

Telomere loss and cancer

SIR — Hastie *et al.* speculated¹ that shortening of chromosome telomeres due to physiological attrition (ageing) may generate tumours. But if the loss or deletion of telomeric sequences due to senescence (or high tissue turnover) were the main factor in tumorigenesis, one would expect a low incidence of tumours in tissues such as those of the central nervous system or bone marrow stroma² normally unable to undergo regeneration. Determination of telomere length in such tissues would represent the only proper falsification context for the above speculation.

Tumours of the central nervous system, whose cells are unable to regenerate, are relatively frequent (overall incidence in the United States being 14,000 cases per year³). Moreover, most cerebral and spinal cord neoplasms are found in children, which argues against the significance of both ageing and cellular turnover in the loss of telomeric sequences and consequent cancer.

It is, therefore, not surprising (at least for a clinician) that the authors of a paper⁴ from the same research centre as that of Hastie *et al.*, suggest that, in mice, telomere size is unaffected by repeated somatic division (cellular turnover) and animal's lifespan (ageing). It appears that, in this case, clinical experience would predict that telomere shortening is unlikely significantly to influence carcinogenesis in men and mice.

Notwithstanding the above criticisms, Hastie *et al.* made an important observation that telomere lengths reflect fairly consistently the past mitotic dynamics of the somatic tissues. This may eventually be of practical help, particularly in the study of subpopulations of haemopoietic stem cells and progenitors. Also, telomere lengths may reflect generation time and cellular dynamics of leukaemic clonogenic cells, thus aiding in the design of therapeutic strategy for individual patients.

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HASTIE *ET AL.* REPLY — We hypothesized that telomere loss may play a part in generating the genetic instability observed in a particular cancer, colorectal carcinoma¹. Jankovic *et al.* attribute to us more far-reaching conclusions than we made from our study. Of course, if telomere length were the main and only factor in generating neoplasia (an improbable suggestion) we might expect a low incidence of tumours in tissues such as those of the central nervous system that have low cellular turnover. We agree that if

telomere reduction does indeed reflect cell turnover, this phenomenon is unlikely to play a role in paediatric tumours and those of the central nervous system. But the fact remains that after lung cancer, the most common cause of death due to cancer in the United Kingdom and the United States remains colorectal cancer; central nervous system tumours are extremely rare by comparison.

We also showed that mouse telomeres are very long even in old animals and concluded that telomere reduction is unlikely to play a role in cancer or ageing in mice⁵. If, as we predict, telomere loss amounts to just four base pairs per somatic cell division, we would not expect to see any measurable reduction in mouse telomeres over a two-year life span, even if such a reduction were occurring.

We feel Jankovic *et al.* are on weak footing when they surmise that if telomere loss does not play a role in carcinogenesis in mice, it is unlikely to play such a role in man. Also, at present we cannot rule out dramatic

telomere loss in mouse cancers.

We feel our most original and interesting conclusion was that telomere loss may reflect the number of cell divisions in a tissue's history, constituting a type of clock. We are now testing this idea by studying telomere length in a wide range of human tissues, including muscle and brain where cellular turnover is low.

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- Hastie, N.D., Dempster, M., Dunlop, M.G., Thompson, A.M., Green, D.K. & Allshire, R.C. *Nature* **346**, 866–868 (1990).
- Ben-Ishay, Z. *et al. Med. Oncol. Tumor Pharmacother.* **7**, 55–59 (1990).
- DeVita, V.T. Jr., Hellman, S. & Rosenberg, S.A. *Cancer* (2nd edn) 1437–1510 (Lippincott, London, 1985).
- Kipling, D. & Cooke, H.J. *Nature* **347**, 400–402 (1990).
- Starling, J.A. *et al. Nucleic Acids Res.* **18**, 6881–6888 (1990).

Measuring air from polar vortices

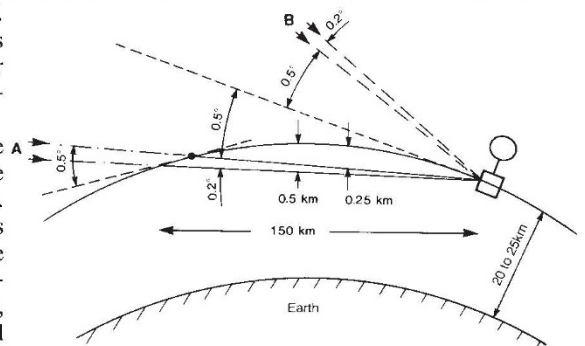
SIR—Tuck has suggested¹ that stratospheric air from within the Arctic winter vortex may be transported into mid-latitudes in cells as small as 200 km horizontally and 3 km vertically. Because such cells contain large amounts of reactive chlorine², they may be important in the ozone depletion in the Northern Hemisphere winter identified by the report of the International Ozone Trends Panel³. Cells of ex-vortex air are also characterized by a reduction in N₂O (ref. 1) and probably in other gases whose source is also in the lower atmosphere (methane, chlorofluorocarbons).

Unfortunately, such cells are barely observable by remote sensors on satellites or balloons. Because limb-sounding sensors observe horizontally through the curved atmosphere, their horizontal resolution is 400 km, which is too large. Their potential vertical resolution is 2–3 km, but, except in the case of a balloon-borne sensor, in practice this is degraded by the field of view to 5–6 km, again too large. Many constituents decrease in concentration below 20 or 25 km, which further degrades the vertical resolution. Conversely, the resolution of measurements of the source gases is improved because their concentration increases below 25 km.

Because limb-sounders are usually specified for maximum sensitivity, they observe the strongest absorption or emission lines. In the infrared, these frequently saturate at the

line centres below 25 km, broadening the atmospheric response function and further degrading the vertical resolution. Below 25 km, the sensitivity and resolution of mid-infrared emission sensors is further reduced because of the low temperature.

In designing limb-sounders to observe these cells, both horizontal and vertical resolution must be improved. The horizontal width of the field of view at the tangent point



A pseudo-*in situ* balloon-borne limb sounder for high-resolution measurements of ex-vortex air would subtract signals emitted from weak infrared or microwave lines at small angles equally above and below the horizontal (A–B). Provided the atmosphere were horizontally uniform for distances of 150 km, the dashed and dot-dashed beams would contribute equal signals; the difference signal would originate within the 0.5 km vertically below the balloon and within 150 km horizontally.

should be less than 200 km; to achieve a vertical resolution better than 3.5 km, the vertical field of view at the tangent point should be less than 1 km. At the expense of signal-to-noise ratio, the vertical resolution could be further improved by oversampling in the vertical plane and subtracting signals in ad-