

Researchers discover signatures predicting therapeutic applications, toxicity of chemicals

September 27 2018



Credit: CC0 Public Domain

To predict the effects of a compound on the human body, researchers assess its biological activity, which requires pinpointing the affected

biological processes within cells. Considering that living cells comprise many biological processes, this is a daunting task. Researchers from Attagene and the U.S. Environmental Protection Agency have found a new, straightforward approach to the assessment of the biological activities of chemicals.

Using Attagene's proprietary technology, the FACTORIAL, the researchers analyzed perturbations of cellular signaling pathways that regulate gene expression. They found that disruption of certain [biological processes](#) produced reproducible patterns of perturbation in cell signaling. Moreover, chemicals disrupting the same bioprocess all produced identical patterns, regardless of where and how they interfered. Thus, the researchers called those patterns "invariant signatures of bioactivities."

Using the invariant signatures, the researchers could accurately identify compounds with specified bioactivities among thousands of uncharacterized chemicals. Moreover, they showed that this approach permitted a straightforward identification of multiple bioactivities of polypharmacological drugs.

The new approach has important ramifications for the drug development process and toxicity testing. The new signatures offer simple and cost-effective solutions to drug discovery, selection of safe [drug](#) candidates and to repurposing of existing drugs for new applications. Furthermore, the new approach enables assessing underlying mechanisms for the toxicity of environmental chemicals.

"Traditional genetic approaches deduce the bioactivity of chemicals by assessing changes in gene expression. These predictions are often imprecise and require complex computations," says senior author and Attagene CEO Dr. Sergei Makarov. "Instead, we assessed the cellular signaling pathways that regulate [gene expression](#)," Makarov says. "As

there are fewer pathways than [genes](#), these signatures are easy to interpret."

"We have identified specific signatures for many bioactivities, including mitochondria, proteasome and HDAC inhibitors, DNA-damaging agents, and cytoskeleton disruptors," says the first author Dr. Alexander Medvedev, Attagene's Director of Research and Development. "Those signatures define the most sought-after classes of anticancer drugs. And this diversity indicates that we will find specific signatures for many other therapeutically relevant bioactivities."

"It has taken a lot of heart and over 10 years of work of an amazingly dedicated group of people to develop this approach," added Dr. Makarov. This research is published in the journal *Science Advances*.

More information: Alexander Medvedev et al. Evaluating biological activity of compounds by transcription factor activity profiling, *Science Advances* (2018). [DOI: 10.1126/sciadv.aar4666](https://doi.org/10.1126/sciadv.aar4666)

Provided by Attagene

Citation: Researchers discover signatures predicting therapeutic applications, toxicity of chemicals (2018, September 27) retrieved 11 July 2024 from <https://phys.org/news/2018-09-signatures-therapeutic-applications-toxicity-chemicals.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.