Culmination of project to share data on the safety of medicines

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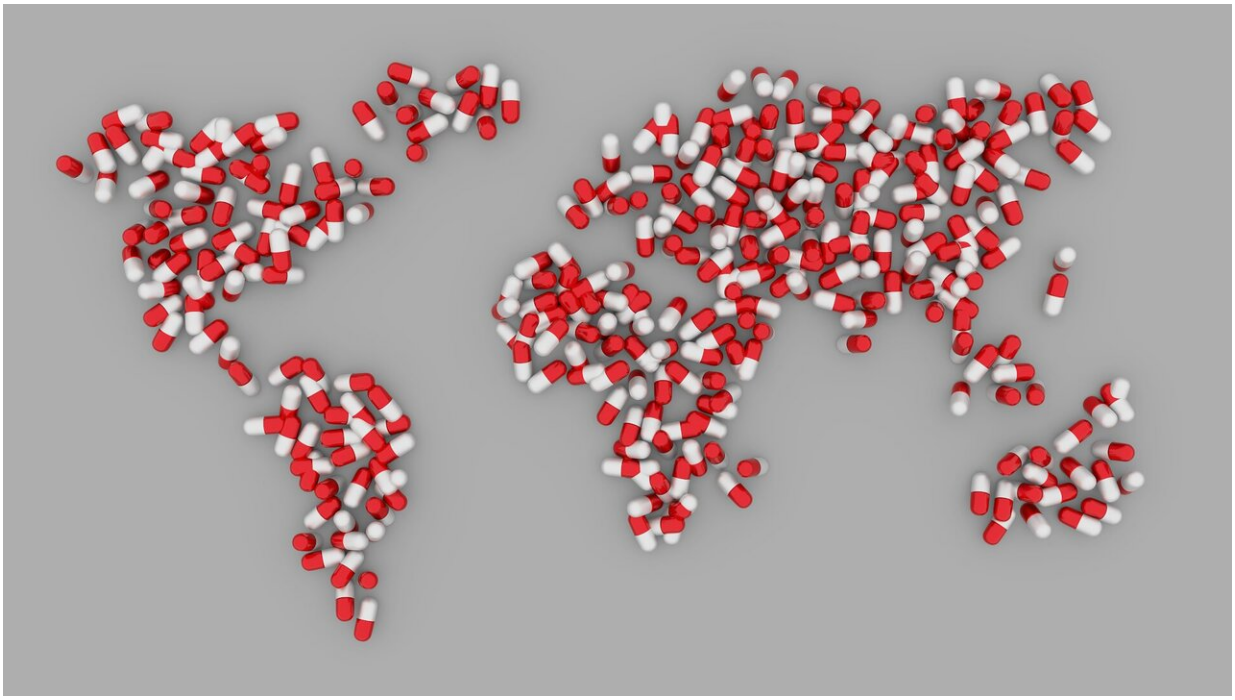

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eTRANSAFE, the European project to share data on the safety of medicines, has come to fruition. On a single platform, the project has integrated data from more than 10,000 pharmacological studies by reference pharmaceutical companies, from a dozen databases that amass public and private information of clinical and preclinical studies. The project has also developed "Flame," an open-source machine learning

application that allows predicting whether future drugs will have adverse effects.

The eTRANSAFE project has involved 13 pharmaceutical companies and a dozen academic institutions, including the GRIB; the research program in Medical Bioinformatics of the UPF Department of Medicine and Life Sciences (MELIS), the Hospital del Mar Research Institute and the spinoff MedBioinformatics Solutions, which emerged from the same program.

"Sharing data is the order of the day. In the academic world, open data is relatively common but in the business world it is more complicated," explains Ferran Sanz, UPF professor and coordinator of the Integrative Biomedical Informatics Research Group at the GRIB. "However, since drug safety is not the main area of competence in the pharmaceutical industry, the possibility of sharing data is more viable, and hence eTRANSAFE was born. From the opportunity to share data and the need to be able to make better predictions of the toxicity of future drugs," adds Sanz, who acted as academic coordinator of the project.

The results of the eTRANSAFE project, published in the journal *Nature Reviews Drug Discovery*, have gathered information from more than 10,000 toxicology studies carried out by 13 benchmark pharmaceutical companies, such as Bayer, Roche and Boehringer. The data collected, along with other data taken from public databases, has been entered into the ToxHub platform; a unique system created so that all the project members can explore and exploit information on drug safety.

The consortium has collected standardized data from preclinical studies, conducted in animals, and clinical and pharmacovigilance studies, in humans, which have been extracted electronically to minimize human error. However, in order to compare all the results, the consortium has had to develop a computer service for the "translation" of standardized

preclinical and clinical concepts they have published in open access.

"When we see scratching behavior in animal studies, we should associate it with what in clinics we call itching. Hence we needed to have a tool to equate these concepts and to be able to compare the results of studies done in animals with humans," Sanz explains.

The joint analysis of preclinical and clinical studies has found that not always are the animals closest to humans the most suitable for predicting the effects of a drug in our species. For example, rats have been found to be better than primates for predicting skin reactions that can be caused by kinase inhibitors, a drug widely used in cancer treatment.

Within the framework of this project, the GRIB has developed Flame, an application to simply build, maintain and share models that predict the biological properties of new compounds. "With this application, in a matter of minutes we can share a model developed at the university with a pharmaceutical company," explains Manuel Pastor, a UPF professor and head of the Pharmacoinformatics Group at the GRIB, who led the development of Flame.

The application, which can be installed on both a laptop and in large cloud servers "presents in a simple and visually attractive way very sophisticated software, so that any researcher can use it".

In the six years that the project has lasted, a prototype has also been made to study virtual control animals, and with the collaboration of partners such as MedBioInformatics Solutions, bioinformatics tools have been developed to identify mechanical biomarkers, which provide information on the mechanism whereby a drug causes adverse effects, and text mining tools to identify the biomarkers used in clinical trials.

All these tools and the databases developed by eTRANSAFE will be

permanently stored at UPF, which is the project's last "honest broker".

"The project has achieved many of the goals set at the beginning and has made it possible to establish direct contact with pharmaceutical companies and develop products based on their real needs," concludes Laura Furlong, co-founder and scientific director of the GRIB spinoff, MedBioinformatics Solutions.

More information: Ferran Sanz et al, eTRANSAFE: data science to empower translational safety assessment, *Nature Reviews Drug Discovery* (2023). DOI: 10.1038/d41573-023-00099-5

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