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Cross-population study links individuals' chemical sensitivity, genes

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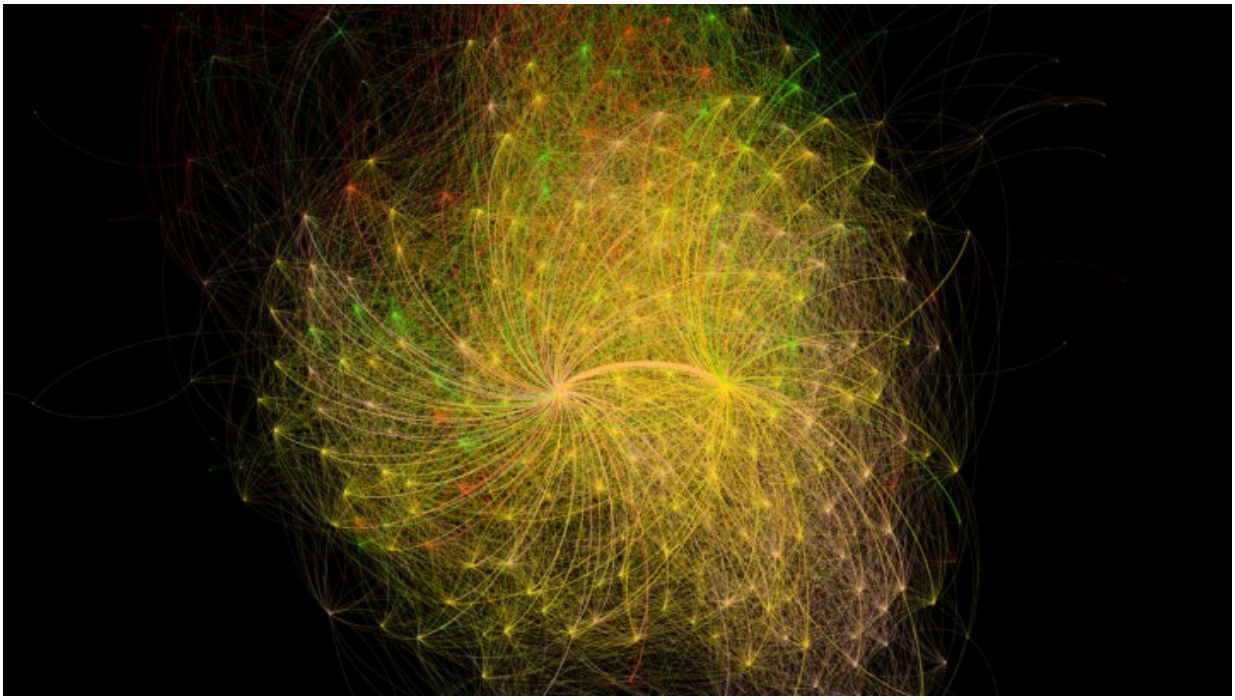

Biological expression network analysis of a portion of the 1000 Genomes cell lines used for testing the effects of environmental chemicals. Credit: Yi-Hui Zhou

Researchers from North Carolina State University and across the U.S. conducted the first large-scale cell-based screening to test variations in environmental chemical sensitivity across a range of human populations and link those variations to genetic data. The data will improve risk

assessment, and shed light on the ways in which our genes interact with certain chemicals.

Testing chemicals for potential human health hazards involves large-scale programs that test hundreds of chemicals in vitro – by exposing a cell culture to differing concentrations of a chemical and recording various responses in hundreds of assays. However, these cell-based tests are usually derived from either rodents or a small sample of humans.

"The current method is good for establishing rough averages in toxicity response, but we know that different people react differently to chemical exposure," says Fred Wright, professor of statistics at NC State and a co-lead author of a paper describing the project. "We wanted to design an experiment that could quickly test a lot of different chemicals against a large variety of populations, both to determine variability among responses and to see if toxicity responses could be linked to specific genes."

Wright and Texas A&M professor of veterinary integrative biosciences Ivan Rusyn, while both on faculty at UNC-Chapel Hill, partnered with the researchers at the National Institute of Environmental Health Sciences and National Center for the Advancement of Translational Sciences to conduct this large-scale experiment. They obtained cell lines from 1,086 individuals who had volunteered their genetic data as part of the 1,000 Genomes Project. The cell lines represented nine different genetic populations spread over five continents. They then exposed cells to 180 different chemicals at eight different concentrations each.

The data revealed that, for some chemicals, the range of sensitivity among individuals was greater than previously thought. The NC State team, including faculty members Alison Motsinger-Reif and Yi-Hui Zhou, was instrumental in discovering several genetic variations that correlated to chemical sensitivity. Most of the genes involved are

associated with the way foreign substances get transported across cell membranes.

'This broad, cross-disciplinary academic-governmental partnership is a model that will fuel important discoveries in environmental health and biomedical sciences," Rusyn says. "We are very grateful to all who committed time, effort and resources to this important undertaking."

"This is a great first step," Wright says, "but ultimately we want to match other biological data and the chemical structures, to find out why genetic differences affect toxicity of some chemicals but not the others. In addition to giving us more personalized information about chemical dangers and helping us determine safe exposure levels for these substances, the data could help us design safer chemicals for everyday use."

More information: "Population-Based in Vitro Hazard and Concentration– Response Assessment of Chemicals: The 1000 Genomes High-Throughput Screening Study," May 1, 2015. *Environmental Health Perspectives* DOI: 10.1289/ehp.1408775

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