Evaluation of deep learning techniques in RNA sequencing data for the prediction of patient response to antiangiogenic treatment

Authors:

Background:

- Antiangiogenic treatments have demonstrated to improve PFS and OS for **metastasis Renal Cell Carcinoma (mRCC)** patients in several phase III clinical trials.
- Current search lines are using **genomic and transcriptomic data** to identify predictors of response to treatments.
- Since healthcare domain data sets are heterogeneous and high-dimensional **Deep learning (DL) approaches** appear to be a consolidated solution to this problem.

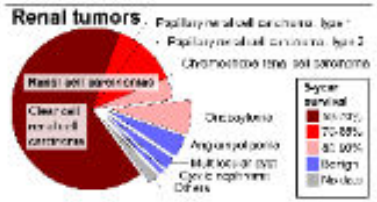

Figure 1:Distribution of renal tumours by relative incidence and prognosis.

Methods:

- **Data set:** **clinical and immune phenotype data and RNA expression (43893 genes) of 181 patients** treated with **NIVOLUMAB**, an antiangiogenic treatment.
- **Procedure:**
  - Creation of 8 data set using combinations of the information above and **classification of patients by their clinical benefit** (CB) using their PFS: CB (PFS < 3m) and no CB (NCB) (PFS > 3m).
  - We compared a generative model (deep autoencoder) and a discriminative model (CNN) with traditional machine learning (ML) models.
  - We came up with an **interpretability analysis** of those black-box models using LIME and SHAP values.

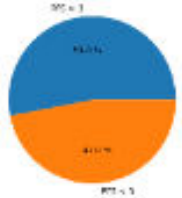

Figure 2: Patients distribution based on their clinical benefit.

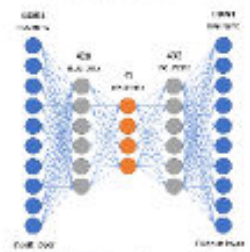

Figure 3: Deep autoencoder structure.

Does our model obtained for NIVOLUMAB treatment really shows the response to the drug?

Yes, concretely the ML classifier which achieved the best result in terms of accuracy was logistic regression classifier with **86.4%** of hit rate.

Are deep learning models the most effective methods for predicting response to NIVOLUMAB treatment?

DL methods have **not** demonstrated to be **significantly better** than traditional ML methods, when predicting the response of patients.

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Results:

Model	Data set	Accuracy
Logistic regression	30 most reliable genes and MSKCC variable.	0,864
Deep autoencoder + Decision tree	30 most reliable genes and 12 clinic variables.	0,689
CNN	400 most reliable genes	0,541

Most relevant genes for the decision making were related with the **immune response and the regulation of kinase** which meets the biological explanation. However interpretability results revealed that **clinic features seemed to have more relevance when making the decision.**

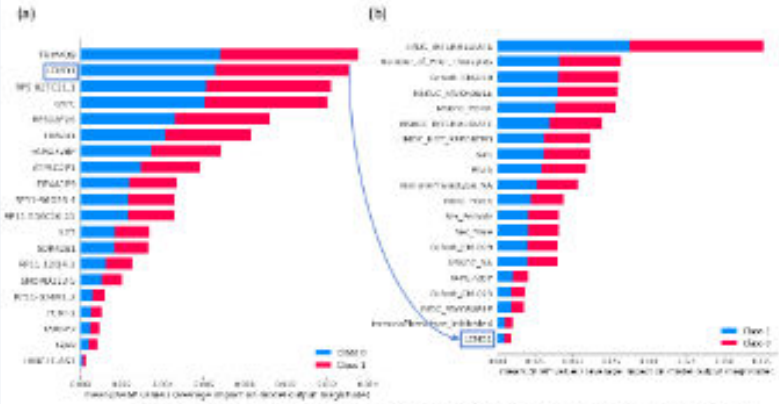
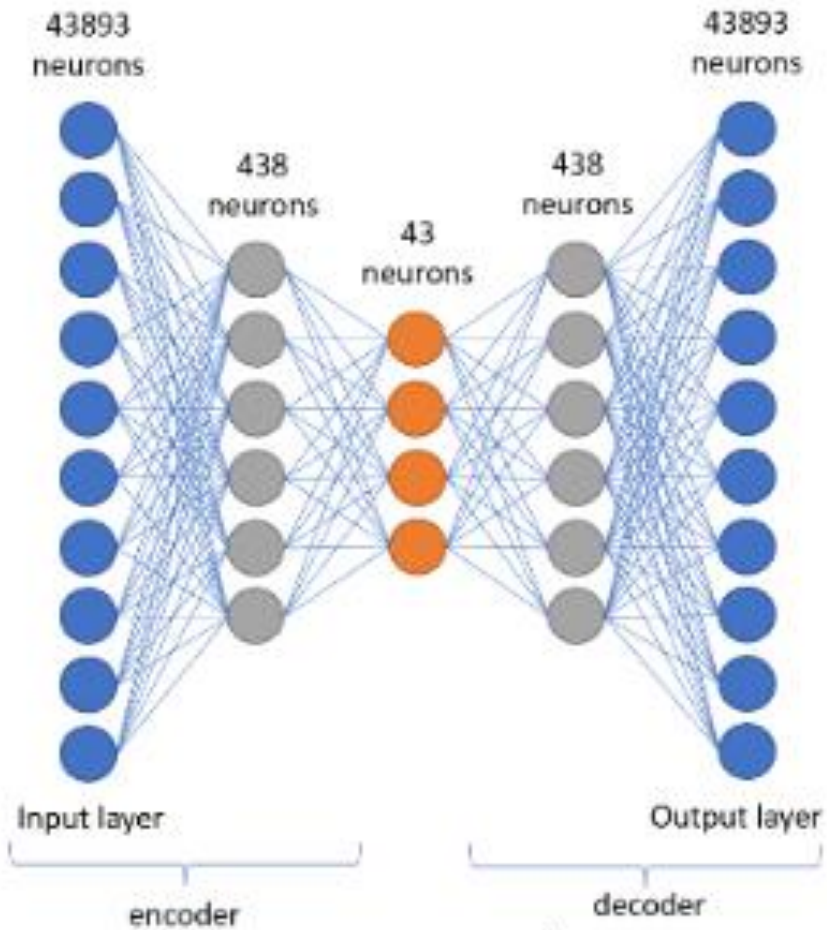


Figure 4: Interpretability results using SHAP values for (a) RNA data and (b) clinic and RNA data.

Future Directions for Research:

- Collect data from more patient samples whose PFS is over 6 months.
- Continue studying more innovative DL techniques.



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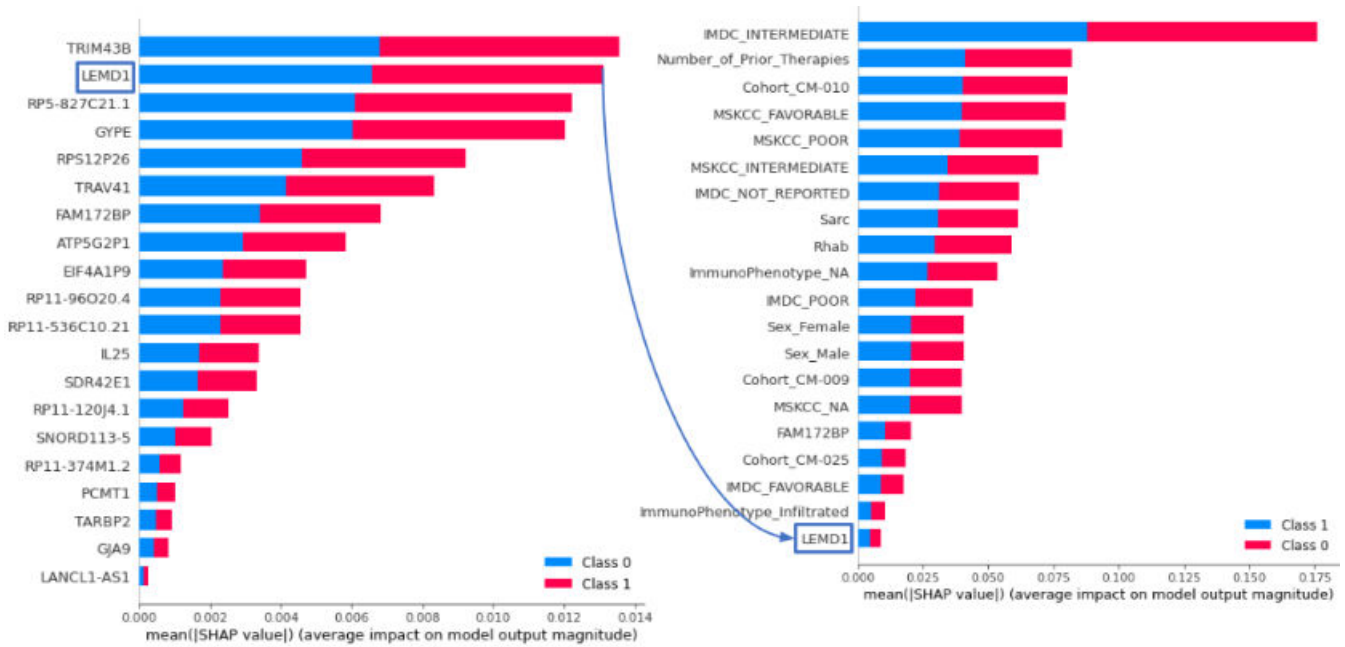

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Gracias!!