EGR1 regulate radiation-induced apoptosis in human head and neck squamous cell cancer

Introduction

The expression and function of EGR1

- EGR1 over-expressed the variable cancer cells (esophagus, prostate, bladder, breast, stomach, colon)
- EGR1 is oncogene or tumor suppressor gene
  - oncogenic function in prostate cancer
  - Positive prognostic effect on survival in nasopharyngeal cancer

Aims

To investigate the early growth response-1 (EGR1) expression in human head and neck squamous cancer (HNSCC) and to evaluate whether EGR1 affects radiation-induced apoptosis and it would thus serves as the proper prognostic biomolecular marker of radiation therapy in human HNSCC.

Results

Table 1. Clinicopathologic variables of 28 patients with advanced hypopharyngeal cancer

<table>
<thead>
<tr>
<th>Variables</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr) median (range)</td>
<td>60(24-80)</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>21/7</td>
</tr>
<tr>
<td>Location (base: supraglottic subglottic)</td>
<td>22/6</td>
</tr>
<tr>
<td>Stage (I-II)</td>
<td>2/6</td>
</tr>
<tr>
<td>T-stage (T1-T4)</td>
<td>1-4</td>
</tr>
<tr>
<td>N-stage (N0-N4)</td>
<td>0-4</td>
</tr>
<tr>
<td>Histopathologic type</td>
<td>2/6</td>
</tr>
<tr>
<td>Tumor response to RT (CR,PR, NR)</td>
<td>4/2:10:16</td>
</tr>
<tr>
<td>Overall response rate (CR,PR,NR)</td>
<td>22:6</td>
</tr>
<tr>
<td>Response (no prior treatment)</td>
<td>15:12</td>
</tr>
<tr>
<td>2 year overall survival (%)</td>
<td>44</td>
</tr>
</tbody>
</table>

![Figure 1](image1)  
Figure 1. Expression of EGR1 in human hypopharyngeal cancer tissue. (A) Immunohistochemistry staining of EGR1 in hypopharyngeal cancer tissue. (B) mRNA expression of EGR1 in hypopharyngeal cancer tissue compared with normal tissues.

![Figure 2](image2)  
Figure 2. Expression of EGR1 and GapDH in human hypopharyngeal cancer tissue. The expression of EGR1 and GapDH was compared at 24 hr after treatment with or without radiation.

![Figure 3](image3)  
Figure 3. EGR1 expression and knock down by siRNA in human head and neck squamous carcinoma cell lines.

![Figure 4](image4)  
Figure 4. Radiation upregulates EGR1 expression in human HNSCC. After 6 Gy and 8 Gy irradiation, mRNA and protein expression of EGR1 increased with peak elevation from 24 hr to 24 h.

![Figure 5](image5)  
Figure 5. The activation of apoptosis related proteins after radiation in human HNSCC cells. (A) Western blot analysis of apoptosis related proteins (Caspase 3, PARP, XIAP). (B) Graph showing the activation of apoptosis related proteins by EGR1 knock down after radiation in human HNSCC cells.

![Figure 6](image6)  
Figure 6. The change of apoptosis related proteins by EGR1 knock down after radiation in human HNSCC cells. The cleaved caspase 3, cleaved caspase 7, cleaved PARP activation was decreased, and XIAP activation was increased by EGR1 knock down after radiation in human HNSCC cells.

![Figure 7](image7)  
Figure 7. Effect of EGR1 on cell apoptosis after radiation in human HNSCC cells. EGR1 knock down (E) inhibited radiation-induced apoptosis compared with control cells (C) in cell apoptosis assay.

Summary

- EGR1 have abundant expression in human hypopharyngeal cancer tissue
- Radiation up-regulate EGR1 proteins in human HNSCC cell lines.
- Radiation up-regulate apoptosis related proteins in human HNSCC cell lines.
- Knockdown of EGR1 inhibits radiation induced apoptosis in human HNSCC cell line.
- Knockdown of EGR1 inhibits the activation of apoptosis related proteins in human HNSCC cell line.

Conclusion

EGR-1 had abundant expression in human HNSCC tissue. EGR-1 knockdown inhibited radiation-induced apoptosis through caspase 3, caspase 7, PARP. EGR-1 may play an important role in treatment response after radiation therapy in human HNSCC.