tion. AJJ is a Lister Institute Research Fellow. The minisatellite probes are the subject of Patent Applications and commercial enquiries should be addressed to the Lister Institute of Preventive Medicine, Brockley Hill, Stanmore, Middlesex HA7 4JD, UK.

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Linkage analysis of neurofibromatosis

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SUMMARY Linkage analysis of neurofibromatosis was performed using genes on chromosomes 1, 8, 11, and 12. No linkage was found between NF and C-myc, AT 3, IGF-1, PTH, and gamma globin genes. Evidence for linkage was found between C-ets 1, on the long arm of chromosome 11 and NF in two families with a lod score of 1.88 at $\theta=0$. More families are being studied to confirm this linkage.

Neurofibromatosis (NF) is one of the common autosomal dominant neurological disorders with a frequency of approximately 1 in 3000. The disease is

mainly characterised by café au lait spots and neurofibromas. These patients have an unusually high frequency of malignancy compared to the normal population. The intriguing question is, what gene do they carry that predisposes them to malignancy? In order to localise the gene for NF, linkage analysis using DNA markers was performed.

Three multi-generation families shown in table 1 were used.

Oncogene C-myc, insulin like growth factor-1, antithrombin-3, parathyroid hormone, and gamma globin genes¹⁻⁵ were not linked to neurofibromatosis in our families. The lod scores are shown in table 2.

We found a positive lod score of 1.88 with oncogene C-ets 1⁶ in two informative families (no recombinants observed in six informative meioses). These data provide suggestive evidence that the NF

TABLE 1 Three multi-generation families used in linkage analysis.

Clinical presentation	No sampled	No affected	No of potentially informative meioses
Family 1 Mainly neurofibromas	20	9	17
Family 2 Café au lait spots and neurofibromas	37	10	14
Family 3 Café au lait spots and neurofibromas	6	3	3

TABLE 2 Lod scores.

Gene	Chromosome	No of informative families	No of informative meioses	0.00	0.05	0.1	0.2	0.3	0.4	$\hat{\theta}$	$\hat{Z}$
C-myc	8q24	3	3	0.84	-2.06	-1.48	-0.89	-0.53	-0.25	-0.50	0
IGF-1	12q22→q24.1	3	11	0.66	-0.78	-0.54	-0.47	-0.39	-0.20	-0.50	0
AT 3	1q23→q25	3	5	0.58	0.54	0.48	0.36	0.23	0.10	0.00	0.58
PTH	11p15.4→p15.1	3	14	0.55	-0.62	-0.31	-0.04	0.05	0.05	0.35	0.06
HbG1	11p15	2	14	—	-1.53	-0.74	-0.08	0.08	0.11	0.36	0.13
HbG2											
C-ets 1	11q23→q24	2	6	1.88	1.68	1.47	1.03	0.57	0.16	0.00	1.88

gene is linked to C-ets 1 on the long arm of chromosome 11 in these families. More families are being studied to confirm the linkage of NF to C-ets 1.

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Genetic linkage studies with neurofibromatosis: the question of heterogeneity

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SUMMARY Three new families are reported for standard gene linkage markers and classical peripheral neurofibromatosis (Von Reckling-

hausen disease). Additional data are summarised for the exclusion map. One family gives slight evidence of close linkage with the Gc locus on chromosome 4, raising again the question of possible genetic heterogeneity in NF.

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