Advanced 3D-Pharmacophores for Bioactive Molecule Discovery and De-Risking Neurotoxicity

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Pharmacophores are widely used in pharmaceutical, agrochemical, cosmetic and nutrition research to identify bioactive molecules using virtual screening (VS) approaches. We have developed advanced 3D-pharmacophore technology to support high performance cloud computing for VS of large libraries. Advanced 3D-pharmacophore technology involves deciphering interactions between protein-ligand and protein-protein interfaces, deriving pharmacophores from empty binding sites and molecular dynamics trajectories to support dynamic, rather than static interpretations and expand opportunities for hit finding. Furthermore, we have utilized advanced pharmacophores for target prediction to support drug repurposing and phenotypic screening analysis.

Recently, we developed the NeuroDeRisk IL Profiler, as one of the results of the NeuroDeRisk Project [1,2]. The adverse effects of pharmaceuticals on the central or peripheral nervous systems are poorly predicted by current preclinical studies. This tool addresses an unmet need by enabling the identification of chemicals with potential risk for adverse events covering seizures/convulsions, psychological/psychiatric effects, and peripheral neuropathies. It provides the ability to profile and rank structures for neuropharmacology and risk and investigate multi-target neurotoxicity. It strengthens the 3Rs approach (“Reduce, Refine, Replace”) and increases productivity towards development of safer pharmaceuticals. Early assessment of risk for neurotoxicity will benefit human volunteers and patients through safer, preclinical candidates and pharmaceutical drugs.

References

[1] The NeuroDeRisk IL Profiler [https://docs.inteligand.com/ndr/il-profiler/]. [2] The NeuroDeRisk Project [https://neuroderisk.eu/].