The NeuroDeRisk In Silico Toolbox: De-Risking Neurotoxicity and 3D-Pharmacophores

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Early assessment of risk for neurotoxicity benefits human volunteers and patients through safer chemicals, clinical candidates and approved pharmaceuticals. Current preclinical studies, performed during drug discovery research, poorly predict the adverse effects of pharmaceuticals on the nervous system and do not integrate sufficient time to mitigate risk by influencing chemical structure design [1].

To address this, we developed the NeuroDeRisk In Silico Toolbox as one of the innovative results of the NeuroDeRisk Project (821528) [2,3]. NeuroDeRisk is a collaborative effort between pharmaceutical industry, SMEs and academia to improve the performance of in vitro models for prediction of adverse effects of pharmaceuticals and eliminate and/or minimize the use of animal models. The NeuroDeRisk Toolbox incorporates LigandScout 3D-pharmacophore technology developed to successfully enable key decisions in drug discovery research and address critical issues including, design, discovery, toxicity, speed, high enrichment, scaffold diversity and accuracy [4,5].

It fulfils an unmet need by identifying chemicals with potential risk for adverse events at an early stage using more than 60 industry validated models and algorithms developed to tackle three of the most challenging adverse effects, namely, seizures/convulsions, psychological/psychiatric effects, and peripheral neuropathies. It provides the ability to:

1) profile and rank chemical structures for risk of neurotoxic adverse events and neuropharmacology;
2) increase productivity and efficiency by supporting early stage decisions on development and commercialization of safer pharmaceuticals and chemicals
3) advance research on molecular initiating events (MIEs), multi-target neurotoxicity related outcomes, and nomination of drugs and compounds for experimental studies to investigate complex mechanisms involved in neurotoxic adverse events.

It strengthens the 3Rs approach (“Reduce, Refine, Replace”) and increases productivity towards development of safer pharmaceuticals and sustainable health.

Bibliography

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