undermethylated in the germ line. More recently Erickson[5] has pointed out that several genes are highly methylated in sperm DNA, a finding which does not support the idea that in these cases a lack of methylation is the cause of the reduced CG suppression.

There are two ways to explain a lack of CG suppression in a particular region. As suggested by Max and explained above this would result if the CGs in that region are not methylated. It would also result if methyl CGs are not deaminated in that region and we have recently presented evidence to support this mechanism[6]. An analysis of various regions of vertebrate genomes demonstrates that CG dinucleotides occur at the expected frequency wherever G+C rich regions occur. (G+C rich regions having a composition of greater than 60% G+C.) The increased stability of the double helix in G+C rich regions will mitigate against the deamination reaction which requires the DNA to be single stranded. Even if heavily methylated, we would predict that CG dinucleotides will be maintained in these very G+C rich regions of DNA and that is what is found.

Deamination of methylcytosine in CG dinucleotides will lead to a decrease in the G+C content of DNA[3] but where these dinucleotides are maintained no change in base composition would be expected. A+T rich regions should remain A+T rich and there is no relevant reason why they should become G+C rich. This implies that those regions which fail to show a suppression of CG dinucleotides have been rich in G+C for a very long time and this may be why they are resistant to deamination. Other events may lead G+C rich regions to mutate to a more average composition which may then allow methylcytosine deamination to occur, thereby accelerating the change to an A+T rich composition. Where a high G+C content is maintained or arises either by chance or because of selection it shows little CG suppression.

CG dinucleotides are highly suppressed in regions of the vertebrate genome containing less than 40% G+C and such regions have little remaining scope to exhibit further base changes as a result of methylcytosine deamination. Such mutations are expected to occur only in regions of intermediate composition where a number of methyl CG dinucleotides still remain in an environment conducive to deamination.

We do not argue against the proposal that lack of cytosine methylation may be the cause of the lack of CG suppression in some cases and indeed Cooper *et al.*[7] have shown that short stretches of unmethylated DNA are present in the vertebrate genome. Nonetheless, we are of the opinion that a simple failure to deaminate methylcytosine in G+C rich regions may be a more general explanation for the absence of CG suppression in G+C rich regions of the vertebrate genome.

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Germ-line gene therapy a misnomer?

SIR — I would like to add to the medical and deontological reservations raised by M.E. Pembrey[1] regarding gene therapy. Two modes of gene therapy are considered: one involving intervention at the level of somatic cells on their immediate precursors (such as bone marrow cells[2]) and the second, modification of the germ line level[3]. The commonly implied advantage of germ-line gene therapy is the the correction of the defect could be made transmissible to further generations.

But, at present, there is no way to control or target the site of gene insertions, which seem to occur at random[4]. Consequently, deficient and inserted loci will, in most cases, lie on different chromosomes (or be separated by a large distance on the same chromosome) and so will segregate more or less independently. Thus, given a homozygous recessive defect, and as long as only a single chromosome can be the target for insertion, descendants will have only a 50% chance of inheriting the correcting locus along with the defective locus. That is, the so-called germ-line gene therapy will effectively control a genetic disease in the corrected individual, but the defective locus and potential for disease will still be transmitted to the progeny. Evidence is also accumulating demonstrating that this randomness of insertion bears a significant mutagenic potential[5]. Multiple independent insertions of the correcting locus would thus not be a solution to this problem, since although increasing the likelihood that offspring receive a "correcting" locus, they would also increase the likelihood of insertional mutagenesis.

Thus, at present, germ-line gene therapy of an individual would not eliminate the necessity to reiterate this therapy in his offspring, since diagnosis for the absence of the correcting gene in the offspring would have to be delayed to the embryo stage with present techniques — too late to apply germ-line gene therapy *de novo*. Arguments for germ-line intervention should thus take into consideration that the benefits are mostly restricted to one generation only. The possibility of insertional mutagenesis, in fact, seems to suggest that germ-line therapy is more likely to increase future genetic problems than it is to cure them.

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Three-dimensional chemical waves in metals

SIR— The review article by Winfree and Strogatz[1] mentions rotating spiral waves in a modified Belousov[2] chemical reagent, in a monolayer of *Dictyostelium discoideum* cells responding to a pulse of cyclic adenosine monophosphate[3] and in successive photographs of the retina of a chicken[4].

The photograph of a scroll wave in modified[5] Belousov-Zhabotinsky reagent is reminiscent of the mechanism by which dislocations may multiply in metals first suggested by Frank and Read[6]. In this model, a line representing a dislocation in a three-dimensional dislocation network in a crystal is successively deformed by a shear stress so as to produce ring dislocations. An unlimited amount of slip my be produced.

The stress required for this process is of the order of Gb/l where G is the shear modulus, b is the Burgers vector, and l is the length of the line. Typically, for a metal $G = 500$ GPa, $b = 0.25$ nm and $l = 100$ μm. This gives a stress of the order of 10^{-6} pascals and an energy of the order of 10^{-10} joules per metre of dislocation line. This corresponds to an energy of approximately 10 eV per atom along the dislocation line.

The value of 10eV is in good agreement with the energy of a typical chemical bond and thus the initial dislocation line may be seen as an organizing centre for the generation of ring dislocations which are analogous to chemical waves travelling through the medium.

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