False hope

Reports show that the majority of research on cancer, taken as promising, end up having no practical application for being of unviable replication. Physicians believe that the reason for the unnumbered failures lies in the scientific publication system.

Every day we are bombarded with the results of the latest and promising studies on cancer. New medicines and therapies for the disease, tested in cells and animals from labs, suggest good effects in humans. The hopeful scenario, however, may be far from clinical application. Reports made by pharmaceutical industries show that most part of the results obtained in such research cannot be replicated.

For ten years the American biotechnology company Amgen has been repeating in its labs research published in scientific magazines on cancer considered unheard and promising. The objective is to take them to the clinical trials phase to, possibly, develop new medicines.

Recently, the company released a report showing that out of the 53 studies tested in the period, only six had their results replicated and confirmed. “Even knowing about the limitations of a pre-clinical trial, this result is shocking” says oncologist Glenn Begley, former head of cancer research at Amgen, who comments on the matter in the current issue of *Nature* magazine.

The replication of scientific studies in specialized publications is the most usual way to validate results of some research. This is fundamental to confirm the results of the original work.

Amgen’s experiments are not the only ones that expose the weaknesses of research on cancer. Last year, a study conducted by a German team from the pharmaceutical company Bayer showed that only 25 per cent of 47 pre-clinical researches on cancer published in high impact journals and tested by them could be reproduced.

Doing right for doing wrong

According to Begley, more than the lack of accuracy of the researchers, the cause for such failure would be a fault in the scientific publication system that puts excessive value on positive results in detriment of the negative ones and eventual errors.

“My opinion is that the principal problem is the pressures that exist within the system that drive investigators to generate and publish positive results”, defends the oncologist. “To obtain financing and promotions, researchers need publications that tell a ‘perfect history’. It’s tempting to publish only the data that matches with that, but there are no perfect histories in biology.”

To Begley, the mistakes and gaps are opportunities to new research and, because of that, they should also have space in scientific articles. The Brazilian oncologist physician Andre Sasse, who keeps a discussion group for studies on cancer based on evidences in the University of Campinas (Unicamp), agrees with this argument, but believes that the introduction of negative results in the publications is far from reality.

“Clinical studies with positive results have four times more chance to be published than the ones presenting negative results”, says. “With pre-clinical studies this must be even worse, because there is no obligation to record and report the mistakes.”

Sasse also highlights that this problem is not exclusive to oncology. “In all specialties there is a little optimism and overvalue to the pre-clinical trials results”, he claims. “This optimism is understandable because if the authors are not more sensitive to the potential of a determined drug, it ends up being discarded, even being promising.”

To the doctor, a standardization of the publication format for pre-clinical research would be a good solution to the issue. “A mechanism like this wouldn’t diminish the importance of potential substances and therapies and would improve the selection of researches that go to clinical trials”, explains.

What about the patients?

The publication of ‘embellished’ articles, which reinforces only the positive results of a research, not only delays the practical application of medicines, but directly damages the patients involved in the clinical trials as well.

Begley reports that some of the researches tested by Amgen were already being used as basis for clinical trials that, probably, didn’t had positive results for the patients. “I understand that the system encourages the publication in any ways, but we must keep focused on cancer research to make the lives of the patients better”, he defends.

A global analysis published in *Nature Reviews* magazine shows that, by lack of rigor in pre-clinical researches, the positive results in clinical trials of new drugs against cancer with humans dropped 10 per cent in the 2008-2010 period, if compared to the 2006-2007.

Currently, there’s no obligation of replication for a pre-clinical trial to proceed to the human testing phase. The approval depends only on the evaluation from the local ethic committees.

Although the potential risk involved in the lack of replication of a study, according to Sasse, it is increasingly more common to skip this step. “If the pre-clinical study shows itself promising, it is directly submitted to clinical study”, says. “Generally, the authors of the pre-clinical study themselves are the first to conduct clinical trials and publish the results, which create more acceptance in the scientific community”.

Independently of the regularization discussion, Begley insists in the rigor of scientific method and its meticulous description as a solution. “Although our report is troubling, I remain very optimistic that the scientific method is the only way to progress the field”, claims. “I hope that the researchers do the necessary changes to improve the reproducibility of experiments. After all, the patients are the ones to beneficiate from that.”

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