region could lead to miscalculation of allele sizes and possible misdiagnosis.

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Mitotic errors in trisomy 21

Sir — In the paper by Antonarkais *et al.* (*Nature Genet.* **3**, 146–150; 1993), it seems that about 5% of trisomy 21 (Down syndrome) cases are due to mitotic errors, as deduced from segregation of DNA polymorphic markers. This analysis, however, cannot detect a substantial proportion of premeiotic mitotic errors (that is, parental gonadal mosaicism). Assuming that, at meiosis, the trisomic cells form one bivalent and one univalent (this configuration seems preferred according to Speed, R.M. *Hum. Genet.* **66**, 176–180; 1984) and considering the three possible random combinations, we can categorize the resulting disomic gametes in the way suggested by Antonarakis *et al.* (their Fig. 1). In this way 5/6 disomic gametes derived from trisomic germline cells are miscategorized as meiotic errors: 3/6 as meiosis I errors without crossover; 1/6 as meiosis I errors with crossover; and 1/6 as meiosis II errors. This potential misclassification could account for the significant excess of non-crossover events reported in Table 1 in Antonarakis *et al.*. Moreover, misclassification of 3/6 mitotic premeiotic errors as meiosis I errors could also account for the lower mean maternal age observed in this group versus the meiosis II errors group.

In short, the overall frequency of mitotic errors (premeiotic and postzygotic) in trisomy 21 is underestimated. Interphase cytogenetic analysis would probably clarify the problem of the frequency of trisomy 21 gonadal mosaicism in humans and its relevance to the incidence of Down syndrome.

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Discrepancy resolved

Sir — In last months issue of *Nature Genetics*, we reported on the *de novo* expansion of the CAG repeat in the Huntington's disease (HD) gene as the cause of sporadic cases representing new mutations in this disorder (Myers, R.H. *et al. Nature Genet.* 5, 168–173; 1993). Although most sporadic cases exhibited CAG repeat expansion, in one exceptional family the repeat length in the affected sporadic case was in the high normal range, and identical to that in two unaffected sibs carrying the same chromosome. We have learned recently that a cell line from a normal sib with the same chromosome was represented to us as deriving from the proband. Moreover, the correct cell line from the proband was assessed independently by Goldberg *et al.* (Goldberg, Y.P. *et al. Nature Genet.* 5, 174–179; 1993) who identified a repeat expansion relative to the normal sib. Consequently, this family does not represent an exception, but rather is consistent with the view that new mutations leading to HD involve expansion of the CAG repeat into the size range normally associated with the disorder.

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