INTERNATIONAL COMPUTATIONAL COLLABORATIONS TO SOLVE TOXICOLOGY PROBLEMS
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Humans are exposed to an ever-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 toxicity of chemicals already in commerce and those 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, these 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, an international consortium of 35 research groups involving over 100 scientists from governmental agencies, academia, and industry was formed to collaboratively develop in silico tools for predicting chemical toxicity. The consortium has 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 the published literature as well as data from 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 thousands of chemicals from the U.S. Environmental Protection Agency's (EPA's) DSSTox database. These models are available for further use through the OPEn structure-activity/property Relationship Application (OPERA), either as a standalone application or via EPA's CompTox Dashboard (https://comptox.epa.gov/).

References
[1] K. Mansouri, et al, Cerapp: Collaborative Estrogen Receptor Activity Prediction Project, *Environ Health Perspect* (2016) 124, 1023-1033
[2] K. Mansouri, et al, Opera Models For Predicting Physicochemical Properties And Environmental Fate Endpoints, *Journal Of Cheminformatics* (2018) 10, na-na