



Microchip developed at the Wyss Institute at Harvard, which simulates the functioning of human lungs

# With help from a computer

Brazilian and foreign researchers discuss ways to reduce animal testing

**Bruno de Pierro**

PUBLISHED IN MAY 2015

The search for alternatives to the use of animals in clinical trials and product testing has intensified in the last decade. One of the best examples of this trend is the Tox 21 Program (21<sup>st</sup> Century Toxicology), which was jointly created by two U.S. federal agencies: the National Institutes of Health (NIH) and the Environmental Protection Agency (EPA). Launched in 2008, Tox 21 uses mathematical and computer models in conjunction with genomics and robotics to study the structure and toxicity of a broad array of chemical compounds. The goal of the program is to understand the ways in which toxins affect organisms and to create methods that can be used to predict whether a potential pharmaceutical should be subject to clinical testing. By ruling out molecules that are dangerous to health, the animal testing of compounds previously classified as toxic can be avoided. In a two-year period, more than 10,000 substances were studied. The results are available in virtual form.

“The success of the next phases of the program will depend on a stronger collaboration that should involve the phar-

maceutical companies,” says Raymond Tice from the National Institute of Environmental Health Science in the United States, one of the institutions involved in Tox 21. Tice participated in a workshop called *Challenges and Perspectives in Research on Alternatives to Animal Testing*, held at FAPESP in March, 2015. Tice believes that the animal testing paradigm does not account for the advances that would make the testing process safer and more precise.

In the workshop, Eduardo Pagani, a drug development manager at the Brazilian Biosciences National Laboratory (LNBio), showed how computer models can compare the structure of a candidate molecule with those of other molecules that have already been tested and determine whether it is worth developing this candidate molecule. The LNBio, which is working in this area, is looking for partnerships, for example, with groups that have mastered the technology known as *organs-on-a-chip*. This technique is currently studied in the United States and Germany and uses cells to grow human tissues. These cells have microchips added and can, therefore, mimic the function of live human organs. “We want to work in the area of tissue mimicry,” Pagani says.

The researchers who participated in the workshop brought new perspectives on the use of animal models in research. These models demonstrate similarities with humans only 60% of the time, according to Thomas Hartung from the Center for Alternatives to Animal Test-

ing at Johns Hopkins University Hospital in the United States. Hartung cited the example of aspirin. Although it has been proven safe for humans, it would have been rejected in animal testing because it leads to fetal deformities in certain cases. “We are trying to show the importance and limitations of using alternative models, as well as the need for a sensible experimental plan, for Brazilian researchers,” said Lorena Gaspar Cordeiro, a professor at the Ribeirão Preto School of Pharmaceutical Sciences of the University of São Paulo (USP), one of the event’s organizers.

Some of the methods presented in the workshop are aimed at finding alternatives to the use of mammals, such as the zebrafish, known in Brazil as the *peixe paulistinha*, and the larvae of the *Galleria mellonella* insect (see *Pesquisa FAPESP* Issue No. 220). “Approximately 75% of the 26,000 genes of the zebrafish are similar to human genes,” says geneticist Cláudia Maurer-Morelli from the University of Campinas (Unicamp). Likewise, the *Galleria* larva has immunological mechanisms similar to those of mammals. “The larva’s cuticle acts like skin. When it is injected with a toxic substance, it reacts and turns darker,” explains Maria José Giannini, a professor at the Araraquara School of Pharmaceutical Sciences of São Paulo State University (Unesp). “Brazil wants to join the path of the United States and European countries,” says Giannini, who coordinated the workshop. ■