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The importance of standardizing drug screening studies

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A bioinformatics expert at the IRCM, Benjamin Haibe-Kains, recently published an article stressing the importance of standardizing drug screening studies in the prestigious scientific journal *Nature*. The study supports the need for further development and standardization to improve the reproducibility of drug screening studies, as they are important in identifying new therapeutic agents and their potential combinations with existing drugs.

Dr. Haibe-Kains's article investigated results from two large-scale pharmacogenomic studies – the Cancer Genome Project (CGP) and the Cancer Cell Line Encyclopedia (CCLE) – published last year in *Nature*. The main goal of these studies was to identify genomic biomarkers that could predict patients' response to anticancer drugs. Because cancer patients often exhibit varied responses to anticancer treatments, and evidence indicates that response is determined in part by patient-specific genome alterations, cancer cell line studies have long been used to test the efficacy of therapeutic agents and explore genomic factors associated with drug response. These two studies screened multiple new and approved drugs on nearly 1,000 panels of cancer cell lines, of which 15 drugs and 471 cell lines were common.

"These studies provided us with a unique opportunity to look at the reproducibility of biomarker discovery in preclinical settings," says Dr. Haibe-Kains, Director of the Bioinformatics and Computational Biology research unit at the IRCM. "Our objective was to examine the uniformities and inconsistencies between results from the two

independent studies, and assess the potential of building predictive models of drug response on the basis of those results."

Dr. Haibe-Kains and his research team observed overall good consistency of genomic profiles, which contain information about all the genes in the body and can be used to determine response to a drug. However, drug sensitivity measurements used in the two studies were highly inconsistent.

"We believe the reasons for such differences include the lack of standardization in experimental assays and data analysis methods," adds Dr. Haibe-Kains. "For example, the studies tested different drug concentrations and used different statistical models to analyze their data. In addition, due to discrepancies in drug sensitivity data, some potential biomarkers were inconsistent between the two studies."

"These pharmacogenomic studies are generally the first step in a larger experimental pipeline where candidate drugs and biomarkers are further validated in animal studies and human clinical trials," explains Dr. Haibe-Kains. "Our findings support the need for standardization of drug-response measurements or the development of new, robust drug sensitivity assays in order to identify reliable genomic predictors of drug response or effectively identify a drug's mechanism of action."

"It is important to note that our study and the resulting observations could not have been possible if the data had not been well documented and made accessible to the scientific community," concludes Dr. Haibe-Kains. "This represents a big success for open data science and reproducible research, and we would like to thank the investigators from the CGP and CCLE studies who made their invaluable data available to researchers everywhere. Without this data, we would not have been able to discover the discrepancies. We now need to work together to improve the reproducibility of large-scale screening studies so that we can

identify new therapeutic agents and their potential combinations with existing drugs."

More information: www.nature.com/nature/journal/ … ull/nature12831.html

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