

Loss in translation: Where will the experimental data of your preclinical and clinical trials go?

Over the past half century, we have witnessed many major breakthroughs in basic neuroscience research that have enriched our scientific knowledge about our nervous systems and the pathology of neurological disorders, including acute and chronic pain. However, like most neurological diseases, chronic pain remains a major medical challenge due in part to the failure of successfully translating the findings of basic neuroscience and pain research into effective treatment or management of chronic pain. Translational research has recently been emphasized and promoted at multiple levels, from funding agencies (e.g., NIH), research institutes, and patient communities. Several compounds, including Lyrica (pregabalin), Neurontin (Gabapentin), and Cymbalta (duloxetine) have eventually been approved by the FDA for clinical uses to treat some forms of chronic pain. However, most translational research has failed to make it into the pipelines of pharmaceutical industries to benefit pain patients and our society. Thus, most chronic pain patients still suffer, opiate overuse remains unavoidable, and society remains helpless to their loved ones. Failure is unavoidable, but lessons must be learned from these failed translational experiments. The question is, where can researchers find out about failed experiments in order to learn the lessons from them? The fact is, most failed preclinical and clinical research is not disclosed to the research community, and the same failures can be repeated over and over again by different research groups. Therefore, it is extremely useful to have an online and open access resource where researchers can learn the important lessons from failed preclinical and clinical trials.

There are many reasons for the failures of developing new pain medicine for treating chronic pain patients. First, there are cultural and motivational differences in drug development among academic basic researchers, pharmaceutical industries, and government regulation agencies. For academic researchers, research activities are often driven by personal curiosity, government funding policy, and personal career establishment. Translation of a basic discovery to clinical treatment is often not a priority for most academic researchers, financially or otherwise. For government regulation agencies and industries, safety and legal concerns as well as stock holder concerns are among top priorities. There are new

compounds that have been prematurely pushed into clinical studies without thoroughly understanding of their basic mechanisms and their potential side effects. For example, many drug companies often target proteins or channels that are important for acute pain for the development of medicine for treating chronic pain. Consequently, many of these candidates failed to pass clinical tests. While there is useful information about the failed candidates in preclinical experiments (such as dogs or monkeys) and clinical trials, results of these experiments are usually locked in file cabinets rather than published or disclosed to open access domains for others to learn the lessons. Failure is the mother of future success, and we believe that it is equally important to publish some of these pre-clinical and clinical studies as it is to publish successes. This may help researchers design better compounds to improve their effectiveness and reduce their side effects.

Molecular Pain has been focusing on the cellular and molecular aspects of pain research since its launch in 2005. Over the past 12 years, we have published many high-impact research articles that elucidate important molecules underlying the development and maintenance of chronic pain. These molecules include receptors, ion channels, and intracellular signaling proteins, which are potentially targeted pharmacologically for treating chronic pain. The discovery of these therapeutic targets logistically would lead to preclinical and clinical studies. Therefore, *Molecular Pain* has now decided to expand our scope from mechanistic study to translational research. From 2017, we will create a new section called “Translational Studies,” which will publish both successful and failed preclinical and clinical studies. We have stressed earlier in this article the important reasons for having an online and open access domain for the failed preclinical and clinical trials. We hope that this new section will help researchers learn valuable lessons from failures and eventually become successful in their own translational research. Manuscripts can be in the form of rapid communication, short research article, or clinical case studies.

Min Zhuo and Jianguo Gu
Editors

