DEEPHIV: DEEP LEARNING TO PREDICT DDI RELEVANCE FOR ARVS

#00430

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INTRODUCTION

❖ **Drug-drug interaction (DDI)**

- DDI can jeopardise the clinical management of multiple therapies and complicate the prescription of treatments for patients [1].
- Clinical studies on DDI between ARVs and drug combinations are challenging due to various constrains such as ethics, time and cost [2].
- Computer-based approaches can support the prediction of relevant clinical DDIs and support a rational management of complex therapies.

❖ **Deep learning**

- Machine learning (ML) is a branch of Artificial Intelligence where the algorithm has an ability to learn from given data and extract patterns to make future prediction.
- Deep learning is a type of ML method inspired by the human neural network [3].

❖ **Aims**

- To rationalise the identification of clinical DDI potential by developing a deep learning algorithm, named DeepHIV, predicting the DDI risk between ARVs and comedications.

DATABASE

❖ **PubChem Compounds and Substances**

- Molecular structure via PubChemPy.

❖ **Liverpool HIV Drug Interaction (Table 1)** [4]

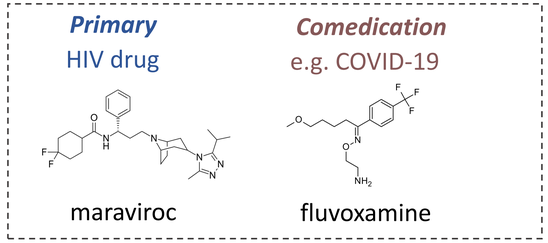
- Primary ARVs: 42 drugs including combination therapy.
- Comedication: 687 drugs (small molecule).
- Total: 28,026 drug pairs with labelled DDI.

Table 1. Degree of DDI from the Liverpool HIV database.

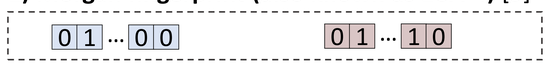
Colour	DDI label
Green	No clinically significant interaction expected
Yellow	Potential interaction likely to be of weak interaction
Amber	Potential interaction that may require close monitoring
Red	Drugs should not be co-administered

METHOD

1) Drug pair of interest



2) Morgan fingerprint (also known as ECFP4) [5]

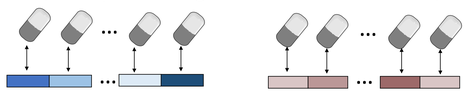


3) Similarity profile (Tanimoto score) [6]

Assume that similar drugs have similar DDIs

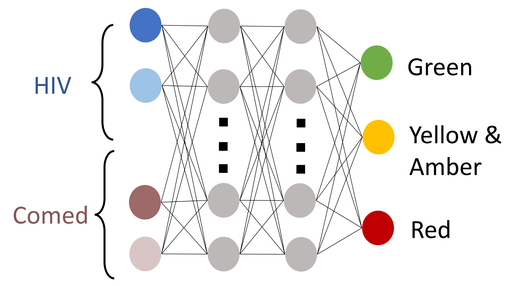
Reference drug list

(Liverpool Drug Interaction database)



4) DeepHIV (feed-forward neural network)

Trained to predict 3 levels of DDI, where ***Yellow and Amber were combined*** based on similar mechanism of DDI. 28,026 drug pairs were split to 80% for training and 20% for testing.



5) Prediction outcome example

Green:

- No clinically significant interaction expected.
- Confidence: 75.18%

RESULTS

- The performance of DeepHIV on the test set (n=5,824) achieved a mean of 85% accuracy, 70% precision, 69% sensitivity and 84% specificity **(Figure 1)**.

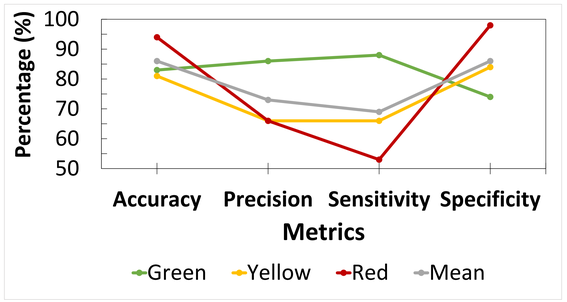


Figure 1. DeepHIV performance on the test set.

- A summary of prediction results versus the actual DDIs was shown as a confusion matrix **(Figure 2)**.
- DDI magnitude between first-line ARVs and comedications was predicted by DeepHIV, with above 80% accuracy, 70% sensitivity and 50% specificity **(Figure 3)**.

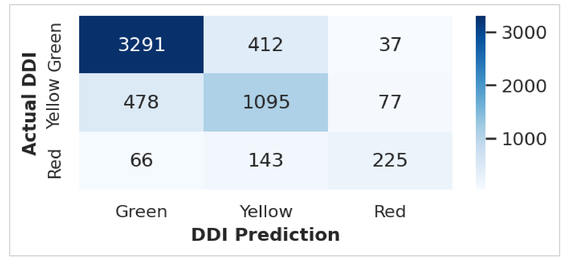


Figure 2. Confusion matrix of prediction versus actual DDI.

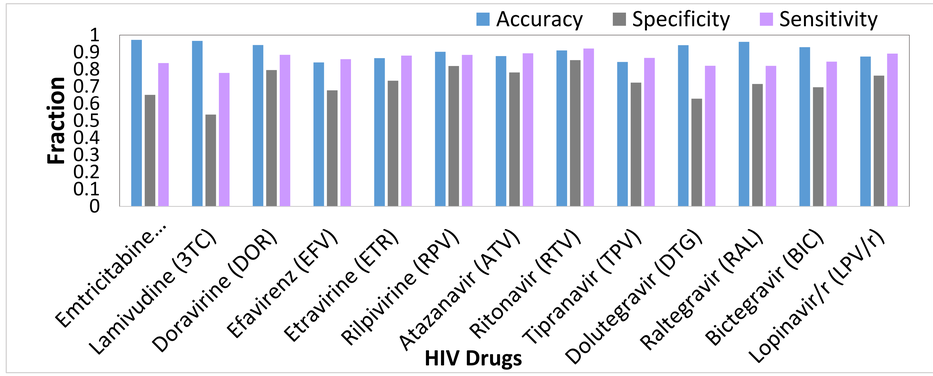


Figure 3. DDI prediction between first-line ARVs and all 687 drugs (comedications) available on the dataset. Evaluation metrics were shown as accuracy and sensitivity, where Accuracy = (TP+TN)/Total, and Sensitivity = TP/(TP+TN)

CONCLUSION

❖ DeepHIV was developed exclusively integrating structural and molecular data, into an automated analytical model, providing an evaluation of ARV DDIs.

❖ DeepHIV represents opportunities for a strategical integration of AI approaches during development of novel therapies as well as the identification and design of clinical DDI studies.

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HIV Website

HIV Drug Interactions