Submission Confirmation for An extracellular matrix-liposome composite: a novel extracellular matrix delivery system for accelerated tissue regeneration (adhm.202101599)

Advanced Healthcare Materials <em@editorialmanager.com> Wed, Aug 4, 2021 at 8:20 PM
Reply-To: Advanced Healthcare Materials <advhealthmat@wiley-vch.de>
To: Agustina Setiawati <nina.lifesci@gmail.com>

You are being blind carbon copied ("bcc:'d") on an e-mail "To" "Kwanwoo Shin" kwshin@sogang.ac.kr

Dear Dr. Shin,

Your submission entitled "An extracellular matrix-liposome composite: a novel extracellular matrix delivery system for accelerated tissue regeneration" has been received by journal Advanced Healthcare Materials. The manuscript number for your submission is adhm.202101599.

To view your submission, please login to https://www.editorialmanager.com/advhealthmat/ by entering your username (********) and password and selecting the "Author Login" option. Please note that the current status of your submission will remain "Under consideration" until an editorial decision is made, at which time you will be notified by e-mail.

If the manuscript is accepted for publication, this author's affiliation will be used to determine eligibility for some open access funding (click here for details).

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This message has been sent to all named co-authors listed in the submission process to serve as notification of submission.

Thank you for submitting your work to the journal.

Kind regards,

Editorial Office

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http://www.advhealthmat.de

Impact Factor (2021 Journal Citation Reports): 9.933

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Please find a copy of the submission questions, which you answered during the submission, for your records:

Additional Information

10. Kwanwoo Shin, Ph.D.

Question	Response
Please submit a plain text version of your cover letter here.	We would like to submit a new manuscript entitled "An extracellular matrix-liposome composite: a novel extracellular matrix delivery system for accelerated tissue regeneration" for publication in Advanced Materials. We designed and formulated a unique combination of lipids for liposomes coated with an extracellular matrix (ECM) and found that this ECM-lipid complex could deliver essential ECM components to cells in the form of native fibrous structures, accelerating cellular activities in the course of wound healing process. This manuscript describes the formulation of the ECM-delivery system that remarkably improves all the aspects in would healing. We encourage you to evaluate Movies S4 first to intuitively appreciate the real-time extracellular matrix formation on the live cell upon the delivery. Below we explain why we believe our research is a novel and technological breakthrough, and why it may capture the

immediate interest of a broad readership in tissue engineering, wound healing, and more importantly, liposomal ECM delivery. Most of the successful or commercialized studies on the liposomal structures have been exploiting the encapsulation ability of liposomes where the assembled hydrophobic lipid boundary encapsulates an aqueous core. The delivery ability of liposomes has been fine-tuned for drug delivery, and researchers continue to envision new applications. For decades, pharmaceutical companies have developed a variety of clinically approved liposome-based medicines. They are Ideal for drugs with poor pharmacokinetics, limited bioavailability, or high toxicity. Very recently, liposomes have become a critical part of COVID-19 vaccines produced by Pfizer and Moderna. Both manufacturers use a specific combination of lipids to protect the delicate mRNA long enough to be delivered to cells.
Indeed, ECM delivery has also been reported in a variety of ways. Nonetheless, direct delivery of the fibrous ECM was not successful because encapsulating the fibrous ECMs in the cramped internal space of the liposome was not suitable.
Be worth of mentioning, however, in 2015, our group have discovered that the negatively charged moieties can unfold globular fibronectins to fibrous fibronectins, and demonstrated for the first time that highly organized extracellular matrix networks can be generated by the presence of negatively charged polymeric materials (Adv. Mat. 27, p2838, 2015). Later, we further discovered that the conformational changes to the fibrous forms from the globular forms must be occurred at the damaged tissue to be healed. Therefore, we naturally hypothesized, if the negatively charged phospholipids can induce those conformational changes, that the injectable ECM-liposomes can be developed as one of the most effective wound healing agents.
Here, we have developed a unique combination of different lipids for liposomes that can promote the adhesion and conformational modification of the extracellular matrix on the surface. Under normal conditions, fibronectin, a protein abundant in the extracellular matrix, remains folded and unfolds only when recruited to the cell surface at the wound site. Therefore, unfolding fibronectin can significantly improve the efficiency of wound healing. In this manuscript, we demonstrated that negatively charged liposomes with our intrinsic lipid composition efficiently bind as well as unfolded fibronectin before delivery to living cells and tissues. This lipid-based substance can induce conformational changes of the fibronectin protein, which is comparable to a potent denaturant. Our system has been successfully applied in vitro to promote healing of cultured fibroblasts. More interestingly, when our composition was applied to an ulcerative rat model to test the system in vivo, the wounds healed much effectively than a control group.

Our results provide a solid background for further development of wound healing extracellular matrix (ECM)-delivery system. The universality of ECM and lipids makes it easy to apply to various diseases without much considering tissue specificity, and synergistic effects can be also expected when combined with target drugs.
Accordingly, we believe that the subject matter and caliber of this work ideally suit it for publication in Advanced Materials.

Sincerely,

Kwanwoo Shin, Ph.D.
Department of Chemistry and Institute of Biological Interfaces, Sogang University Phone : +82 10 6214 8213 Email : kwshin@sogang.ac.kr

Kevin Kit Parker, Ph.D.
Disease Biophysics Group, John A. Paulson School of Engineering and Applied Sciences, Harvard University, Cambridge 02138, USA

Chang-Ju Kim, Dr. Ph.D

	Department of Physiology, College of Medicine, Kyung Hee University, Seoul 02447, Republic of Korea
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Please confirm that ethical approval from the national or local authorities was obtained prior to the research, and that this is included in the Experimental section of your manuscript. as follow-up to "Does the research described in this manuscript include animal experiments?"	Yes, I confirm
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If available, please provide the assigned approval/accreditation number of the laboratory/investigator in the textbox below, as well as in the Experimental section of your manuscript. as follow-up to "Please confirm that ethical approval from the national or local authorities was obtained prior to the research, and that this is included in the Experimental section of your manuscript."	KHUASP(SE)-15-085
Does the research described in this manuscript include human research participants (including for experiments with sensors or wearable technologies) or tissue samples from human subjects (including blood or sweat)?	No
Do you or any of your co-authors have a conflict of interest to declare?	No. The authors declare no conflict of interest.
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FW: Acceptance of your submission to Advanced Healthcare Materials (adhm.202101599R1) - [EMID:10ca0b738379d393]

Kwanwoo Shin <kwshin@sogang.ac.kr> Tue, Nov 16, 2021 at 6:10 PM
Reply-To: kwshin@sogang.ac.kr
To: "Lee, Gilyong" <gilyong_lee@g.harvard.edu>, Agustina Setiawati <nina.lifesci@gmail.com>, Huong Nguyen <huong.nguyen200291@gmail.com>, 정원희 <whjung@cau.ac.kr>, "Parker, Kit" <kkparker@g.harvard.edu>, "김창주(의과대학 의예과)" <changju@khu.ac.kr>, 남소정 <sojeong3110@naver.com>, 김민영 <yeoderae@naver.com>

Dear Colleagues,
I just received that our SUV-ECM delivery system to ulcerative colitis has been accepted in Advanced Healthcare Materials. Thank you for your years-long process. Thank you.

Kwanwoo.

-----Original Message-----
From: em.advhealthmat.0.775f56.2a0fd33b@editorialmanager.com <em.advhealthmat.0.775f56.2a0fd33b@editorialmanager.com> On Behalf Of Advanced Healthcare Materials
Sent: Tuesday, November 16, 2021 6:01 PM
To: Kwanwoo Shin <kwshin@sogang.ac.kr>
Subject: Acceptance of your submission to Advanced Healthcare Materials (adhm.202101599R1) - [EMID:10ca0b738379d393]

Dear Dr. Shin,

Thank you for submitting your manuscript entitled "An extracellular matrix-liposome composite: a novel extracellular matrix delivery system for accelerated tissue regeneration" (Research Article, No. adhm.202101599R1) to Advanced Healthcare Materials. The reviewer report and comments are included at the end of this e-mail.

I'm pleased to inform you that your manuscript has been accepted for publication without change.

The final version of your article can only be published once we have received a signed license agreement. You will soon receive an email invitation to register or log in to Wiley Author Services (https://authorservices.wiley.com). After logging into Wiley Author Services, please follow the on-screen instructions to sign the appropriate license agreement.

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Congratulations on your results, and thank you for choosing Advanced Healthcare Materials for publishing your work. I hope you will consider us for the publication of your future manuscripts.

Yours sincerely,

Ulrike Kauscher Pinto

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REVIEWER REPORT:

Please note that reviewers may not be numbered consecutively.

EVALUATION:

Reviewer's Responses to Questions

Please rate the importance compared to published work in this subject area.

Reviewer #1: Outstanding - Top 5% in the subject area

Reviewer #2: High - Top 15% in the subject area

Please rate the novelty compared to published work in this subject area.

Reviewer #1: Outstanding - Top 5% in the subject area

Reviewer #2: High - Top 15% in the subject area

Which aspects of scholarly presentation require improvement (if any)?

Reviewer #1: (No Response)

Reviewer #2: (No Response)

Do the methods, data and analysis (including statistical analysis where applicable) adequately test the hypothesis and support the conclusions?

Reviewer #1: Yes

Reviewer #2: Yes

Are the methods, data and analysis described in sufficient detail to be reproduced?

Reviewer #1: Yes

Reviewer #2: Yes

Is the research reported clinically relevant?

Reviewer #1: Yes

Reviewer #2: Yes

Where applicable, have the requested revisions been adequately addressed?

Reviewer #1: Yes

Reviewer #2: (No Response)

COMMENTS TO AUTHOR:

Reviewer #1: the authors have addressed my concerns. the revised manuscript is clearly improved and should be published in its current form

Reviewer #2: The authors did a very thorough job responding to my prior comments. Their answers were thoughtful and the changes that were made in the manuscript resulted in significant improvements.

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