Genomics study finds shared disease pathways for humans and environmental test organisms

29 September 2022

Blurs the line between human toxicology and ecotoxicology

Dr Emma Davies
Reporter

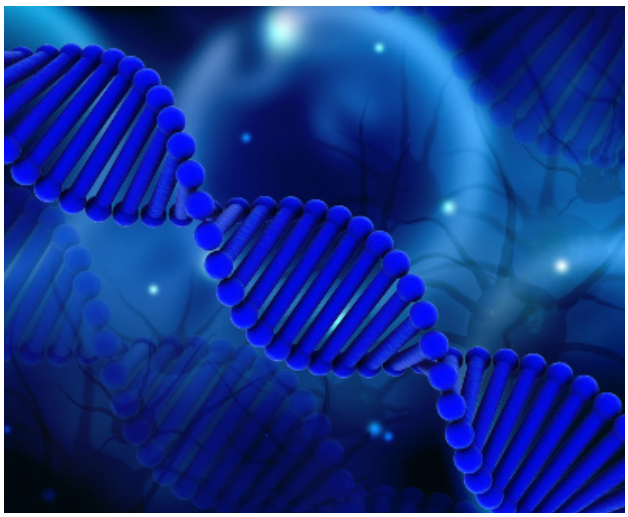
Chemicals toxic to humans may be picked up by tests on environmental model species, thanks to shared disease pathways, according to work part-funded by the EU's PrecisionTox project. The work "blurs the line" between human toxicology and ecotoxicology and paves the way to "species-agnostic" adverse outcome pathways (AOPs), said lead author John Colbourne from the University of Birmingham, UK.

A team from Birmingham and its spin-off Michabo Health Science collaborated with scientists from the US EPA, Indiana University and Unilever to search public databases and compare the genomes of different species, including humans and insects. The results show that a variety of animal species share more than 70% of gene families associated with disease.

"Because we know so much about human disease pathways, we are able to investigate to what extent the genes within human pathways are in fact preserved and likely to function in the same way in other species," said Professor Colbourne.

Published in the journal Environmental Advances, the study shows that genes linked to human disease are "more highly conserved" across animal genomes than those that are not disease related.

The team also investigated interacting genes that form networks to perform specific biological functions, finding them to be more strongly conserved across animal species than individual genes. As a result, the researchers suggest that chemical hazard assessments based on molecular key events in AOPs are likely to be informative for a greater range of species than currently used.



The work highlights how "unnatural" the current division between human toxicology and ecotoxicology is, said Professor Colbourne. Developing a greater understanding of fundamental pathways that can be perturbed by exposure to chemicals and are "predictive of adversity for a whole swath of animal diversity that includes humans" can help to bridge the divide, he added.

PrecisionTox

The University of Birmingham, Michabo Health Science and Indiana University are also partners in PrecisionTox, which launched in 2021. The project aims to predict adverse health effects in humans without using mammalian tests. It hopes to do this by identifying molecular biomarkers of key events in toxicity pathways. Biomarkers include changes in the regulation of genetic and metabolic pathways triggered by chemicals.

PrecisionTox researchers hope to develop "biological read-across" in chemical hazard assessment between humans and other mammals and ecological test species, such as water fleas (Daphnia). "The thing about comparative toxicology that is exciting is that those commonalities that we have among species will mostly be reflected at a mechanistic, molecular level, through these conserved,

shared pathways that we have," said Professor Colbourne. As a result, the project will identify new molecular key events for AOPs, as well as expand existing pathways.

Project teams have been preparing to collect vast amounts of biomolecular data on the effects of 250 selected chemicals on a wide range of species, amounting to a total of 21,000 samples. The project expects to release its first reports next year.

PrecisionTox is one of the ASPIS cluster of EU-funded new approach methodology projects, all of which have a strong focus on AOPs.