

The long road to retraction

In the current issue of *Nature Medicine*, we are publishing the retraction of a paper by Kugler et al., titled “Regression of human metastatic renal cell carcinoma after vaccination with tumor cell–dendritic cell hybrids.” The study, published in March 2000, reported the results of a small clinical trial involving kidney metastatic cancer patients vaccinated with hybrid cells produced by the fusion of autologous tumor cells and mature allogeneic dendritic cells. The authors reported that of 17 patients, 4 treated with the hybrid vaccine completely rejected all metastatic tumor lesions, 1 presented a “mixed response,” and 2 had a tumor mass reduction of greater than 50%. A rather promising outcome for one of the first human applications of a hybrid cell vaccine.

The paper received enormous attention from both the research community and the mainstream press. But soon after it appeared, there were indications that all was not well. Some researchers voiced dissatisfaction with the scientific quality of the paper, expressed doubt that the protocol could actually succeed as hypothesized and criticized the limited information provided in the Methods section. In particular, experts in the field decried the incomplete characterization of the cell products the authors used for their therapy.

As in this case, editors are sometimes faced with rumors of bad science in their pages. But retracting a paper without a full investigation can unjustly destroy the authors’ credibility and careers. At the same time, delaying retraction lends a paper credibility that it may no longer deserve. In summer 2001, the ombudsman committee at Kugler’s institution, Göttingen University, began investigating the paper. The investigation was sparked by a scientist’s observation that a picture showing fused cells in another of Kugler’s papers had been directly downloaded from the Internet. We chose to wait for the committee’s full report before deciding on a course of action.

In November 2002, the committee completed the investigation and did not find scientific misconduct, but instead found negligence in the preparation of the manuscript and a failure to meet the requirements of good scientific practice.

A detailed look at the committee’s report exposed several deficiencies in the manuscript: inaccurate primary data in the publication, insufficient documentation of laboratory work and patient vaccination, and inclusion of patients that did not fulfill the criteria described in the Methods section. Perhaps the most significant fault was that the authors developed a pro-

tol for using dendritic cells that was not approved by the ethics committee.

Would a correction be more appropriate than a retraction? Should the paper be retracted by the authors or by the editors? How should editors decide whether to retract a paper? These were questions we posed as we tried to decide how to proceed.

Editors, publishers or funding agencies can decide to retract a paper, but the usual policy is that the authors themselves must retract. Only in extreme circumstances would an editor retract a paper without the agreement of the authors, although it is very rare that authors will voluntarily retract.

In this case, the large number of errors in the data published, together with the lack of ethical approval for the described trial, contrary to the authors’ statement in the paper (which alone would make the paper unacceptable to *Nature Medicine*), meant a retraction was necessary. We also felt strongly that the retraction had to be signed by all the authors, as coauthorship implies shared responsibility for the content of a paper.

It took several months to convince all the authors that a retraction was necessary, and several more months for all authors and editors to reach a compromise on the specific wording to accompany the retraction: “The authors unanimously wish to retract this paper because of several incorrect statements and erroneous presentation of primary data, results and conclusions.”

In the 3.5 years it has taken from publication of the paper to retraction, one lesson we have learned is that the community is perplexed by the editorial process. People have speculated that we were reluctant to withdraw the paper because we were afraid it would negatively influence the journal’s impact factor, or because we were embarrassed. Neither is true.

We feel responsible and compelled to make the biomedical community aware of errors of this nature published in our pages, and to make the public and patients knowledgeable on the promise (or lack thereof) of a cancer therapy. We are confident that we made the right decision and that we arrived at our conclusion in the fairest manner possible.

According to a recent analysis in the *Journal of the American Medical Association*, many retracted articles continue to be cited and, in most cases, treat the retracted article as if it were valid research. We now look to the community to place the results of the Kugler article in the right context. Whether their method is a good cancer strategy is an important question. It may be, but this paper should no longer be cited as evidence.