# Melodrama in research publication

The excitement of a rapidly advancing research field may be swamped by the confusion generated by the competition of researchers (and journals) to be the first in print.

MYOTONIC dystrophy is the most common form of muscular dystrophy, affecting one in 8,000 among the people in whom the incidence has been carefully studied. It is genetically determined, indeed dominantly so. But in contrast with many other inherited diseases, the symptoms of myotonic dystrophy may make their first appearance at any age between infancy and middle life.

There are also great variations in the severity of the disease, provoking questions such as why throwing a kind of genetic switch should have an uncertain outcome. More puzzling still is the observation that, in families carrying the aberrant gene, the symptoms of myotonic dystrophy should become more severe as generations succeed each other. Clinical geneticists have a word for that: "anticipation".

These curious features of myotonic dystrophy were unexplained until a few weeks ago, when this journal published a group of three letters describing attempts to identify and characterize the aberrant gene, known for some time to be located on human chromosome 19 (Harley *et al.*, Buxton *et al.* and Aslanidis *et al.* **355** 545, 547 and 548; 6 February 1992). All three reports came to the same conclusion: the myotonic dystrophy gene is closely linked with a region of DNA that is unstable in the sense that its length can differ between a person and his or her offspring.

At the same time, it became plain that the length of this variable region of DNA is positively correlated, in those with myotonic dystrophy, with the severity of the symptoms. So the question naturally arises of whether the aberrant gene differs from the normal simply in the length of this variable region. That, of course, complicates textbook notions of what aberrant genes are like: mutations consisting of the replacement of one nucleotide by another are the simplest, deletions of a group of three nucleotides (leading to the omission of a single amino acid from the product protein) the next simplest, and so on.

Aberrancy that consists of variability in the length of a piece of DNA is clearly in a different category, provoking several interesting questions. What does the variability of length consist of, and how does it arise? By what mechanism does the supposed product protein cause the symptoms of myotonic dystrophy? And so on.

For what it is worth (which may be a great deal), similar questions have previously arisen. Thus the origin of the X-linked genetic disease known as Kennedy's disease, a form of motoneuron disease, was shown last year (La Spada *et al.*, *Nature* **352**, 77; 1991) to consist of a doubling of the length of a stretch of the X-chromosome which normally consists of an average of 21 repeated nucleotide triplets CAG (for cytosine, adenine and guanine). The consequence is an extra stretch of repetitive glutamic acid in the structure of the cell-membrane receptor for androgen.

The appearance of extra nucleotide triplets ("expansion" is the new word) in the X-chromosome is also linked with the condition known as fragile X-chromosome (one of the commonest forms of genetic mental defect), but in that case the extra triplets consist of CGG (Oberlé *et al. Science* **252**, 1,097; 1991).

So there are good reasons why people should be excited by the discovery that myotonic dystrophy is somehow linked with the phenomenon of genetic expansion. And it is far from irrelevant that myotonic dystrophy is the most common cause of muscular dystrophy. But does this sense of excitement justify the melodrama lavished on the problem in the past few weeks by various journals (this one included)?

This is what happened. A week ago, *Science* told journalists that it was "lifting the embargo" on two articles concerned with myotonic dystrophy due to be published in its issue of 6 March, roughly two weeks later. Like other journals, *Science* looks askance at premature references to what it is about to publish. So why lift that constraint? Because, it emerged, *Cell* was due to publish last Friday (21 February) an even fuller account of the origin of myotonic dystrophy (Brook *et al. Cell* **68**, 799; 1972) than the two articles in *Science*'s pipeline. What neither journal knows is that *Nature* then decided not immediately to proceed with the publication of an article provisionally scheduled for 5 March so that its authors could pay attention to some perceptive comments on it.

Happenings of this kind, increasingly commonplace, are demeaning for all concerned — not just for authors, but for the journals in which they seek to publish. Everybody will agree that, in getting to grips with the understanding of an important disease, rapid publication is important; otherwise, physicians will not know what is going on. But how quick is rapid, or can a few days matter all that much? Especially when even the precipitating cause of last week's melodrama, Brook *et al.*, amounts to an excellent sharpening (but not a resolution of) the questions people have been asking?

The timing of the articles concerned is interesting. The three articles published in *Nature* on 6 February arrived last year on 2 December (Harley *et al.*), 4 December (Buxton *et al.*) and 19 December (Aslanidis *et al.*). The two articles due to appear in *Science* on 6 March were received on 21 January (Fu *et al.*) and 31 January (Mahadevan *et al.*) respectively. *Cell* says that the article by Brook *et al.* was received on 5 February, a mere 16 days before publication. At this rate, bystanders will suppose, delays for research articles on myotonic dystrophy will be down to zero a few weeks from now.

Each of these articles has (or will have) conveyed important news. The two articles to be published in *Science* show that the lengthening repetitive DNA is a replicating nucleotide triplet (in this case, CTG) and that the product of the myotonic dystrophy gene is probably a protein kinase, an enzyme likely to be involved in the tissue-specific regulation of cell activity. Brook *et al.* go further in an interesting way, by confirming what others have concluded and then disentangling the degree to which CTG triplets have expanded on the two separate chromosomes-19s in each cell nucleus.

The way in which these research articles tread on each others' heels must engender as much confusion as enlightenment in the minds of readers. Are we heading for a state of affairs in which what tends to be published is not the 'minimum publishable unit', a slice of salami, but a more substantial record of discovery with something novel tagged onto the end? Those concerned cannot be accused of duplicate publication, because the overlapping parts have not yet appeared in print.

Confusion is further aggravated by the overlapping membership of the author groups. Three of the signatories of Fu *et al.* are also signatories of both Mahadevan *et al.* (in *Science*) and Aslanidis *et al.* (in *Nature*), suggesting that apparently competing groups knew in advance of the overlapping parts. There is nothing wrong with that either, except the hint of a suspicion that people out to maximize the publicity attending discovery have taken to playing tricks on journals. There are two remedies: journals must watch out, especially for the quality of what they publish, and must be uniformly faster.

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