Title of Research:

16_PT01-02-2

Construction of prediction models for toxicities induced by drugs and chemicals based on chemical structures and AOP

Principal Investigator:

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Summary of Research:

Quantitative structure–activity relationship (QSAR) analysis uses structural, quantum chemical, and physicochemical features calculated from molecular geometry as explanatory variables predicting physiological activity. Recently, deep learning based on advanced artificial neural networks has demonstrated excellent performance in the discipline of QSAR research. While it has properties of feature representation learning that directly calculate feature values from molecular structure, the use of this potential function is limited in QSAR modeling. The present study applied this function of feature representation learning to QSAR analysis by incorporating 360° images of molecular conformations into deep learning. Accordingly, we successfully constructed a highly versatile identification model for chemical compounds that induce mitochondrial membrane potential disruption with the external validation area under the receiver operating characteristic curve of ≥0.9.

Timeline:

March, 2017 – February, 2018

Topics:

Uesawa, Y., inventor; Meiji Pharmaceutical University, assignee. Prediction systems, prediction methods, prediction programs, learning model input data generation systems, and learning model input data generation programs. Pending Japanese patent application 2017-129823. 2017.

Publications:

1. Yuki Asako, Yoshihiro Uesawa, “High-Performance Prediction of Agonists on Human Estrogen Receptor Based on Chemical Structures”, Molecules, 23;22(4). pii: E675, 2017
2. Adverse effect predictions based on computational toxicology techniques and large-scale databases, 137th annual meeting of the pharmaceutical society of Japan, symposium, Sendai Japan (invited), 2017/3
3. “Application of JADER in palliative pharmacy care”, The 11th Annual Meeting of Japanese Society for Pharmaceutical Palliative Care and Sciences, symposium, Sapporo, Japan(invited), 2017/6
4. “Drug toxicity predictions based on databases for adverse effects and chemical structures”, The 24th HAB annual meeting, Tokyo, Japan(invited), 2017/6
5. “Analyses of adverse outcome pathways based on artificial intelligence”, The 44th Annual Meeting of the Japanese Society of Toxicology, Yokohama, Japan(invited)2017/7
6. “Construction of prediction models for toxicity reactions based on AOP and chemical structures”, Japan Chemical Industry Association LRI symposium, Tokyo, Japan(invited) 2017/8
7. “Application of AI technology in liver toxicity prediction via adverse outcome pathways”, Informatics In Biology, Medicine and Pharmacology2017, Sapporo, Japan(invited) 2017/9/
8. “The future of toxicity prediction developed by artificial intelligence”, 196th R&D Conference, Tokyo, Japan (invited)2017/12
9. Yurie Yoshida, Ryota Higuchi, Jun Teraoka, Yuhei Mashiyama, Hajime Kagaya, Yoshihiro Uesawa, “Comprehensive analysis of drug-induced thrombocytopenia in Japanese Adverse Drug Event Report database with chemical-structural information”, 137th annual meeting of the pharmaceutical society of Japan, , Sendai Japan, 2017/3
10. Yuhei Mashiyama, Yurie Yoshida, Ryota Higuchi, Jun Teraoka, Hajime Kagaya, Yoshihiro Uesawa, “Comprehensive analysis of drug-induced erythema exudativum multiforme major in Japanese Adverse Drug Event Report database with chemical-structural information”, 137th

annual meeting of the pharmaceutical society of Japan, , Sendai Japan, 2017/3