

International computational collaborations for predictive toxicology

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Humans are exposed to an increasing number of chemicals, but only a fraction of these have been evaluated for potential risks to human health and the environment. Thus, both regulators and manufacturers need rapid and efficient approaches to evaluate the potential toxicity of thousands of chemicals already in commerce and others in development. Advances in information technology and machine learning have fostered the development of in silico approaches that leverage the relationships between chemical structures and their biological activities. However, individual predictive computational tools are associated with certain limitations, and they are only as good as the input data upon which they are built. To address these challenges, international consortia involving over 100 scientists from governmental agencies, academia, and industry were formed to collaboratively develop in silico tools for predicting chemical toxicity. These consortia have successfully concluded three projects: the Collaborative Estrogen Receptor Activity Prediction Project (CERAPP), the Collaborative Modeling Project for Androgen Receptor Activity (CoMPARA), and the Collaborative Acute Toxicity Modeling Suite (CATMoS). These projects used data from both the published literature and the ToxCast/Tox21 programs curated to meet defined quality specifications. Limitations of individual modeling approaches were overcome by establishing consensus models that leveraged each model's strengths. The resulting consensus models have been used to screen hundreds of thousands of chemicals from the U.S. Environmental Protection Agency's (EPA's) DSSTox database. These models are freely available for further use through the OPEn structure-activity/property Relationship Application (OPERA), as an open-source standalone application and by querying the EPA's CompTox chemistry Dashboard (<https://comptox.epa.gov>) and NTP's Integrated Chemical Environment (<https://ice.ntp.niehs.nih.gov>).