Identification of Slow Cycling Cells in Rat Vocal Folds

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Abstract

Purpose
As in other organs, cell therapy is one of the promising treatments in restoring the injured vocal folds (VFs). Indeed some cells including mesenchymal stem cells were used in attempt to restore scarred tissue or to prevent scarring, showing their potential in experimental models. Considering the ethical issues in cell transplantation, the tissue specific stem cells which reside in the VFs are expected to be a potent option in the establishment of therapeutic strategies for VF scarring, however tissue specific stem cells in VF have not been identified so far. Stem cells normally proliferate at a slow rate in adult organs, and the slow cycling cells of some organs are recognized as stem cells. Slow cycling cells in the VFs have not be well documented and represent an important subject for investigation. Purpose of this study was to clarify the distribution of slow cycling cells in rat VFs. Materials and methods
Adult SD rats were administered with intra-peritoneal injections of exogenous proliferation marker, 5’-bromo-2’-deoxyuridine (BrdU). After a certain period, VFs were harvested and double-stained with BrdU and a second endogenous proliferating marker Ki-67 in order to exclude the cell populations which stopped proliferation just after the injections. Additionally, lateral VF incision was performed to investigate the transition of slow cycling cells in tissue regeneration.

Result 1

1. Detecting the distribution of slow cycling cells in rat VFs.
2. Investigating the transition of slow cycling cells in the course of tissue regeneration.

Material and Method 1

Animal: 13 weeks old male Sprague Dawley rat n=9(2 for day 1, 5, and 15. 3 for day 10)

<table>
<thead>
<tr>
<th>Day 0</th>
<th>1</th>
<th>5</th>
<th>10</th>
<th>15</th>
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<tbody>
<tr>
<td>I % BrdU</td>
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<tr>
<td>Intra-peritoneal injection 50 μg/g/day 7 consecutive days</td>
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<tr>
<td>Harvest of larynges on day 1, 5, 10</td>
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Material and Method 2

Animal: 13 weeks old male Sprague Dawley rat n=6( 3 per each time point)

<table>
<thead>
<tr>
<th>Day 0</th>
<th>7</th>
<th>9</th>
<th>10</th>
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</thead>
<tbody>
<tr>
<td>I % BrdU</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Intra-peritoneal injection 50 μg/g/day 7 consecutive days</td>
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<td>VF epithelium incision on day 7, 9</td>
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<td></td>
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<tr>
<td>Harvest of larynges on day 10</td>
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Result 2

Discussion

Slow cycling cells were mainly distributed in the epithelium of the VFs. Considering the scariness of slow cycling cells in lamina propria, these results suggest the important role of VF epithelium for homeostasis and repair.

Enhanced proliferation caused by inflammatory or regenerative cytokines is a possible explanation for the reduced number of slow cycling cell in incised VFs.

Conclusion

Slow cycling cells, putative stem cells, were mainly distributed in the epithelium of the VFs.

Injury enhanced the proliferative characteristic of slow cycling cells.

References

1. Cotsarelis G. et al. (1989) "Existence of slow-cycling limbal epithelial basal cells that can be preferentially stimulated to proliferate: implications on epithelial stem cells." Cell. 57(2):201-9