

NEUROTOXICITY DE-RISKING IN PRECLINICAL DRUG DISCOVERY

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The adverse effects of pharmaceuticals on the central or peripheral nervous systems are poorly predicted by the current *in vitro* and *in vivo* preclinical studies performed during research and development process. Increasing the predictivity of the preclinical toolbox is a clear need, and would benefit to human volunteers/patients (safer drugs) and pharmaceutical industry (reduced attrition). The NeuroDeRisk Consortium consists of 18 academic, pharmaceutical industry and small and medium enterprise partners within the Innovative Medicines Initiative project (2019-2022). University of Belgrade – Faculty of Pharmacy is the partner that leads the work package devoted to preclinical prediction of mood and cognitive adverse effects. The other two groups of challenging adverse effects tackled by the project are seizures and peripheral neuropathies. By employing a plethora of experimental techniques and numerous pharmaceuticals previously connected with each of major adverse effects examined, the project looks for innovative tools, assays and protocols, which cover *in silico*, *in vitro*, *in vivo* and *ex vivo* approaches. Besides widening the knowledge on many widely used pharmaceuticals, the major goal of the project is to develop an integrated platform for better risk-assessment in exploratory and regulatory studies in the future.

References

1. Andronis C, Silva JP, Lekka E, Virvilis V, Carmo H, Bampali K, Ernst M, Hu Y, Loryan I, Richard J, Carvalho F, Savić MM. Molecular basis of mood and cognitive adverse events elucidated via a combination of pharmacovigilance data mining and functional enrichment analysis. *Arch Toxicol* 2020; 94: 2829-2845.
2. Takahashi K, Sato K. [Strong demands for the new preclinical assessment system of the CNS adverse effects]. *Nihon Yakurigaku Zasshi* 2020; 155: 295-298. Japanese.

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PREKLINIČKO PREDVIĐANJE NEŽELJENIH EFEKATA LEKOVA NA NERVNI SISTEM

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Postojeće in vitro i in vivo prekliničke studije koje se sprovode tokom procesa istraživanja i razvoja teško mogu predvideti neželjene efekte farmaceutika na centralni i periferni nervni sistem. Postoji jasna potreba za povećanjem prediktivnosti prekliničkih oruđa, što bi bilo korisno za humane volontere/pacijente (bezbedniji lekovi) i farmaceutsku industriju (smanjena stopa neuspeha). NeuroDeRisk konzorcijum se sastoji od 18 akademskih institucija, kompanija farmaceutske industrije i malih i srednjih preduzeća u okviru projekta Inicijative za inovativne lekove (2019-2022). Univerzitet u Beogradu – Farmaceutski fakultet jeste partner koji predvodi radni parket posvećen prekliničkom predviđanju neželjenih efekata na raspoloženje i kogniciju. Druge dve grupe izazovnih neželjenih efekata koje projekat obrađuje jesu konvulzivni napadi i periferne neuropatije. Korišćenjem mnoštva eksperimentalnih tehnika i brojnih farmaceutika koji su prethodno povezani sa svakim od ispitivanih velikih neželjenih efekata, projekat traga za inovativnim oruđima, esejima i protokolima, koji pokrivaju in silico, in vitro, in vivo i ex vivo pristupe. Mimo širenja znanja o brojnim široko korišćenim farmaceuticima, glavni cilj projekta jeste razvoj integrisane platforme za bolju procenu rizika u budućim eksploratornim i regulatornim studijama.

Literatura

1. Andronis C, Silva JP, Lekka E, Virvilis V, Carmo H, Bampali K, Ernst M, Hu Y, Loryan I, Richard J, Carvalho F, Savić MM. Molecular basis of mood and cognitive adverse events elucidated via a combination of pharmacovigilance data mining and functional enrichment analysis. *Arch Toxicol* 2020; 94: 2829-2845.
2. Takahashi K, Sato K. [Strong demands for the new preclinical assessment system of the CNS adverse effects]. *Nihon Yakurigaku Zasshi* 2020; 155: 295-298. Japanese.

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