Data analysis of genomic alteration by environmental toxicant

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1 Introduction

The primary toxicity of estrogen disruptor in males involves the induction of reproductive system abnormality. Although the male reproductive toxicity induced by endocrine disruptor chemicals (EDCs) has been investigated, the molecular mechanisms are unclear.

2 Methods and Results

In present study, we performed Y chromosome abnormality test using by a Y chromosome microdeletion detection kit for evaluation of the direct effects on the Y chromosome associated with reproduction. However, Yq abnormality as the result of BPA exposure was not detected. Also, to evaluate genomic alteration as component of our toxicity assessment, we carried out high-density oligonucleotide array-based comparative genome hybridization (CGH). We performed quadruplicate trials to verify the reliability of array-data by individual variation.

2.1 Tables

We used the ADM-2 (aberration detection module-2) finding method algorithm, threshold: 5.0, to select copy number variation, and used GEAR (Genomic Enrichment Analysis of Regional DNA copy number changes) as a statistical method (hypergeometric distribution, uncorrected P-values < 0.02). The ADM-2 algorithm searches for intervals in which a statistical score based on the average quality weighted log ratio of the sample and reference channels exceeds a threshold 5.0. A total of seven features were detected in the regions of DNA copy number variation in the BPA-treated mice.

Table 1: List of genomic altered-region

<table>
<thead>
<tr>
<th>Chromosome</th>
<th>Cytoband</th>
<th>#Probes</th>
<th>Amp/Del</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chr2:77739470-77848433</td>
<td>qC3</td>
<td>5</td>
<td>-2.337</td>
<td>7.54e-24</td>
</tr>
<tr>
<td>Chr5:128329169-128329869</td>
<td>qG1.2</td>
<td>1</td>
<td>-2.573</td>
<td>1.86e-15</td>
</tr>
</tbody>
</table>
2. Figures

Figure 1. GO ontology was analyzed by GeneSpring, Java-based ArrayToGo (Genochek.co.Ltd., Korea) software and used GeneOntology database (www.godatabase.org). Pheromone response-related genes and signal transduction-related genes are substantially included in the region of genomic alteration by BPA treatment.

3. Discussions

Seven observed features were gains or losses in chromosomal DNA (P-value < 1.0e-5, average log2 ratio > 0.2). consequently, chr7q1-qA2 in cytoband were a commonly observed amplification (P-value 3.69e-10). Another region, chr14qA1 in cytoband was also commonly amplified (P-value 2.93e-12, average of log2 ratios in segment > 0.3786). These regions include many genes associated with pheromone response and signal transduction using Java-based ArrayToKegg software. From these results, we could understand the molecular mechanisms underlying the reproductive effects induced by BPA.

References

