cence literature. The products of a single mitosis may differ widely in replicative lifespan[9]. Random genetic damage certainly fits better with that picture than does a telomere clock. Indefinite division, which is characteristic of established cell lines, does not mean that cells are not dying; it means that replication in a population outstrips death.

It is flatly incorrect to state that any damage other than telomere erosion is insufficient to halt cell division in vitro because the overt expression of the *ras* gene[10] and the inhibition of phosphatidyl kinase[11] each induce the senescent phenotype almost immediately.

The rationalization invoked to dismiss the failure of Cristofalo et al. to observe an inverse correlation between human donor age and skin fibroblast lifespan[12] is logically bizarre. Kipling et al. state that there is no significant decline in division potential in vitro of these cells with human age because there is minimal turnover in vivo. Yet Cristofalo et al. used cells from the same sites that were used by those who did report an inverse relation[3,4].

In the most frequently quoted of the latter[13], most of the specimens came from cadavers, and those that came from living persons showed no age-related decrease in replicative lifespan (George Martin, personal communication). This may be because replicative life span of a primary culture is due to the selective outgrowth of the longest surviving clones[6], which are rare and therefore easily lost in cadavers. In any case, lymphocyte stem cells certainly have a high turnover rate in the body, yet mass cultures fail to exhibit the inverse life span with donor age[14]. If neither fibroblasts nor lymphocytes *reliably* demonstrate the relationship, then what cell type does?

The claim of erosion of telomeres with human age, or as a function of cell divisions in vivo, also fails critical analysis. The foundation paper for this claim failed to show any telomere erosion in skin fibroblasts beyond 20 years of donor age (ref. 15, Fig. 1C). Human leukocytes had no telomere shortening for 20 years beyond the donor age of 4 years[16], yet their bone marrow precursors are continuously replenishing the short-lived supply. A more recent report finds no significant difference whatever in telomere length of leukocytes from young and old donors[17].

Are fibroblasts and leukocytes to be considered exceptions to the telomere clock hypothesis and, if so, exceptions to what cells?

The possibility that the life-extending effect of telomerase transfection on foreskin fibroblasts[18] is an artifact cannot be waved away in the light of the recent finding that primary culture of chicken embryo fibroblasts results in a severe downregulation of telomerase activity[19]. Were this happening in the BJ foreskin fibroblasts used for telomerase transfection, it would cause an artifactual requirement for telomerase that is satisfied by transfecting the gene[18].

That of course does not explain the extended lifespan of the cells, but plausible genetic explanations for that are not hard to imagine[4]. In any case, there is no evidence that telomere length maintenance extends the life span of cells other than those in primary cultures suffering from premature stochastic decay. An artifact for an artifact?

The recent claims of normalcy of the telomere-extended cells[20,21] bypass the stringent test for true normality that was first validated in skin fibroblasts from patients bearing internal cancers or genetically predisposed to them[4]. These cells, which behave normally except for an extended life span, have their preneoplastic nature unmasked by progressing neoplastically after treatment with mutagens, carcinogens, oncogenes, or long-term crowding[4]. Such stringent testing should certainly be applied before therapeutic intervention with the cells is approved for commercial use.

I suggest the cell senescence workers acknowledge findings that challenge their basic preconceptions. Such prudence would spare them the ad hoc backtracking they are forced to make, as in their last paragraph, that is, that not every cell shows telomere dependence, nor does every animal. Instead of plunging head-on in their preset course, they would do well to heed the advice of that sage of modern science, Alfred North Whitehead, namely, "An unflinching determination to take the whole evidence into account is the only method of preservation against the fluctuating extremes of fashionable opinion."[22]

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Food safety regulations

To the editor:

Henry Miller is correct in stating that agricultural biotechnology is delivering important benefits to the world's consumers and farmers (*Nat. Biotechnol.* **17**, 113, 1999). However, he ignores legitimate public interest and community needs when he argues that health, safety and environmental regulations are a "gratuitous" entry barrier in the biotechnology industry. Prudent regulations protect the public, secure public confidence in the food supply, and are a necessary cost of doing business. One only needs to look to Europe, as Miller has in previous columns, to observe the devastating effect on consumers caused by the erosion of trust in food safety regulators.

In the coming years, many companies will offer numerous beneficial biotechnology products both here and abroad. The regulatory reviews that these products will receive will give consumers confidence that these products of this new technology are safe as any foods we eat.

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Errata

In "This Month in Nature Biotechnology" (*Nat. Biotechnol*. **17**, 214, March 1999), a brief describing a research article on directed DNA evolution of thymidine kinase incorrectly stated that the viral form of the enzyme has lower substrate affinity than the human form. The viral form actually has lower substrate specificity.

Several reference errors occurred in a recent commentary by Richard C. Strohman (*Nat. Biotechnol*. **17**, 112, February 1999). In the text (para. 4), ref. 8 should be ref. 9; (para. 6) ref. 4 should be ref. 9; (final para.) refs 9–12 should be refs 10–13, respectively. Changes to the listed references 2 and 8, and an additional ref. 13 are printed below:

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In the February 1999 issue of *Nature Biotechnology*, a chart listing recent IPOs gave the incorrect location for Centaur Pharmaceuticals. Centaur Pharmaceuticals is based in Sunnyvale, CA, and is not affiliated with Centaur, Inc. of Overland Park, KS.