Direct reprogramming of human cardiac fibroblasts to cardiomyocytes using microRNA mimics

Abstract Submission Form: TERMIS EU 2019, 27th to 31st of May 2019, Rhodes, Greece

Abstract Submission Form Guidelines

TERMIS EU 2019 invites abstracts in all areas of tissue engineering and regenerative medicine research, development and clinical translation. Abstract with educational, career development and societal impact are also welcomed. If you are interested in submitting an abstract, please complete the abstract form and submit it to termis@nuigalway.ie by **Friday, the 28th of December 2018**.

Submitted abstracts will be evaluated on the basis of the following criteria:

- Relevance to tissue engineering and regenerative medicine research;
- Scientific / technological / clinical / educational / societal impact.

Submitted abstracts will be reviewed and considered for podium or poster presentation. Please indicate whether you want your abstract to be considered for podium or poster presentation by ticking either of the boxes below.

☐ Podium presentation.

☒ Poster presentation.

Notification of acceptance or rejection will be communicated to the authors in January 2019. Instructions to podium and poster presenters will be sent to the authors in March 2019.

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☒ I am student (1) or young investigator (2) and I want my abstract to be considered for an award.

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(1) Any individual who is engaged as a full-time undergraduate or graduate in a university or college program and is actively involved in research in the field of tissue engineering and regenerative medicine. You will be asked to submit a copy of your student identification card in the registration form.

(2) Any individual who is employed by an academic institution in the field of tissue engineering and regenerative medicine, who has been awarded their doctoral degree within the past 3 years and who is not holding an appointment as faculty or academic staff. Young investigators are required to have their advisor / supervisor send a letter as proof of the bona fide status of the young investigator.

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TERMIS EU 2019 assumes that all authors have approved the submitted abstract. All abstracts must be submitted electronically using the template below. All abstracts must be written in English.

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PLEASE ADHERE TO THE GUIDELINES BELOW

Abstracts must not exceed one page.

All abstracts must be formatted for only A4 paper (210 x 297 mm).

Margin sizes must not be altered and are set to 25 mm.

The title should be in bold, 14 size Times New Romans font, center alignment.

The author should be listed consecutively by initials and last name.

The name (first name second name) and email of the presenting author must be indicated.

Affiliation should be indicated with superscripted suffix Arabic numerals. Do not append degrees, professional designations, etc., to names.

Affiliations should be listed consecutively.

The body of the document should be set in size 11 Times New Roman, justified, with single line-spacing.

Figures should have the caption below them.

Tables should have the caption above them.

References: A maximum of three references may be used. In the text, indicate references by number(s) in square brackets in line with the text (e.g. [1]). In the list, number the references (numbers in square brackets) in the order in which they appear in the text. Please use the following format: [1] Satyam A et al. Adv Mater. 2014; 26(19):3024-34

The abstracts must not exceed 5MB in size.

Rename the file using the presenting author's first name second name (e.g. Diana Gaspar).

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Direct reprogramming of human cardiac fibroblasts to cardiomyocytes using microRNA mimics

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INTRODUCTION: The combination of four different microRNAs (miR-1, 133, 208 and 499), named "miRcombo", has been used for the direct reprogramming of murine fibroblasts into cardiomyocytes (CMs) for myocardial infarction (MI) treatments.[1,2] Here, we evaluated miRcombo mediated reprogramming of human adult cardiac fibroblasts (AHCFs) into CMs in 2D and 3D culture.

METHODS: For digital droplet PCR (ddPCR) analysis, $3x10^5$ AHCFs were plated in 6-well plates, for Immunocytochemistry (ICC) $5x10^4$ cells were plated in 24-well plates. AHCFs were transfected with miRcombo (mirVana) using DharmaFECT1 (Dharmacon). Untrasfected and NegmiR (mirVana) transfected AHCFs were used as controls. After 24 hours, medium was changed to medium with 1 μM Jak1 Inhibitor for 4 days for 2D experiments; for 3D experiments, cells were cultured in fibrin-based hydrogels.

RESULTS: ddPCR analysis showed significant increase expression of early cardiac transcription factors (TFs) Hand2 and Mef2c ($p < 0.005$) slight increase expression of Tbx5 and Nkx2.5, although non-significant ($p > 0.05$), and reduced Vimentin expression ($p < 0.05$) in miRcombo-transfected AHCFs compared to controls after 4 days in 2D culture. ICC analysis showed increased expression of late cardiac markers α-sarcomeric actinin and cTnT in miRcombo-transfected AHCFs after 10 and 20 days of culture in 2D. However, ddPCR showed no significant differences of late cardiac markers Myh6 and cTnI expression between the groups after 15 days in 2D culture. On the other hand, cells cultured in 3D fibrin-based hydrogels showed enhanced cardiac TFs expression compared to 2D. However, miRcombo transfection did not significantly enhance cardiac gene expression in AHCFs cultured in 3D hydrogels respect to controls after 4 days. After 15 days, AHCFs cultured in 3D hydrogels showed a strongly enhanced expression of cardiac genes such as cTnI and Myh6 compared to 2D.

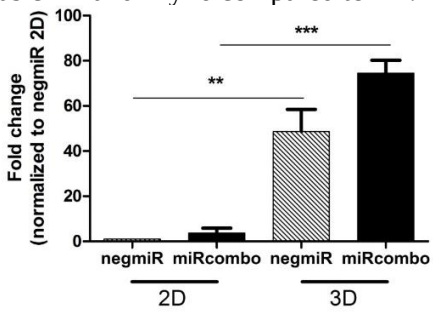

Figure 1: Fibrin-based 3D hydrogels significantly enhanced Myh6 expression in AHCFs compared to negmiR in 2D culture after 15 days.

DISCUSSION & CONCLUSIONS: Together, these results showed that a 3D environment was found to play a key role in enhancing direct reprogramming of AHCFs into CMs.

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REFERENCES

[1] Jayawardena TM et al. *Circ Res.* **2013**, *110*, 1465–1473
[2] Li Y et al. *Sci. Rep.* **2016**, *6*, 1–11