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

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The Space Radiation Environment

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.

- **SOLAR PARTICLE EVENT** (Protons to Iron Nuclei)
- **GALACTIC COSMIC RADIATION (GCR)** (Protons to Iron Nuclei)
- **INNER RADIATION BELT** (Protons)
- **OUTER RADIATION BELT** (Electrons)
- **SOUTH ATLANTIC ANOMALY** (Protons)
Galactic cosmic radiation

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

- Relative Abundance vs. Atomic Number (Z)
- Differential Flux vs. Kinetic Energy (MeV/Nucleon)
DSB induction

High-LET

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

Analysis of truly incomplete exchanges using telomere probes
Telomere Analysis

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.

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

Complex type aberrations

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

Centromere probes were used.

<table>
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<th>Radiation</th>
<th>Dose (Gy)</th>
<th>Harvest method</th>
<th>F ratio</th>
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<td>$\gamma$ ray</td>
<td>2</td>
<td>PCC</td>
<td>$15.3\pm6.3$</td>
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<td>$\gamma$ ray</td>
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<td>Meta</td>
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<td>PCC</td>
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<td>3</td>
<td>PCC</td>
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<td>1 GeV/u Fe</td>
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Wu, George, Kawata, Willingham and Cucinotta, Rad. Res. 2001
mBAND analysis

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<tr>
<th>FITC</th>
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<td>Normal</td>
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<td>Inversion</td>
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Inter- vs. intra chromosome exchanges (mBAND)

![Graph showing aberrations in chromosome 3/cell vs. dose (Gy) for inter- and intra-exchange under different radiation sources: $^{137}$Cs $\gamma$-ray and Fe (600 MeV/n).]
Most inversions were involved with other inter- and/or intra-chromosome rearrangements.

mBAND analysis
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