A MAPPING BASED ON PHYSICO-CHEMICAL FEATURES: LESSONS LEARNT

Ouédraogo, Gladys[1]; Detroyer, Ann[1]; Bourouf, Linda[1]; Nocairi, Hicham[1]; Loisel, Sophie[1]; Chettaoui, Chafika[1]; Note, Reine[1]; Ringeissen, Stéphanie[1]; Meunier, Jean-Roch[1]; Berthe, Pascal[1]; Reif, David[2]; Martin, Matt[2]; Richard, Ann[2]; Judson, Richard[2]; Dix, David[2]; Kavlock, Robert[2]

[1] L'Oréal, Aulnay-sous bois, France; [2]National Center for Computational Toxicology, ORD, US EPA, RTP, USA

The ban on animal testing of cosmetic products for systemic toxicity in Europe is foreseen in 2013. Several research programs involving the public and private sectors have been initiated with the aim of fulfilling regulatory requirements and complying with this transformative shift in toxicology. L'Oréal has been promoting such efforts with an emphasis on developing capacity for predicting the toxicity of the so-called "real-life"chemicals. Many efforts have been made in order to handle the complexity, diversity and specificity of cosmetic ingredients in terms of chemical reactivity, classes and solubility profiles.
The present study was an exploration of the chemical space being used to develop predictive models for systemic toxicity using the US EPA's ToxCast™ high throughput screening data, beginning with the 309 compounds of ToxCast Phase I for the training set. In order to enrich the chemical selection list and eventually expand the applicability domain of the proposed model, a comparative study of the ToxCast Phase II and L'Oréal chemical spaces (673 and 708 compounds, respectively) has been completed using a panel of 19 calculated structural and physico-chemical properties.
While the simple comparison of the two inventories by strict structural similarity (CAS) yielded a poor overlap, using the physico-chemical properties showed a high degree of overlap-indicating that the knowledge and models derived from the Phase I and Phase II Toxcast effort could be extended to a broader chemical space. This result will help define a rationale for selecting additional compounds for ToxCast in order to enrich the training set of the proposed model. However, future work is required to identify physico-chemical properties that are best associated with systemic toxicity, and extend the exercise to categories like mixtures and polymers which are commonly used in consumer products.