

Aging Pathobiology and Therapeutics

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Submission To Be Reviewed

Title Targeted regulation of senescence-associated secretory phenotype with an aptamer-conjugated activatable senomorphic
Journal Section Research Article
Abstract

Background: Senomorphics have been considered as an effective alternative paradigm of senotherapeutics to regulate cellular senescence by inhibiting the deleterious effects of senescence-associated secretory phenotype (SASP) components secreted by senescent cells without. However, current senomorphic drugs usually exhibit low selectivity towards senescent cells and inevitably cause unwanted side effects, highlighting the need to develop innovative senomorphic strategies for the specific regulation of cellular senescence.

Methods: To address this challenge, here we design a novel class of senomorphics with active cell targeting and activatable activities for silencing SASP by conjugating a senescent cell-targeted aptamer with a SA- β -gal-activated H2S donor. Using senescent BJ cells as a cell model, assays were performed to evaluate the performance of the engineered senomorphic (Apt-H2SD) for cell-specific regulation of SASP during cellular senescence.

Results: Apt-H2SD demonstrated specific binding and accumulation to senescent cells over proliferating cells through the aptamer-mediated internalization, Apt-H2SD was efficiently activated by the accumulated SA- β -gal in senescent cells, leading to the release of H2S precursor suppressing the expression of three important SASP factors (IL-6, IL-1 β and MMP3) at the mRNA level.

Conclusion: Our results strongly support the potential of Apt-H2SD as a valuable senomorphic. With rational design of the molecular structure, we provide a general strategy to construct advanced senescence-targeted activatable senomorphics for precise intervention of cellular senescence diseases.

Keywords: Senescence-associated secretory phenotype, senomorphics, L1CAM, cellular senescence

Submission Editor Warren Ladiges 
 editor apt 

Submission Metadata


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Review Schedule

Editor's Request 2023-05-23
Your Response 2023-05-25
Review Submitted 2023-06-07
Review Due 2023-06-06

Review Steps

1. Notify the submission's editor as to whether you will undertake the review.
 Response [Accepted](#)
2. If you are going to do the review, consult Reviewer Guidelines below.
3. Click on file names to download and review (on screen or by printing) the files associated with this submission.

Submission Manuscript	650-3088-2-RV.DOCX	2023-05-04
Supplementary File(s)	None	
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5. In addition, you can upload files for the editor and/or author to consult.

Uploaded files	None
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6. Select a recommendation and submit the review to complete the process. You must enter a review or upload a file before selecting a recommendation.

Recommendation	Revisions Required	2023-06-07
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