Cell contamination leads to inaccurate data: we must take action now

Sir— In 1981, Nelson-Rees *et al.* found that many cell lines had been unwittingly switched or cross-contaminated with HeLa cells[1]. Despite that warning, the number of published cases of cross-contamination is still increasing. Reference culture collections use techniques including DNA fingerprinting to authenticate their cell stocks[2–4] and continue to discover HeLa contamination[2,5]. In such cases, the only remaining characteristic of the original cultures is their name!

Misrepresentation of such cultures is perpetuated in scientific publications where the original designation is retained, including several HeLa derivatives of established value as reference cells, for example Hep2c, INT407 and KB — used respectively in virology, bacterial studies and cancer research[5].

The American Type Culture Collection (ATCC) recently found 15 cases that were not authentic among newly acquired cell lines (see http://www.atcc.org). Furthermore, a recent survey of 252 human tumour cell lines, performed by the German Collection of Microorganisms and Cell Cultures (DSMZ), identified 45 (18%) that had been cross-contaminated by their originators[6].

It is high time that the true origins of 'cross-contaminated' cultures are acknowledged, for transparency and to raise awareness amongst those new to cell culture. Action at several levels is required.

We recommend clear identification of cross-contaminated cultures in catalogue entries of culture collections. Thus, we propose that HeLa-contaminated cultures should carry the appendage '(HeLa)' in addition to the official cell name.

Resource centres and scientific organizations (such as the World Health Organisation international cell banks) should collaborate to authenticate cell stocks and ensure unrestricted access for research.

When new cell lines are established, representative samples of the original tissue, cells or DNA should be archived by originators for later authentication of cell stocks.

Authentication of new cell lines should be a prerequisite for publication. We strongly recommend that this should be by submission to a culture collection (not necessarily for immediate release to other investigators). This protects the intellectual investment of the originator and is a prerequisite for certain patents.

Cell lines should be disseminated only if they are from authenticated sources, such as bona fide culture collections; recipients should refer to guidelines on best practice in cell culture, such as those produced by the UK Co-ordinating Committee on Cancer Research and the US Food and Drug Administration[7,8].

Proper documentation must accompany a cell line being transferred between laboratories, including a description of the cell line, its origin and provenance, confirmation of authenticity and freedom from mycoplasma, and biohazard information.

Such precautions could save months or years of wasted work. Those using cell culture in research and development should remember a phrase coined in information technology: "garbage in, garbage out".

G. N. Stacey
National Institute for Biological Standards and Control, Blanche Lane, South Mimms, Herts EN6 3QG, UK

Other signatories of this letter:
J. R. W. Masters *Institute of Urology, University College London, 67 Riding House Street, London W1P 7PN, UK*
R. J. Hay *American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209, USA*
H. G. Drexler, R. A. F. MacLeod *German Collection of Microorganisms and Cell Cultures, Mascheroderweg 1b, 38124 Braunschweig, Germany*
R. I. Freshney *CRC Department of Medical Oncology, University of Glasgow, Garscube Estate, Bearsden, Glasgow G61 1BD, UK*

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Mitchell saw the new vista, if not the details

Sir— For a researcher in the area of bioenergetics, like myself, it was a delight to read Leslie Orgel's Millennium Essay[1]. Peter Mitchell's formulation in 1961 of the chemiosmotic theory as an alternative to the covalent intermediate opened a completely new vista in the field.

But Mitchell never suggested that the electron-transfer complexes in respiration and photosynthesis function as proton pumps; in fact, he was an ardent opponent of the idea of redox-linked proton pumps. For example, after Wikström reported[2] that cytochrome oxidase is a proton pump, Mitchell wrote an article called "Cytochrome *c* oxidase is not a proton pump"[3]. Mitchell's idea of how the proton gradient across the membrane is created was the 'redox loop'. According to this concept, a hydrogen atom is first transferred from one side of the membrane to the other, where it is split into a proton and an electron; the electron is then transported back across the membrane, leaving the proton behind. The difficulty with this clever mechanism is that it can only have a H^+/e^- stoichiometry of -1, which would mean that about half of the energy available from the electron-transfer reactions would be wasted.

The Royal Swedish Academy of Sciences awarded Peter Mitchell the Nobel Prize for Chemistry in 1978, on the recommendation of its Nobel Committee for Chemistry, of which I happened to be chairman at the time. The committee was well aware of the fact that Mitchell was wrong about how the proton gradient is created (proton pumps rather than redox loops) and how it is utilized to make ATP (conformational coupling rather than mass action). This is why the academy's citation read rather vaguely "for the contribution to the understanding of energy transfer through the formulation of the chemiosmotic theory".

As Mitchell was right only on the phenomenological and not on the mechanistic level, one could argue that he should have been given the Nobel Prize for Physiology or Medicine instead. As one of my teachers used to say: "Physiology is that part of biochemistry which we do not yet understand".

Bo G. Malmström
Department of Chemistry (Biochemistry and Biophysics), Göteborg University, PO Box 462, SE-405 30 Göteborg, Sweden

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Give credit where it's due (not to me, this time)

Sir— In his interesting review of Stan Prusiner's *Prion Biology and Diseases*[1], Colin Masters inadvertently gave me credit for showing "that accessory chaperones… may facilitate the conversion of a normal host-cell protein into a pathogen". Although I can take credit for discovering that [URE3] and [PSI] are prions of yeast, the credit for discovering the role of chaperones in this phenomenon goes to Yury Chernoff and colleagues[2–4].

Any chagrin I may feel at being inappropriately credited is measurably mitigated by the knowledge that there will inevitably be occasions when I will be 'unintentionally' ignored.

Reed B. Wickner
Laboratory of Biochemistry and Genetics, NIDDK, National Institutes of Health, Bethesda, Maryland 20892-0830, USA

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