Investigators at VIB and UGent have developed a tool for more accurate interpretation of biomedical research

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Investigators affiliated with VIB and UGent recently achieved great success with a study involving biomedical research on mouse models. The research group of Prof Peter Vandenabeele (VIB/UGent) recently used tangible examples to demonstrate how the side effects of genetic modification of mice can complicate the interpretation of biomedical research. The team developed a web tool that allows scientists to estimate the impact of this phenomenon more accurately. Their findings were recently published in the medical journal *Immunity* and received ample attention by a preview in *Immunity* and a comment in *The Scientist*.

Tom Vanden Berghe (VIB/UGent): "Our research will have a profound retro-active impact on the interpretation of a great deal of scientific research. In addition, it will also aid in explaining controversies in scientific literature surrounding certain disease models. Finally, in the long term, these results can contribute to an improved translation of findings from lab animals to humans."

Tests on mice are an important tool for research into diseases and drugs. By deactivating a specific gene in mouse strains, the investigators can study the effect of this gene on the development of a disease.

Translation from animals to humans

However, mouse models alone are not sufficient to reach irrefutable scientific conclusions. Clinical studies using human cells remain essential to validate the research results. These studies often produce different conclusions. An important reason for this is that the genetic modification of mouse strains not only changes the target gene, but also causes changes in the neighboring genes. Geneticists are familiar with this phenomenon, but it is sometimes overlooked.

Comparative analysis of mouse strains

In order to clarify this problem, the research group of Prof Peter Vandenabeele (VIB/UGent) performed a comparative analysis on the genetic information from various mouse strains.

Peter Vandenabeele (VIB/UGent): "Our bioinformatics analysis revealed that each mouse strain contains approximately one thousand genes that result in an abnormal protein. About a hundred of these could actually be attributed to a functional defect. In the first generation of a genetically modified mouse strain, the so-called recombinant congenic mice, we almost always see various other defective genes close to the inactivated gene. This means that in certain cases, researchers cannot be certain whether the inactivated gene, or the dysfunctional neighboring genes (or a combination of both) is/are responsible for the observed effect."

Online tool to support biomedical research

Post-doctoral researcher Tom Vanden Berghe supported this supposition with several tangible examples. In this way, he illustrated how this strongly underestimated problem in fundamental scientific research can result in false positives and premature conclusions.

Tom Vanden Berghe then worked with bio-informaticists Liesbet

Martens and Paco Hulpiau to develop a web tool that helps researchers to estimate the impact of this phenomenon correctly. The tool gives researchers insight into the possible abnormalities and the potential effect of these on their research results. Tak Wah Mak, a top-scientist from Ontario Cancer Institute, concludes his preview on Vanden Berghe's article as follows: "The wake-up call represented by this Immunity article on the importance of the passenger genome therefore does a great public service to the research community involved in the analysis and generation of gene targeted mice."

More information: "Passenger Mutations Confound Interpretation of All Genetically Modified Congenic Mice." *Immunity*. 2015 Jul 21;43(1):200-209. DOI: 10.1016/j.immuni.2015.06.011

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