Innovative test to predict drug-induced neurotoxicity and psychiatric side effects

D Weissmann
Alcediag, France

Severe drug-induced psychiatric side effects as depression and suicide recently resulted in market withdrawal of compounds like Rimonabant, emission of FDA alerts (Champix, Roaccutane) or law suites (Paxil). Current non clinical safety studies, whether safety pharmacology or toxicity studies cannot detect these severe side effects leading to dramatic human deaths and expensive late withdrawals. RNA editing of the serotonin 2C receptor (5-HT2cR) has been shown to be altered in postmortem brains of depressed patients and suicide committers. Alcediag has characterized a specific RNA editing signature of the 5-HT2cR linked to depressed/suicide patients. By using next generation sequencing technology (Illumina), Alcediag determined the editing profiles of the serotonin 2C receptor in SH-SY5Y human neuroblastoma cell line, treated with 54 market approved drugs at 3 concentrations. These compounds were selected from various therapeutic classes (antidepressant, antipsychotic, anti-obesity, antiviral, anti-inflammatory, anti-fungal, antiepileptic, mood stabilizing agents and others) as potentially inducing suicidality (FDA warning label) or not (no psychiatric side effects reported). The screening could identify a specific ‘at risk signature’, similar to that found in post mortem brain of suicide patients. Clear dose-effect relationships were observed. An algorithm was generated to identify ‘at risk’ compounds with 80% sensitivity and 90% specificity. This test is the first in vitro test able to characterize a potential pharmacotoxicity on the brain. Based on the same approach, a blood test was developed to assess the suicide risk in patients. First data exhibit high sensitivity and specificity. Taken together, these tests open new perspectives in personalized medicine in psychiatry.

Biography
D. Weissmann is General Manager at Alcediag, a company dedicated to innovation in diagnostic, and co-director of SYS2Diag, a joint venture between Alcediag and the CNRS dedicated to the biology of complex systems. Before Alcediag, she has served as Biocortech CEO and Chairman since 2001 and began her career as a Senior Scientist at Roussel Uclaf (now Sanofi-Aventis). Her research background includes an appointment as Research Director at the CNRS. As a co-founder of the CNRS Neuropharmacology lab at Lyon University, she was appointed by the French Ministry of Research to define the new national strategy for research and innovation.

dweissmann@alcediag-alcen.com

Notes: