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
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.

False incomplete exchange
Most of the incomplete exchanges analyzed with FISH are actually complete.
• 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>
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<td>Meta</td>
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</tr>
</tbody>
</table>

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