

Sister chromatid exchange in dyskeratosis congenita lymphocytes¹

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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 5.4 SCE per mitosis and 5 patients with Fanconi's anaemia averaged 7.6 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 tumours (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 broad spectrum antibiotics. There was no family history of consanguinity. Four patients were diagnosed as having Fanconi's anaemia on the basis of pancytopenia, *cafe-au-lait* spots, and increased chromosome breakage. 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 Freedlander (1974). Parallel cultures grown without BrdU were examined for chromosome breaks and other aberrations.

The dyskeratosis congenita patient had a mean of 12.2 SCE per mitosis based on the examination of 42 and 62 mitoses from 2 cultures set at a 6-week interval. The mean for the 5 Fanconi's anaemia patients was 7.6, while our normal controls averaged 5.4 (See Fig. and Table).

The mean SCE value in the dyskeratosis congenita patient represents at least a twofold increase over the control value. This increase is related to a population of mitoses with raised SCEs. In sampling (a), 26% and in sampling (b), 23% of the mitoses contained over 15 SCEs, whereas none of the controls had over 15 SCE per mitoses (Table). No evidence of bimodal frequency distribution was apparent in either of the dyskeratosis congenita cultures. By Wilcoxon rank sum test, the difference between SCEs in our patient and controls has been found significant at the $P = 0.06$.

Only 1 break and 1 dicentric were found in 200 mitoses grown without BrdU from the dyskeratosis congenita patient. The Fanconi's anaemia patient had 6 to 10 breaks per 100 mitoses, as well as 1 to 4 quadriradials. Breakage in normal controls was within the range of 0 to 2.5%.

According to Sirinavin and Trowbridge (1975) dyskeratosis congenita and Fanconi's anaemia can be distinguished through pedigrees and physical findings. Chromosomal analysis offers additional help. Fanconi's anaemia is characterized by breakage rates up to 50% (Schroeder *et al.*, 1964; Bloom *et al.*, 1966). Only Morrison (1974) has shown increased breakage in dyskeratosis congenita, while none of Sirinavin and Trowbridge's (1975) patients nor our

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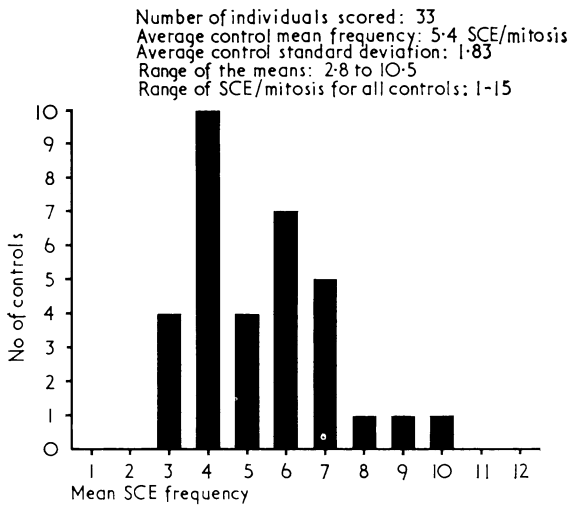


Fig.

Table SCE frequencies in dyskeratosis congenita and Fanconi's anaemia

	Patient	No. of cells scored	Mean SCE	Standard deviation	Range
Dyskeratosis congenita	*(a)	42	12.3	4.8	4-25
	(b)	64	12.1	3.9	4-22
	Mean:		12.2		
Fanconi's anaemia	(1)	2	7.5	4.9	4-11
	(2)	24	7.9	2.8	4-16
	(3)	24	6.5	2.4	3-13
	(4)	69	7.5	3.3	2-16
	(5)	6	8.7	4.6	4-15
	Mean:		7.6		
Grouped controls	33	780	5.4	1.9	1-15

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

patient 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.

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