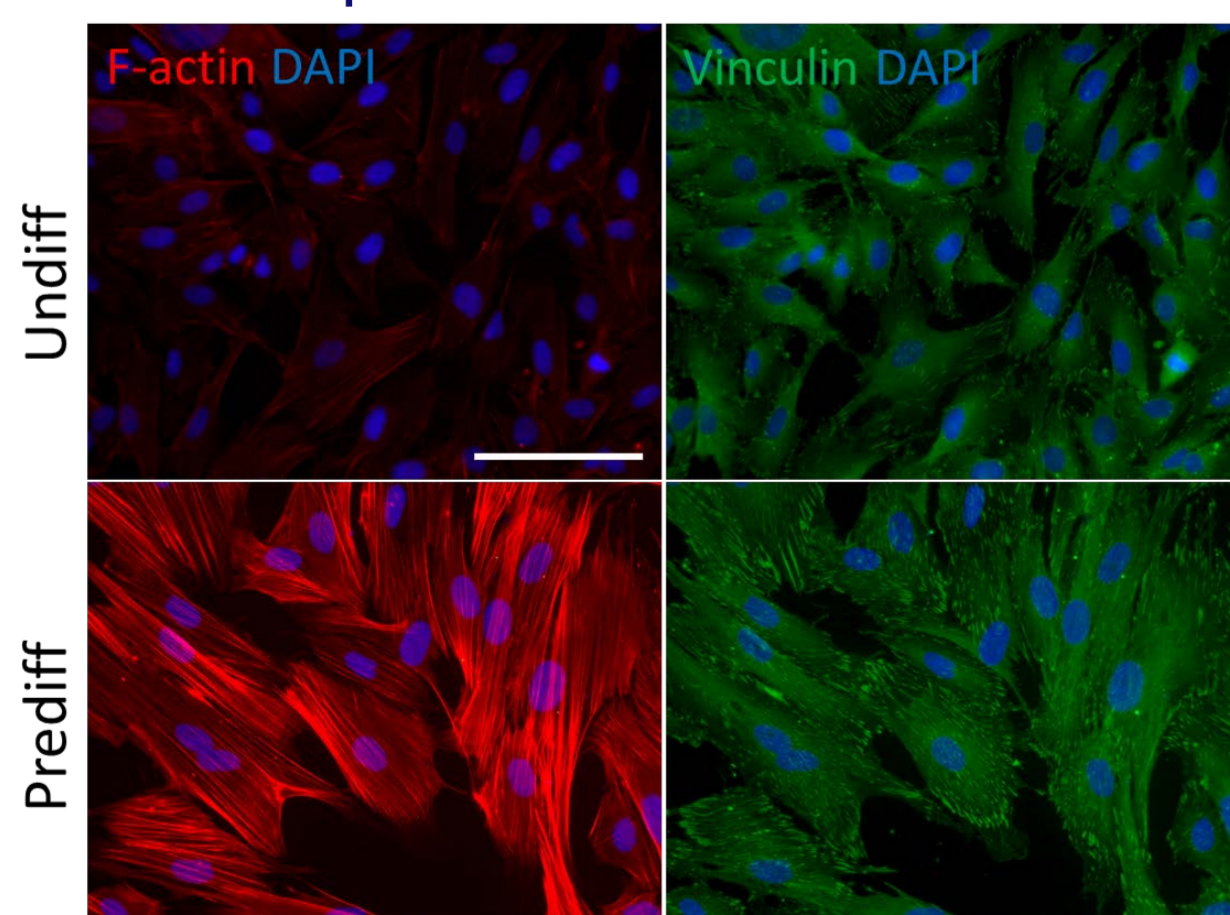


Figure 2: F-actin and vinculin expression in undiff and prediff CMPCs 24h after seeding on collagen IV-coated cover glasses. Scale bar 100 μ m.

Conclusions and future outlook

Our results indicate that human CMPCs are able to sense and respond to external mechanical cues only when cardiomyogenic differentiation is biochemically induced, thanks to the mechanosome development that follows differentiation. The occasional strain avoidance displayed by undifferentiated CMPCs might be due to strain-induced differentiation. This 2D study represents a first step toward future experiments in 3D, niche-like environments.

CMPC response upon cyclic strain

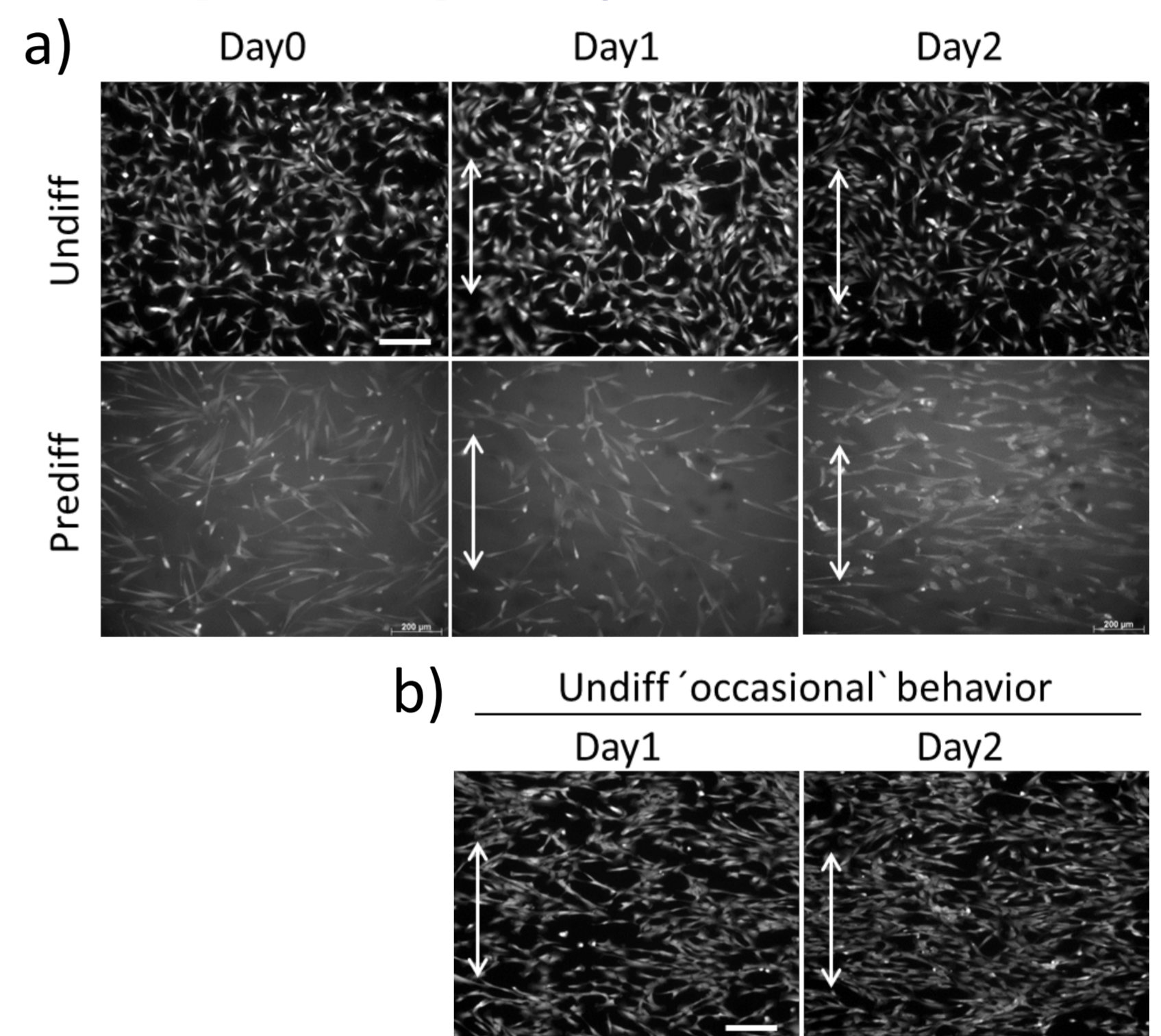


Figure 3: **a)** After one day of applied cyclic strain (Day1), both undiff and prediff cells mainly kept a random orientation. After two days of straining (Day2), prediff CMPCs showed a main orientation perpendicular to the strain direction (strain avoidance), whereas undiff CMPCs displayed the same behavior as Day1. **b)** Occasionally, undiff CMPCs showed strain avoidance at Day1, depending on their localization in the well plate, and maintained the same behavior at Day2. Scale bar 200 μ m.

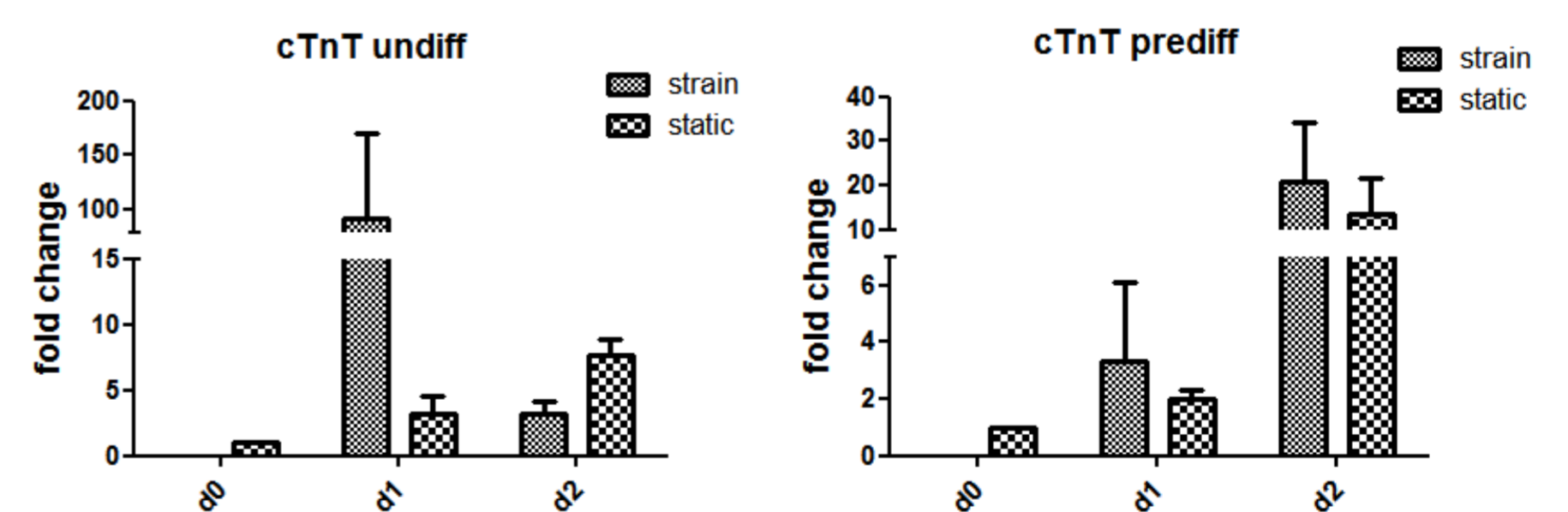


Figure 4: Upregulation of the late cardiac gene cTnT after one day of strain in undiff CMPCs suggests that cyclic strain might induce CMPC differentiation. Strain-induced differentiation might be responsible for the occasional cell alignment in response to mechanical loading.

References:

- [1] Pijnappels DA et al., Ann. N.Y. Acad. Sci. 2010;1188:7-14
- [2] Kanchanawong P et al., Nature 2010;468:580-586
- [3] Smits AM et al., Nature Protocols 2009;4(2):232-243
- [4] Bax N, Marion MH et al., JMCC 2012;53:497-508