Painting analysis of chromosome aberrations induced by energetic heavy ions in human cells

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Representation of the major sources of ionizing radiation of importance to manned missions in low-Earth orbit. Note the spatial distribution of the trapped radiation belts.
Galactic cosmic radiation

Figure D.1. Abundances (a) and Energy Spectra (b) of GCR
DSB induction

High-LET

Low-LET
Complex aberrations
Radiation-induced chromosome aberrations in lymphocytes in vitro

Analysis of truly incomplete exchanges using telomere probes
Human lymphocytes exposed to 2 Gy gamma rays. Chromosomes #2 and #4 were painted.
Most of the incomplete exchanges analyzed with FISH are actually complete.

Figure 4. Percentage of complete and incomplete exchanges from the sum of the data. (A) The percentage of incomplete exchanges was 27% without the consideration of telomere probes. (B) With false incomplete exchanges included as complete, the percentage of incomplete exchanges decreased to 11%. (C) The estimated percentage of true incomplete exchange was 3%. (bar = 1 SD)

Wu, George and Yang, IJRB (1998, 1999)
• The fraction of unrejoined chromosome breaks are higher for high LET.

• Unrejoined breaks and incomplete chromosomal exchanges are possible biosignatures of high-LET radiation.

High-LET radiation induces more unrejoined DNA double strand breaks

Desai, Davis, O’Neill, Durante, Cucinotta and Wu, Rad. Res. 2005
Complex aberrations -- mFISH analysis

BIOSIGNATURE OF HIGH-LET RADIATION

mFISH showed a higher fraction of complex and incomplete exchanges for high-LET
Interphase vs. metaphase: Issues of biosignature

Centromere probes were used.

<table>
<thead>
<tr>
<th>Radiation</th>
<th>Dose (Gy)</th>
<th>Harvest method</th>
<th>F ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>γ ray</td>
<td>2</td>
<td>PCC</td>
<td>15.3±6.3</td>
</tr>
<tr>
<td>γ ray</td>
<td>2</td>
<td>Meta</td>
<td>12.5±5.9</td>
</tr>
<tr>
<td>γ ray</td>
<td>5</td>
<td>PCC</td>
<td>8.2±2.0</td>
</tr>
<tr>
<td>γ ray</td>
<td>5</td>
<td>Meta</td>
<td>9.1±2.5</td>
</tr>
<tr>
<td>1 GeV/u Fe</td>
<td>3</td>
<td>PCC</td>
<td>5.2±0.9</td>
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<tr>
<td>1 GeV/u Fe</td>
<td>3</td>
<td>Meta</td>
<td>9.1±2.2</td>
</tr>
</tbody>
</table>

Wu, George, Kawata, Willingham and Cucinotta, Rad. Res. 2001
mBAND analysis

Normal

Inversion
Inter- vs. intra chromosome exchanges (mBAND)
Most inversions were involved with other inter- and/or intra-chromosome rearrangements.
Summary

• FISH, mFISH, mBAND, telomere and centromere probes have been used to study chromosome aberrations induced in human cells exposed to low- and high-LET radiation in vitro

• High-LET induced damages are mostly a single track effect

• Unrejoined chromosome breaks (incomplete exchanges) and complex type aberrations were higher for high-LET

• Biosignatures may depend on the method the samples are collected

• Recent mBAND analysis has revealed more information about the nature of intra-chromosome exchanges