blood samples from her relatives. The prevalence of the mutations in the *TIGR* gene was 4.0% (2/50 families), which was comparable to that reported in a previous study (Stone et al. 1997).

The present study has revealed that mutations in the *TIGR* gene are also responsible for familial POAG in Japan. The mutations in the third exon of the *TIGR* gene were found to be associated with ~4% of Japanese familial POAG patients. The prevalence of the mutations in the gene was comparable in Japanese patients and in the population previously studied. The mutated sites, however, were different from those reported in the previous study, and no common mutations were found. Therefore, the distribution of the mutated sites in the *TIGR* gene in Japanese POAG may be different from those in other races. Known mutated sites in the *TIGR*-gene disease alleles are at the 364th, 367th, 368th, 370th, and 437th amino acid residues. The apparent focus of the reported mutations—around the 367th amino acid residue—indicates that the amino acid change around this position may play a critical role in the pathogenesis of POAG. The TIGR-protein product is overexpressed with glucocorticoid stimulation and is thought to contribute to steroid-responsive intraocular-pressure increase, by the obstruction of aqueous outflow (Nguyen et al. 1993; Polansky et al. 1997). Further investigations of the *TIGR* gene will reveal more information about the pathogenesis of POAG.

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Childhood Cancer and Neural Tube Defects

To the Editor:

In the March 1997 issue of the *Journal,* Narod et al. (1997) concluded that cases of spina bifida and of abnormalities of the eye, ribs, and spine were more common in children with cancer than among population-based controls. In an invited editorial in the same issue, Friedman (1997) called for additional work to define more clearly the associations between congenital anomalies and cancer and to differentiate those associations that are spurious from those that are biologically important.

I wish to comment on the reported association between spina bifida and cancer, which was based on comparison of the relative frequency of specific types of anomalies in children with cancer who were diagnosed in Great Britain during the period 1971–86 with the corresponding relative frequency in liveborn children born in British Columbia during the period 1969–88. In addition to the differences in methods of ascertainment discussed by Narod et al. (1997), this comparison appears to be inappropriate, since the prevalence of neural tube defects at birth was markedly higher in the British Isles than in Canada, from the 1950s to the early 1980s (Little and Elwood 1992). This difference was apparent despite the decline in the prevalence of these defects at birth in the British Isles since the early 1970s. In Canada, there has been a persistent east-west gradient, with the prevalence at birth declining from the east toward the west.

In the study by Narod et al. (1997), when the 275 cases with an established genetic cause were excluded, the prevalence of neural tube defects at birth among children diagnosed with childhood cancer was 1.2 per 1,000 births. As noted by Narod et al., anencephalus is associated with a high rate of infant mortality, and most children with neural tube defects are likely to have had

spina bifida. In studies of births in Great Britain prior to 1979, the prevalence of spina bifida at birth was within the range of 1.5–4.1 per 1,000 births, and, in studies in the early 1980s, the prevalence was within the range of 0.7–1.9 per 1,000 births (Little and Elwood 1992). Some of these infants would have been stillborn. For example, in Northern Ireland during the period 1974–79, 15.5% of 569 cases of spina bifida or encephalacoele were stillborn (Little and Nevin 1989). In Glasgow and Liverpool during the period 1980–92, when fetuses from terminated pregnancies were excluded, 16% of 262 cases of spina bifida were recorded to have resulted in fetal deaths (EUROCAT Working Group 1995). Therefore, it appears that the proportion of cases of childhood cancer with neural tube defects is similar to what would be expected on the basis of data on the prevalence of these defects at birth, in Great Britain.

In the study by Narod et al. (1997), eight of the children with tumors of the brain or of the spinal cord were recorded as having spina bifida, compared with the 5.6 expected on the basis of the frequency of spina bifida among children with other types of cancer in Great Britain and with the 2.4 expected on the basis of the data for British Columbia. Again, the proportion of children with tumors of the brain or of the spinal cord who were recorded as having spina bifida (1.7 per 1,000 births) would appear to be within the range of prevalences at birth reported for Great Britain during the period in which the children included in the study by Narod et al. would have been born. Thus, the study by Narod et al. does not appear to support the hypothesis of a common maternal factor for brain tumors and spina bifida.

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Reply to Little

To the Editor:

My colleagues and I thank Dr. Little (1997 [in this issue]) for his important data. We saw an excess of neural tube defects in children with cancer, in the United Kingdom, compared with healthy controls from British Columbia. It is unclear to what extent the control group from British Columbia was comparable to the children from Britain, and our approach is inadequate when the baseline rates of disease differ for the two countries. Unlike the rates of other malformations, the rate of spina bifida was not significantly greater in children with solid tumors than in those with leukemia. We agree that our data do not allow us to conclude that there is an excess of cancer among children with neural tube defects.

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Lafora Progressive Myoclonus Epilepsy: Narrowing the Chromosome 6q24 Locus by Recombinations and Homozygosities

To the Editor:

Lafora disease (LD) is an autosomal recessive and rare but fatal epilepsy syndrome characterized by stimuli-sensitive myoclonus, absence and grand mal seizures, progressive intellectual and neurological deterioration, and periodic acid Schiff (PAS) stain–positive intracellular inclusion bodies. Eighty-four years after Gonzalo Lafora