

Don't be misled by citation figures! (7)

Highly cited – ...but wrong!

In contrast to the previous articles of this column the following example relates to a true story. The reason is that one could hardly devise a better story to document more strikingly the fact that highly cited papers need not necessarily be correct.

The whole story took place roughly between 1986 and 1992. Before that time nobody knew exactly what it was in the genome that makes a man a man. And it is easy to imagine that there were many researchers keen to revel in the glory of being discoverer of the “male factor(s)”.

It had to be a gene for a transcription factor, so everybody presumed at that time. This factor should function as a kind of master switch in activating a cascade of further factors at a certain point in development - culminating in the production of a whole battery of proteins, which finally act in concert to create the complete set of male sexual organs. So much for the theory.



At that time it was also already known that the sex of us humans wasn't simply determined by the pure number of X-chromosomes, but rather it was clear that one or more “male master genes” had to be hidden somewhere on the Y-chromosome. Through much laborious groundwork, the region on the Y-chromosome containing the presumed master gene(s) was continuously narrowed down until one day in 1987 there seemed to be a final

breakthrough. David Page and his team from the MIT in Boston were apparently successful. They identified, in exactly the right region of the Y-chromosome, a gene encoding a protein that included a zinc finger domain, a typical motif for a certain family of DNA-binding transcription factors. They called it ZFY and, of course, Page *et al.* postulated this protein as constituting the “testis determining factor” (TDF) in their 1987 *Cell* paper.

However, shortly thereafter ZFY would prove not to be the TDF, after all. Only one year later a British team localised ZFY-homologue sequences exclusively on the autosomes of marsupials. This, however, was not to remain the only subsequent counter-argument. In 1990, a British group led by Robin Lovell-Badge and Peter Goodfellow found another TDF-candidate within the critical region of the Y-chromosome, SRY, standing for “sex-determining region Y”. Yet another year later the same team finally succeeded in transforming XX-mice into males by inserting the SRY-gene into their genomes.

That meant, that David Page *et al.* weren't exactly “wrong” but had definitely drawn the wrong conclusions from their “TDF-paper”. Nevertheless, it was among the most-cited articles of the late Nineteen-Eighties.

Of course, such “wrong” papers might often prove to be absolutely essential for the further progress in research; in which case they might even be highly cited for all the right and good reasons. However, that doesn't change the fact that what is highly cited, need not necessarily be correct.

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