Sister chromatid exchange in dyskeratosis congenita lymphocytes

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SUMMARY Sister chromatid exchange (SCE) frequency in chromosomes from lymphocytes of a patient with dyskeratosis congenita was 12.2 per mitosis. Our 33 normal controls had a mean of 5.0 ± 1.7 SCE per mitosis and 5 patients with Fanconi’s anaemia averaged 7.6 ± 0.7 SCE per mitosis. The rate of chromosome breakage was only 0.5% in the dyskeratosis congenita patient and 0 to 2.5% in controls, while the Fanconi’s anaemia patients showed higher values.

Dyskeratosis congenita is a rare genodermatosis with skin, nail, and mucous membrane changes, as well as pancytopenia (50% of cases) and solid tumors (17%) (Sirinavin and Trowbridge, 1975). Because of the skin changes and pancytopenia, dyskeratosis congenita has often been compared to Fanconi’s anaemia. We compared sister chromatid exchange (SCE) frequencies in chromosomes from lymphocytes of a dyskeratosis congenita patient with those of 5 patients with Fanconi's anaemia and 33 normal controls.

The dyskeratosis congenita patient was a 29-year-old man with reticulated hyperpigmentation, absent nails, leukoplakia, epiphora, and pancytopenia. The latter had been treated with corticosteroids and androgens for many years; a more recent and eventually fatal pneumonitis required supportive care. None of the controls had any of these findings. The dyskeratosis congenita cultures contained 29-year-old lymphocytes, cafe-au-lait spots, and increased chromosome breaks. They, too, were being treated with corticosteroids and androgens.

Lymphocytes were cultured with 10⁻⁴ molar bromodeoxyuridine (BrdU) for 72 hours and harvested by routine methods; slides were prepared following the SCE procedure of Korenberg and Freedlender (1974). Parallel cultures grown without BrdU were examined for chromosome breaks and other aberrations.

1This paper is supported in part by USPHS Grants No. TO1 AM 05560 (WB) and ST01 GM 01156 (KK).
Received for publication 25 June 1976
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Number of individuals scored: 33
Average control mean frequency: 5.4 SCE/mitosis
Average control standard deviation: 1.83
Range of the means: 2.8 to 10.5
Range of SCE/mitosis for all controls: 1-15

![Graph showing the number of controls vs. mean SCE frequency]

Table: SCE frequencies in dyskeratosis congenita and Fanconi’s anaemia

<table>
<thead>
<tr>
<th>Patient</th>
<th>No. of cells scored</th>
<th>Mean SCE</th>
<th>Standard deviation</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dykeratosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>congenita</td>
<td><em>(a)</em></td>
<td>42</td>
<td>12.3</td>
<td>4.25</td>
</tr>
<tr>
<td></td>
<td><em>(b)</em></td>
<td>64</td>
<td>12.1</td>
<td>3.9</td>
</tr>
<tr>
<td></td>
<td><strong>Mean:</strong></td>
<td>12.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fanconi’s</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>anaemia</td>
<td>(1)</td>
<td>2</td>
<td>7.5</td>
<td>4.11</td>
</tr>
<tr>
<td></td>
<td>(2)</td>
<td>24</td>
<td>7.9</td>
<td>2.8</td>
</tr>
<tr>
<td></td>
<td>(3)</td>
<td>24</td>
<td>6.5</td>
<td>2.4</td>
</tr>
<tr>
<td></td>
<td>(4)</td>
<td>69</td>
<td>7.5</td>
<td>3.3</td>
</tr>
<tr>
<td></td>
<td>(5)</td>
<td>6</td>
<td>8.7</td>
<td>4.6</td>
</tr>
<tr>
<td></td>
<td><strong>Mean:</strong></td>
<td>7.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grouped controls</td>
<td>33</td>
<td>780</td>
<td>5.4</td>
<td>1-15</td>
</tr>
</tbody>
</table>

*(a) and (b) represent two cultures from the same individual.

Our patients showed an increase in chromosome breakage rate.

We are unaware of SCE frequencies being reported for dyskeratosis congenita. Of the chromosome breakage syndromes, only Bloom’s syndrome has shown both increased breakage and SCE frequencies ranging up to 12 times normal (Chaganti et al., 1974). Normal SCE rates have been reported in Fanconi’s anaemia (Chaganti et al., 1974; Sperling et al., 1975; Latt et al., 1975; Hayashi and Schmid, 1975), xeroderma pigmentosum (Wolff et al., 1975), and ataxia telangiectasia (Galloway and Evans, 1975; Hook et al., 1975). All these disorders are characterized by high chromosome breakage rates.

Our patients offer additional evidence that SCE and chromosome breakage do not always correlate. Perhaps the increased SCE frequency in dyskeratosis congenita, in analogy to the chromosomal instability in the chromosome breakage syndromes, offers a clue to the predisposition of these patients to malignancies.

References


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