<table>
<thead>
<tr>
<th>Title</th>
<th>Timeless interacts with Parp1 to promote homologous recombination repair</th>
</tr>
</thead>
<tbody>
<tr>
<td>Author(s)</td>
<td>Xie, S; Mortusewicz, O; Ma, K; Poon, R; Hellday, T; Qian, C</td>
</tr>
<tr>
<td>Citation</td>
<td>The 2014 Hong Kong Inter-University Biochemistry Postgraduate Symposium, Hong Kong, 14 June 2014. In Program Booklet, 2014, p. 24, poster no. 24</td>
</tr>
<tr>
<td>Issued Date</td>
<td>2014</td>
</tr>
<tr>
<td>URL</td>
<td><a href="http://hdl.handle.net/10722/203758">http://hdl.handle.net/10722/203758</a></td>
</tr>
<tr>
<td>Rights</td>
<td>This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.</td>
</tr>
</tbody>
</table>
Using Polyanionic Heparin Mimetics for the treatment of COPD

KLK Wu*, SCH Chan*, JCL Tan^, JCW Mak^, DCL Lam^, MSM Ip^, DKY Shum*
Departments of Biochemistry* and Medicine^, LKS Faculty of Medicine, The University of Hong Kong, Sassoon Road, Hong Kong, China.

COPD patients suffer from sustained inflammation leading to airway damage and deteriorating lung function caused by unopposed protease activity resulting from α1-antitrypsin resistant supramolecular complexes of neutrophil elastase and shed syndecan-1 in the airway. It was further shown that the action of the GAG digesting enzyme heparanase facilitates syndecan-1 shedding.

We hypothesize that the use of a polyanionic heparin mimic would 1) displace neutrophil elastase from syndecan-1 rendering it susceptible to α1-antitrypsin inhibition and 2) inhibit heparanase activity in the airway.

In vitro tests show that the heparin mimic successfully displaced neutrophil elastase from syndecan-1 rendering it susceptible to α1-antitrypsin inhibition and 2) inhibit heparanase activity in the airway.

To assess the feasibility of using the mimic as a treatment for COPD, we treated cigarette smoke-induced COPD rats with an aerosol preparation of the mimetic. Preliminary results indicated that the number of neutrophils and neutrophil elastase amount in the lung was significantly decreased compared to rats treated with carrier alone. This suggests that our preparation can serve as a potential drug for the treatment of COPD.

Timeless interacts with Parp1 to promote homologous recombination repair

Si Xie1*, Oliver Mortusewicz2*, Ken Ma3, Randy Poon3, Thomas Helleday2, Chengmin Qian1
1Department of Biochemistry, The University of Hong Kong
2Department of Medical Biochemistry and Biophysics, Karolinska Institute, Sweden
3Institute of Life Science, Hong Kong University of Science and Technology
*These authors contribute equally to the study.

Both Parp1 and Timeless have been implicated in DNA damage response, while there is no report that Parp1 could function together with Timeless. We have, for the first time, provided the evidence that Parp1 binds to Timeless both in vitro and in vivo. In addition, we present the crystal structure of Timeless in complex with Parp1, and demonstrate that Timeless-Parp1 complex facilitates homologous recombination repair.