Citation Classics – Amusing sidelights

Prof Guido Pontecorvo (Ponte), the eminent geneticist who was a Raman Professor at the Indian Academy of Sciences, is a man of great sense of humour and . . . of heart.

In a letter to me he wrote: 'I have just come across your most interesting article on "The quality of scientific journals published in India – some random thoughts" (Curr. Sci., 1992, 63, 529–534). I share 99% of your random thoughts. On one point (SCI and Citation Classic) you might be amused about the enclosed reprint [reproduced below] and particularly my last para. I also enclose an amusing letter to Nature [reproduced below] by a man whom I do not know. I entirely agree with the reaction of his 24 young scientists. My paper required no thinking and only about a week of tests: I consider it a trivial contribution, though it has had very wide appreciation'.

— Editor

Fusing cultured mammalian cells with polyethylene glycol*

Guido Pontecorvo

After the pioneer work by G. Barski, S. Sorieul, and Boris Ephrussi in the early 1960s, cultures of 'hybrid' somatic cells originated from fusion of cells of different species or tissues became extensively used for research in cell biology and genetics. The low rate of spontaneous fusion was overcome dramatically in 1965 by treating the cells to be fused with inactivated Sendai virus[1]. A great expansion of the work occurred after M. C. Weiss and H. Green's[2] demonstration that man/mouse hybrid somatic cells could be used very effectively for assigning human genes to each chromosome.

However, inactivated Sendai virus has several disadvantages as a 'fusogen', including its variability and cost. Thus, prior to 1975 attempts at replacing it by chemical treatment were made but had only limited success.

In 1974 I was working at the Imperial Cancer Research Fund in London on mammalian, including human, somatic cell hybrids. The aim was to apply to man the type of genetic analysis that bypasses sexual reproduction developed in the 1950s in my laboratory at the University of Glasgow. For cell fusion I was using *faute de mieux* inactivated Sendai virus. Having oscillated all my life between research on plants and animals, I stumbled on a botanical paper from O. L. Gamborg's laboratory[3]. It showed that plant protoplasts could be fused very efficiently by brief treatment with polyethylene glycol (PEG). Clearly this treatment was worth testing on mammalian cells. As I had all the required techniques in operation, I carried out the test, admittedly with considerable reluctance. It took a few days and very little work to find that PEG worked wonderfully on all combinations of cells tested. These included fibroblasts of man, mouse, or hamster and human lymphocytes. The hybrid cells so produced were capable of prolonged multiplication, a point not yet verified for the plant protoplasts in the original work.

In the naive belief that my finding should be made available for immediate use by all those working on mammalian hybrid cells, I submitted a very short note for prompt publication in the *Proceedings of the Royal Society*. Quite promptly it was rejected (a new experience for me!), and a referees's comment was: 'The present paper does not permit one to decide whether polyethylene glycol will prove to be no better than others that have been tried and rejected'. The specialist journal to which I then sent the note published it immediately.

As I expected, PEG quickly went into general use, among others in the extensive development of monoclonal antibodies. I am glad that **this intellectually trivial** transfer of a botanical technique to mammalian cells has been so useful[4].

This experience supports two prejudices of mine. One is that the wall between plant and animal research workers, very effective in the past, still is so, hopefully with exceptions at the level of molecular biology. The other is that technical papers are more likely to end up as *Citation Classics* than papers proposing and testing new good ideas. Is there a tendency to shift the balance towards technology in the essential reciprocal interaction between it and science?

1. Harris, H. and Watkins, J. F., Hybrid cells derived from mouse and man artificial heterokaryons of mammalian cells from different species *Nature*, 1965, **205**, 640–664 (Cited 500 times).
2. Weiss, M. C. and Green, H., Human–mouse hybrid cell lines containing partial complements of human chromosomes and functioning human genes *Proc Nat. Acad. Sci. USA*, 1967, **58**, 1104–1111. (Cited 470 times)
3. Kao, K. N. and Michayluk, M R, A method for high-frequency intergeneric fusion of plant protoplasts. *Planta*, 1974, **115**, 355–367. (Cited 390 times) [See also Kao, K N, Citation Classic (Barrett, J. T., comp) *Contemporary classics in plant, animal, and environmental sciences* Philadelphia ISI Press, 1986, p 118]
4. Bodmer, W, Somatic cell genetics and cancer *Cancer Surv.*, 1988, **7**, 239–250

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Recognizing good work*

Robert Brown

Few people in research would argue with Maddox[1] about a lot of published research being impenetrable to readers. The question is what to do about it. I spend a lot of my time teaching scientists how to publish 'reader-friendly' papers; one of the tools I use is to get them to review well-written papers, such as Watson and Crick's classic[2], slices of Einstein's theory of relativity[3] and so on.

The problem is that they know the work is good and they often adjust their opinions accordingly, so I recently did something different. I gave 24 scientists a copy of a paper by Pontecorvo[4] and asked them to read it and to analyse it according to what they thought was good or poor I gave them no other information about the paper or why I had chosen it, but they were given as much time as they wanted to come to a decision. (The main text is about a thousand words and most were done in 20 minutes.)

I then asked them to assemble along a line ranging from 'great' to 'rubbish' with the mid-point being the dividing line between when an editor should accept it or reject it. Only one person thought it should have been published, and most of the rest clustered near 'rubbish'. We had a good exchange of views from both sides but nobody elected to change camps.

Then I told them that I had chosen it because *Current Contents* had listed it as a citation classic (that is, a paper cited more than 400 times) and because it is a well written paper. They were surprised and confused, and found these facts difficult to accept.

My own interpretation (which I discussed with them at the time) is that their judgment was clouded by a mixture of inexperience and perfectionism. Perfectionism is an occupational hazard in science; scientists can easily get hooked into rejecting anything that has a demonstrable flaw. (Pontecorvo writes well, but the perfect paper has yet to be written, so my group could all find plausible – to them – grounds for rejection.)

I think this shows a weakness in the way in which we educate researchers, which is not confined to Australia. Too often, students are left to use osmosis to learn how to publish, but this is turning out a proportion (most?) who cannot recognize good papers when they see them. If they cannot do that, what are they going to model their own papers on?

My suggestion is that academics and anyone else involved in the management of research should spend time with students and less experienced scientists to analyse important papers in order to understand how the authors made their points, not just what the points were This should be an integral part of any higher education and my concern is that too few do it.

1 Maddox, J , *Nature*, 1983, **305**, 477–478
2 Watson, J. D. and Crick, F H , *Nature*, 1953, **171**, 737–738
3 Einstein, A , *Relativity: the special and general theory* (Authorised translation by Robert W Lawson)
4 Pontecorvo, G , *Somatic Cell Genetics*, 1975, **1**, 397–400.

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