

is premature to attribute it entirely to the Chernobyl accident.

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SIR — V. S. Kazakov *et al.* and K. Baverstock *et al.* (*Nature* 359, 21–22; 1992) report a sudden, unexpectedly large increase in the number of thyroid cancer cases in children in some areas of Belarus, starting about four years after the Chernobyl accident — considerably earlier than expected. The data provided in these reports are limited and preliminary in that they do not allow one to state whether the suggested increase in thyroid cancer cases is unequivocally attributable to radiation exposure. Many questions need to be answered, including the following.

Information on radiation dose (not reported by either Kazakov *et al.* or Baverstock *et al.*) is critical in determining the relationship to radiation exposure. In the case of children in Belarus, the focus of interest is the internal radiation exposure from radioactive iodine. However, several dosimetric problems remain. For example, it is difficult to examine the relative contribution of <sup>131</sup>I and other short-lived radioiodines in exposed individuals. Also, uptake and elimination rates of iodine will be affected by iodine deficiency, which may occur in children from some of the affected areas, further complicating dose estimation. Efforts are now being undertaken by various groups to reconstruct the radiation doses of exposed individuals, including thyroid doses in children in the affected areas. It would be worthwhile to determine the thyroid cancer incidence in those children in Belarus for whom reliable thyroid doses are available.

Another question is whether the increased number of thyroid cancer cases reported in recent years really represents an increased incidence of this disease in a defined population. Efforts undertaken by expert pathologists to verify diagnoses is obviously an important first step in trying to answer this question. Detection of thyroid cancer is highly dependent on the intensity of medical screening because many of these cancers are clinically dormant and progress very slowly. Any attempt to estimate the true incidence of thyroid cancer after Chernobyl should carefully consider the potential effect of the increased general concern over thyroid cancer and the introduction of widespread medical screening for this cancer in the affected areas. The intensity of case ascertainment may also vary in different areas. It

is important to undertake a systematic ascertainment of cases, including thyroid tumours and other thyroid disorders. Kazakov *et al.* and Baverstock *et al.* seem to downplay the role of improved case ascertainment as the explanation for the increased number of recorded cases, but we do not know how many of the recorded cases were detected as a result of the medical screening and how many cases clinically manifested themselves. Finally, and most important, how will these numbers be expressed in terms of incidence rates in exposed and non-exposed populations?

We fully agree with Baverstock *et al.* that “understanding the consequences of Chernobyl will provide an important basis for preventive action in future”. However, we would add that studies of these consequences must be carefully pursued and based on scientific methodologies. One should not be overly alarmed, nor feel unjustifiably secure, on the basis of evidence that is not definitive. As in the past, our foundation is prepared to make its expertise, obtained in our long years of research on atomic-bomb survivors, available to assist in resolving some of the problems we have identified above.

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## DNA fingerprints of cell lines

SIR — Few will disagree with the view expressed by researchers at the European Collection of Animal Cell Cultures (ECACC) that DNA profiling will transform authentication of cell cultures<sup>1</sup>. But when? For the technique to fulfill its undoubted potential requires persuading originating investigators to publish DNA profiles of cell lines — itself contingent on standardization of probes and methods. Neither prospect is in sight. Hitherto, DNA profiling has been only fully effective in revealing those (presumably infrequent) contaminations occurring after accession of cell lines by cell banks themselves.

Although original cell lines will have highly specific DNA profiles, in the absence of any reference standards, these cannot be used *per se* to exclude contamination by unknowns. By contrast, isozyme typing (for quick and inexpensive species confirmation), cytogenetics (derived by the ECACC) or immunophenotyping (which they do not perform) are able to yield early clues to possible contamination. In this cell bank

we have been able to detect contaminated, wrongly identified or incorrectly characterized cell lines using some or all of these methods together with DNA profiling. Given the wide variety of cell lines held by large facilities, no single method could cope with the almost unlimited possibilities for contamination — a point emphasized by the US Foods and Drugs Administration in its guidelines for authenticating cell lines.

The ECACC's conclusion that cytogenetics lacks the capacity to provide “new approaches” for characterizing cell lines is open to question. The development of chromosome “painting” by fluorescent *in situ* hybridization allows for the first time the unambiguous identification of marker chromosomes and small unbalanced translocations (notorious bugbears of permanent cell lines) — and is potentially amenable to a far higher degree of automation than possible hitherto.

It remains to be seen whether the present domination by commercial interests of probe methodologies will promote or hinder standardization. Until then cell banks would be wise to hold on to their microscopes (and their DNA samples).

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STACEY *ET AL.* REPLY — MacLeod's comments, although valid in some circumstances, can only serve to mislead if, as in our article<sup>1</sup>, the problem of identity testing the increasing diversity of cell cultures is to be addressed. Our conclusions were drawn from experience in a service department handling 1,100 different cell lines from at least 44 different animal species, which represents a wider range than that experienced in many laboratories. Few, if any, publicly funded culture collections have the necessary resources to carry out diverse and time-consuming cytogenetic techniques such as chromosome painting, fluorescence-activated chromosome sorting or analysis of interphase nuclei.

It is our experience that scientists need their cultures “this week” and although it is necessary to be pragmatic to meet this demand, it does not have to be at the expense of quality. We cannot attempt to duplicate depositors' research analyses; nevertheless we can maintain each culture stably and use a combination of isoenzyme analysis and DNA fingerprinting to identify cultures and exclude cross-contamination. Additional techniques (for example immunological analysis) are used when they are considered to be essential<sup>2</sup>. Therefore the