

Pontecorvo G. Production of mammalian somatic cell hybrids by means of polyethylene glycol treatment. *Somat. Cell Genet.* 1:397-400, 1975.
[Imperial Cancer Research Fund, Lincoln's Inn Fields, London, England]

Polyethylene glycol (PEG), previously known to promote fusion between plant protoplasts, was tested in 1974 for fusion of mammalian somatic cells in culture. The results were very successful. PEG soon came into general use for the production of hybrid somatic cells. [The SCI® indicates that this paper has been cited in over 400 publications.]

Fusing Cultured Mammalian Cells with Polyethylene Glycol

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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's² 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 Uni-

versity 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 referee'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 & Watkins J F. Hybrid cells derived from mouse and man: artificial heterokaryons of mammalian cells from different species. *Nature* 205:640-6, 1965. (Cited 500 times.)
2. Weiss M C & Green H. Human-mouse hybrid cell lines containing partial complements of human chromosomes and functioning human genes. *Proc. Nat. Acad. Sci. USA* 58:1104-11, 1967. (Cited 470 times.)
3. Kao K N & Michayluk M R. A method for high-frequency intergeneric fusion of plant protoplasts. *Planta* 115:355-67, 1974. (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.* 7:239-50, 1988.