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In Silico Method for determining Cancer Diagnosis from Patient Blood mi RNA Levels

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ABSTRACT

Cancer has been a prevalent medical concern among many scientists. Despite modern treatments, many patients still have a low recovery rate due to late diagnosis. MicroRNAs (miRNAs) are endogenous non-coding functional RNAs that regulate gene expression by inhibiting/promoting certain signaling pathways.[5] They could be a potential indicator of cancer and can be detected from miRNA screening of patients' blood samples. This indicator could allow scientists to detect potential cancer at an early stage and begin targeted therapy or early treatment. In this project, the aim to was to improve the understanding of gene expression in relation to cancer, using machine learning to identify key miRNAs with a high relatedness to cancer and find pathways connected to the relatively novel field of miRNAs. We carried out data collection (data from Toray Industries, Japan, for three cancers: lung, esophageal, and gastric cancer), model development, pathway analysis, and app development along with generating figures such as variable importance and partial dependence plots. The models averaged a very high AUC of 0.99. All of this allowed for a further understanding of miRNAs in relation to gene expression. Crucial statistics such as specific threshold levels of miRNA expression most indicative of cancer were generated. Overall, this project serves as a prototypical model which has a high diagnostic accuracy for predicting cancer outcomes from patient miRNA data, and an app displaying the gene targets and basic descriptions of said targets was produced.

Keywords:- *miRNA, Machine Learning, Liquid Biopsy, Lung Cancer, Esophageal Cancer, Gastric Cancer*.

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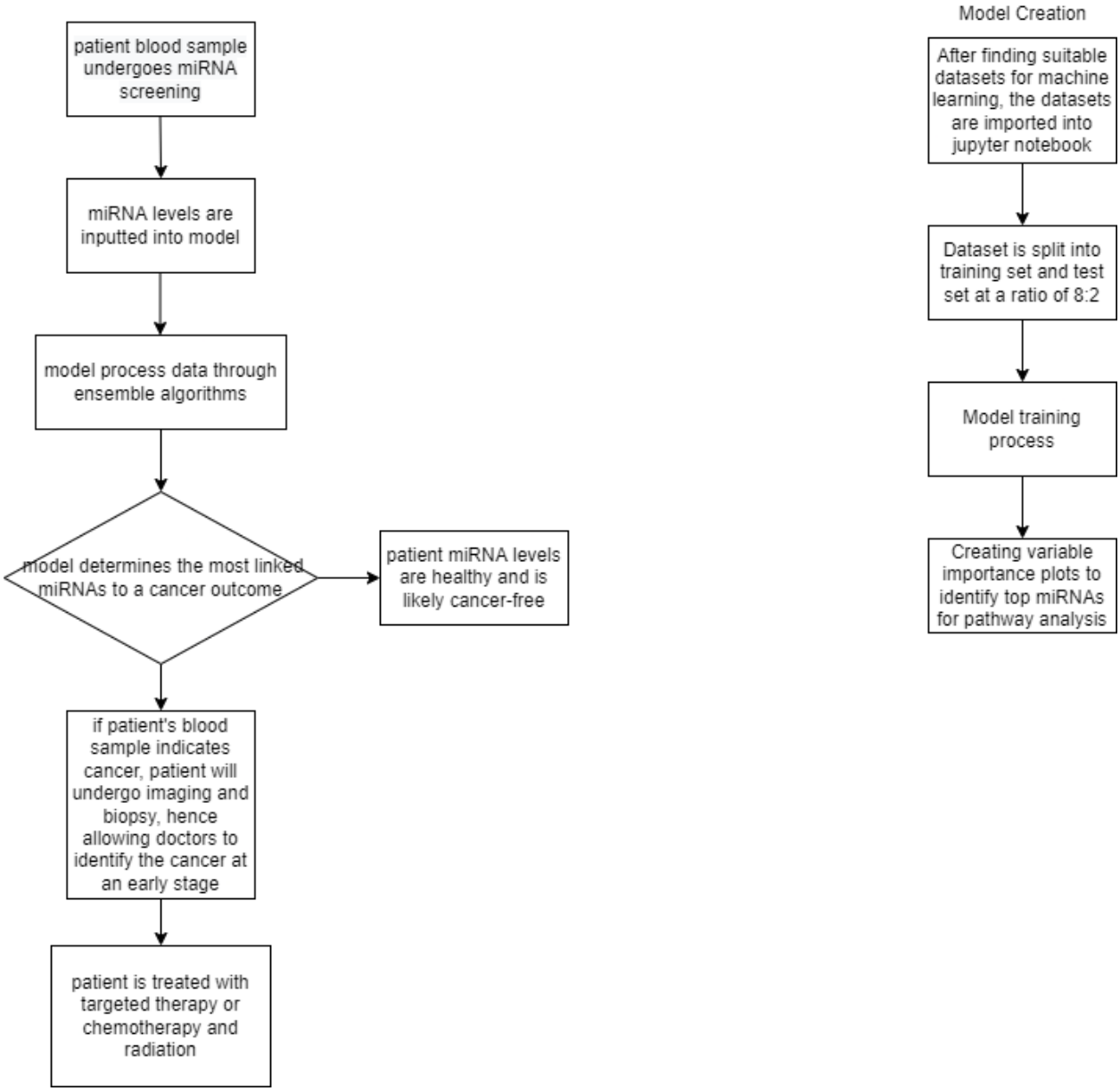

Paper 0.1: Overview of the model usage process (left) along with the model creation process (right)

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CHAPTER ONR

INTRODUCTION

A. Background

Lung cancer(25%),[9] esophageal cancer(5%),[12] and gastric cancer(8.3%)[3] are responsible for around 38.3% of cancer-related deaths worldwide, a large percentage of overall cancer-related deaths.

Lung cancer mainly refers to tumors growing in the parenchyma or within the bronchi.[9] It is the second most prevalent disease in both men and women — above which is prostate cancer in men and breast cancer in women. It also constitutes an alarming 25% of all cancer-induced deaths, more than prostate and breast cancer combined.[12]

The singular leading cause of lung cancer is smoking, which results in approximately 90% of lung cancer cases.[12] However, it is not the only cause. Other notable factors include air pollution, radiation, secondary smoking, and other lung-affecting diseases, such as pulmonary tuberculosis. These lung diseases increase the chance of lung cancer development.

The lethality of lung cancer can be attributed to the ineffectiveness of current treatments, such as chemotherapy, given lung cancer's resistance. More than two-thirds of patients are only diagnosed at the late stages of lung cancer, meaning that lung cancer has already spread too far past the point of treatment, leading to the survival rates of lung cancer being extremely poor.[9]

Esophageal cancer is a malignancy with a staggeringly low survival rate, even when the patient undergoes treatment. Currently, esophageal cancer is the sixth most common cancer in the world. In fact, the number of people getting esophageal cancer each year has been increasing. Esophageal squamous cell carcinoma is generally caused by smoking, alcohol, or extremely unhealthy diets.[6]

Gastric cancer is the fifth most prominent cancer in the world, and third in cancer-caused deaths.[10] The reason the cancer-caused deaths are so high is that there are not a lot of successful treatments for gastric cancer.

Due to this issue, most patients are instead offered life-prolonging palliative treatment. As of the moment, surgery is the only way to fully cure gastric cancer and is dangerous and expensive.

Another hindering factor is the difficulty in diagnosing cancer.[12] The most obvious way to do it is a physical examination, where the doctor will check the outer body for abnormalities such as skin deformation or lumps, but not all types of cancer show outer-body symptoms. Then there are screening methods such as CT and MRI scanning, but they are expensive and inaccessible, along with exposing patients to unnecessary amounts of radiation. The most used is a biopsy, where doctors collect a tissue sample from the body, and test it in a laboratory, but this requires the mass to already be located, making it unviable as an early diagnostic method.

A promising new method for diagnosing cancer is looking at circulating RNAs in the patient’s blood, which has been undergoing a lot of research over the past decade.

B. Context

MicroRNAs (miRNAs) are endogenous non-coding functional RNAs that regulate gene expression.[4] They are essential to biological processes such as cell division and cell differentiation, cell death, and DNA repair.[5] In the context of cancer, miRNAs could act as tumor suppressors and promoters, but also could be an indicative factor of the presence of cancer.

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Failure to regulate miRNAs is a possible cause of non-small cell lung cancer (NSCLC), gastric cancer, and esophageal cancer.[5] If miRNAs are aberrantly expressed, they could inhibit the pathway that regulates cancer, leading to tumors forming. When miRNAs are overexpressed, they could inhibit processes in the cells that regulate tumor suppression. When miRNAs are underexpressed, there could be overly high amounts of protein produced, which also leads to cancer.

The reason we chose miRNA as the biomarker to perform data analysis for many reasons. The first is the small size of miRNAs. This factor, along with their association with proteins, prevents them from being degraded by RNases and hence enhances their stability within the blood, making them a strong candidate as a biomarker. On top of this, miRNAs can be directly extracted from patient blood samples, making it accessible and relatively inexpensive to test for blood miRNA levels. Extracting miRNAs from blood samples is also much less invasive than other methods such as biopsies. Lastly, compared to other circulating materials such as non-coding RNA, there were more available datasets with much higher amounts of cancer patients, making it more viable for this study, as machine learning is based purely on data.

C. Goals

The major goals of this project were to improve understanding of gene expression in relation to disease and cancer. After using data on miRNA blood levels that are publicly available from real patient blood samples, machine learning was employed to identify the most prominent cancer-inducing miRNAs. We can then analyze the shared targets between these miRNAs and find novel pathways. A primary goal to produce a small simple model that maintains high diagnostic accuracy, a potential development for the therapeutic field.

D. Personal context

My initial interest in cancer diagnosis and therapy stemmed from my mother, who was diagnosed with cancer when I was a child. Although not malignant, she suffered from the tumor and stayed in the hospital for almost a year, and she sacrificed her career for treatment. The indirect financial, physical, and emotional effects caused by cancer could be described as detrimental to her job and well-being, along with her not being with me for the year. This event showed me the extent to which cancer can affect not just the patient but the entire family, and how devastating the effects can be. From here, going through middle and high school, I invested time to read about cancer treatment and diagnosis, eventually being interested in biomarkers and RNA biology.

Parallel to my interest in cancer is my passion for machine learning. This was provoked by a school called AWS deep racer, an introductory machine learning club to program self-driving cars. I soon realized that machine learning could yield inhuman levels of accuracy and speed, going beyond the limits of our mental capacities, and hence discovered the field of computational biology.

After doing more reading on papers and research on suitable datasets, I eventually settled for the biomarker miRNA and initiated this project.

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CHAPTER TWO

MATERIALS AND METHODS

A. Data Collection

The first step of Data collection was sourcing datasets from GEO datasets (https://www.ncbi.nlm.nih.gov/gds). The criteria ensured the data was up to standards and high quality enough to be processed by machine learning.

The first criterion was large amounts of data points for both negative-controls and cancer-positive patients. To increase the accuracy of training, we created balanced sets of each dataset, where the number of control patients was the same as cancer patients, this was done randomly so as not to bias. We chose to look at a binary outcome rather than a multivariate outcome by focusing on one cancer per model, to make our analysis less convoluted. All three of the datasets come from New Frontiers Research Laboratory in Kanagawa, Japan. This laboratory used reagents and an array chip developed by Toray Industries, meaning that the same miRNAs were screened for each site. The reason for this is taking all three datasets from the same provider allows us to ensure standardized testing methods and accurate results.

The process begins with data processing. This includes organizing and transposing the matrix and splitting it into frames for training. Then we import the data onto Jupyter notebook for the model.

First Dataset:[1] GSE122497 Esophageal cancer, *Homo Sapiens*, 5531 samples, 566 Esophageal cancer patients, 4965 non-cancer controls. Data was obtained using Serum miRNA profiling.

Second Dataset:[2] GSE137140 Lung cancer, *Homo Sapiens*, 3924 samples, 1566 preoperative Lung cancer patients, 180 postoperative Lung cancer patients 1774 non-cancer controls. Data was obtained using Serum miRNA profiling.

Third Dataset:[3] GSE164174 Gastric cancer, *Homo Sapiens*, 2940 samples, 1423 Gastric cancer patients, 50 Esophageal patients, 50 Colorectal cancer patients, 1417 non-cancer controls. Data was obtained using Serum miRNA profiling.

B. Model development

We began model development by using the Google Collab notebook:

Pycaret was the package initially used for machine learning, and we had to install packages including pandas, NumPy, warnings, and Pycaret. These packages were used as the basis of all other codes. The training for this model was multi-algorithmic so that we could choose the best algorithm for processing miRNA data, along with seeing if the trendlines were the same across multiple algorithms.

The next step was to import and set up the dataset, the term binary refers to the column that shows 1 if the patient has cancer, or 0 if they are a control. 80% of the dataset was used as the training set and the other 20% was used as a test set for verifying and refining the model.

After the dataset was set up we proceeded to explore different machine learning algorithms to compare their levels of accuracy, the value that was used for overall model accuracy was the 'AUC,' which is the amount of area under the ROC curve. It is the measure of how well the classifier can distinguish different classes. The higher the value of the AUC, the better the performance of the model.

The next step was model evaluation and predictions to finally generate the feature importance plots and partial dependence plots for the miRNAs. However, a bug on the developer's side resulted in an error. This was when we switched the platform to another machine-learning platform called H2O.

Same as before while using Pycaret, installing and importing packages was the first step of the new code. Then we imported the dataset into Jupyter. Just as before, the dataset was split into an 80% train set and a 20% test set. After that, instead of training on Pycaret, we trained on H2OAutoML. After training was completed, the explain function revealed the feature importance plots, the confusion matrix, and the partial dependence plots.

Creating a feature importance plot helped to identify the most predominant miRNAs and to be able to perform pathway analysis on their gene targets. The confusion matrix shows the accuracy of the model, and the partial dependence plots reveal the levels of how much these miRNAs are expressed to yield certain results (cancer or cancer-free).

After the training and the plots were generated, model consolidation was performed by taking the top two miRNAs and training a model using a dataset using only the top two. This allowed a model that used only two features versus the many more in the original models and also allowed for further evaluation of model accuracy and the contribution of specific miRNAs.

C. Pathway analysis

We found the gene targets of the most prevalent miRNAs using the model and used mirBase to find the gene targets. Using Excel, we were able to deduce the shared gene targets between the different miRNAs. Then, we used pathway analysis to find protein targets, and deduce what effect miRNAs had on tumor development/suppression.

Using Reactome (the program used for pathway analysis, https://reactome.org/), we identified potential pathways by identifying pathways with a high "entity found" value, meaning a high number of gene targets in a pathway. After locating novel pathways, we were able to find pathway diagrams of the entire web of signaling targets that a pathway has, then we could begin to create pathway plots based on specific entities present within the web of signaling targets.

D. Therapeutic proposal

We aim to apply machine learning methods to accurately identify cases of lung, esophageal, and gastric cancer among patients at a very early stage. This could potentially allow early intervention and insight into potential targeted therapy. For example, several targeted therapies are approved for lung cancer,[14] such as immunotherapy. In development are antisense oligonucleotides, an experimental strategy to approach cancer. The overall concept of this is that antisense oligonucleotides bind to the miRNA which then prevents miRNA from binding to mRNA, hereby potentially able to limit protein generation and the pathogenesis of many diseases.[13] When the model identifies oncogenic pathways, antisense oligonucleotides could be a future option, as long as delivery systems are properly applied.

Another potential method of treatment that can be applied to early-diagnosed cancer patients is the bifunctional molecule RIBOTAC, a chimera molecule that targets miRNAs by recruiting a ribonuclease.[8] This was designed to work against breast cancer by exterminating breast cancer oncogenic miRNAs to cause rapid malignant cell death, but could be repurposed to target other miRNAs.[11]

Another method for miRNA function suppression is via miRNA sponges.[15,16] miRNA sponges serve the goal of being able to continuously inhibit miRNA function. miRNA sponges contain mass amounts of complementary binding sites for miRNAs of interest and are produced within transgenes of cells. A single miRNA sponge can block out an entire miRNA along with the family of related miRNAs.[16] The biggest advantage of miRNA sponges is that it affects mature miRNA. The implication that arises from this is that since many precursor miRNAs are produced in clusters, interacting with these precursor miRNAs during production may lead to unintended consequences on the processing of other miRNAs. However, since miRNA sponges interact with mature miRNA, this issue regarding precursor miRNA is avoided.

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In contrast to miRNA function inhibition, in the case where a miRNA is underexpressed in cancer, miRNA replacement therapy can be applied to increase the level of blood miRNA.

miRNA mimics are synthetic miRNA molecules.[17] Unlike typical miRNAs, they are double-stranded and are classified as RNA rather than miRNA, stimulate endogenous miRNA, and can bind to mRNA strands to suppress gene expression, similar to the function of a regular miRNA.

miRNA agomirs are similar to mimics but have more chemical modifications.[17] These chemical modifications will enhance the stability of these artificial strands beyond that of a typical mimic, allowing it to be used for effectively upregulating specific miRNAs.

Although these are potential options for the upregulation of blood miRNA levels, there are caveats to this.[17] An efficient delivery system is required for the delivery of any foreign genetic material, as they are subject to degradation in the blood, and also may trigger an immune response. There are also many different approaches to delivery systems such as viral vectors and liposomes, but this process is still under development and undergoing clinical trials.

E. Obstacles

During the project, we encountered a few major obstacles that set back progress. First of all, there was a Pycaret update that caused a bug in the software, which led to the original code based on Pycaret not being able to run without error. After a long debugging process and eventually realizing the issue was not on our end of the code but rather a bug that was not yet fixed, we switched to an alternative called H2O. During the process of model creation on H2O, we also got many errors during the training process due to incompatibilities with syntax inside the imported matrices, we fixed this by standardizing the datasets so that they could be compatible with the functions.

Apart from the coding process, sorting through the noise and the messiness of the pathway analysis website (Reactome) proved to be a very tedious task.

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CHAPTER THREE

RESULTS

The final results consist of a few components: ROC plots, variable importance plots, partial dependence plots, and potential novel pathway plots.

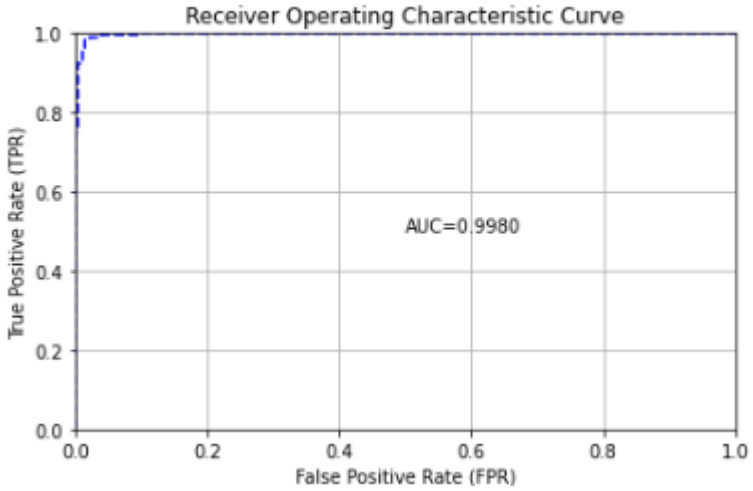

Fig. 1: The ROC Curve above is representative of all 3 models(lung, esophageal, gastric cancer), this shows an extremely high model accuracy rate for the datasets we trained on. AUC results are from the test set

The AUC is a performance metric that measures model accuracy or the area under the ROC curve. The ROC curve is calculated by plotting the true positive rate (TPR), against the false positive rate (FPR). TPR can be calculated by:

$$TPR = \text{Sensitivity} = \frac{TP}{TP + FN}$$

And false positive rate can be calculated by:

$$FPR = 1 - Specificity = \frac{FP}{FP + TN}$$

To understand these equations fully we must refer to the confusion matrix, which follows this format:

Predicted Values \ Actual Values	Positive (1)	Negative (0)
Positive (1)	TP	FP
Negative (0)	FN	TN

The TP (true positive) is when a model predicts a positive result, and the actual result is positive, the opposite for TN (true negative). By the same logic, a false positive and a false negative is when the model wrongly predicts either a negative or positive result. This is displayed below in the confusion matrices.

Confusion Matrix (Act/Pred) for max f1 @ threshold = 0.5777988994718207:

	Esophageal_cancer	Non-cancer	Error	Rate
Esophageal_cancer	110.0	0.0	0.0	(0.0/110.0)
Non-cancer	0.0	117.0	0.0	(0.0/117.0)
Total	110.0	117.0	0.0	(0.0/227.0)

Fig. 2: The confusion matrix for the esophageal cancer model. The confusion matrix depicts the rate of the inaccuracy of the models. From this example, there was no inaccuracy when the model used the test set. There could, however, be a rating that is lower if we used a larger dataset (10,000+ data points)

Confusion Matrix (Act/Pred) for max f1 @ threshold = 0.9993215949255042:

	Lung cancer	Non-cancer	Error	Rate
Lung cancer	317.0	0.0	0.0	(0.0/317.0)
Non-cancer	0.0	325.0	0.0	(0.0/325.0)
Total	317.0	325.0	0.0	(0.0/642.0)

Fig. 3: Confusion matrix for the Lung Cancer model

Confusion Matrix (Act/Pred) for max f1 @ threshold = 0.9373178332975879:

	Control	Gastric Cancer	Error	Rate
Control	293.0	0.0	0.0	(0.0/293.0)
Gastric Cancer	0.0	284.0	0.0	(0.0/284.0)
Total	293.0	284.0	0.0	(0.0/577.0)

Fig. 4: Confusion matrix for the Gastric Cancer model

From the above images, we can get an overall impression on the high level of accuracy the model possesses. To put this into perspective, the plot below demonstrates the AUC curve of random miRNAs taken from a dataset.

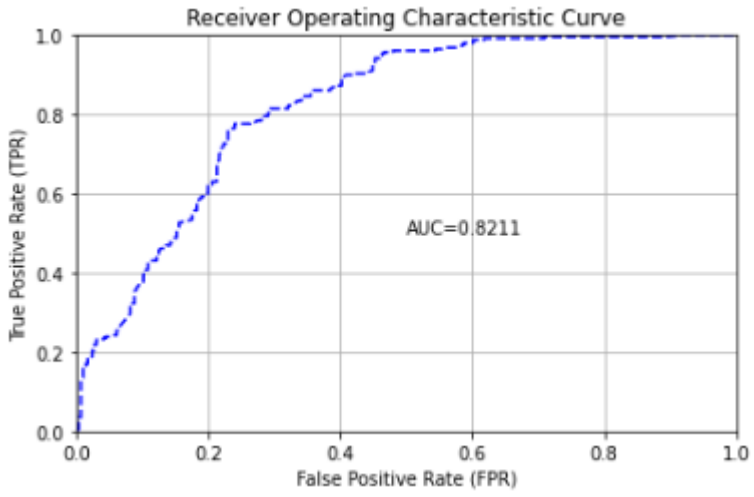

Fig. 5: Control AUC curve to provide information on the default levels of AUC

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On top of using a control AUC curve to compare how accurate the AUC curves we obtained were, we took further measures to ensure unbiased results by taking the top 2 miRNAs from each cancer, and running them in a separate dataset. If this still yielded high AUC levels then it shows that the top 2 miRNAs are in fact prevalent in cancer.

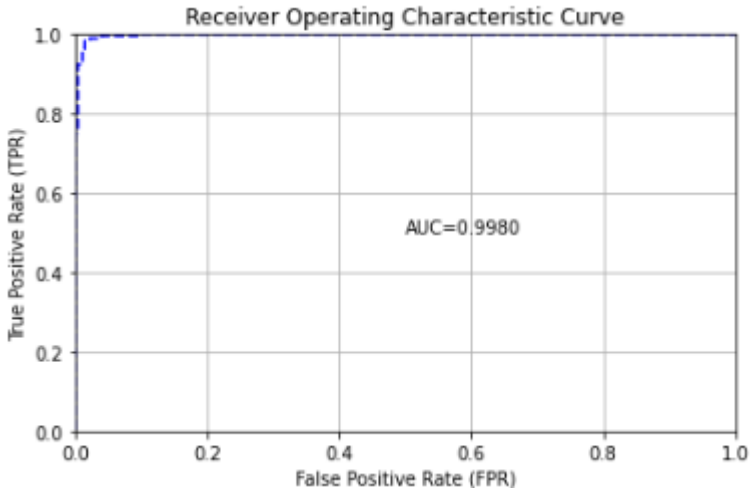

Fig. 6: AUC curve for lung, gastric, and esophageal consolidative model, taking only top 2 miRNAs

Confusion Matrix (Act/Pred) for max f1 @ threshold = 0.42189956390750893:

	Control	Gastric Cancer	Error	Rate
Control	761.0	360.0	0.3211	(360.0/1121.0)
Gastric Cancer	105.0	1052.0	0.0908	(105.0/1157.0)
Total	866.0	1412.0	0.2041	(465.0/2278.0)

Fig. 7: Confusion matrix for the Gastric cancer consolidative model

Confusion Matrix (Act/Pred) for max f1 @ threshold = 0.07191671406388075:

	Lung cancer	Non-cancer	Error	Rate
Lung cancer	310.0	2.0	0.0064	(2.0/312.0)
Non-cancer	0.0	304.0	0.0	(0.0/304.0)
Total	310.0	306.0	0.0032	(2.0/616.0)

Fig. 8: Confusion matrix for the Lung and Esophageal cancer mixed consolidative model

After the consolidation and verification process, we moved on to the feature importance plots from the models.

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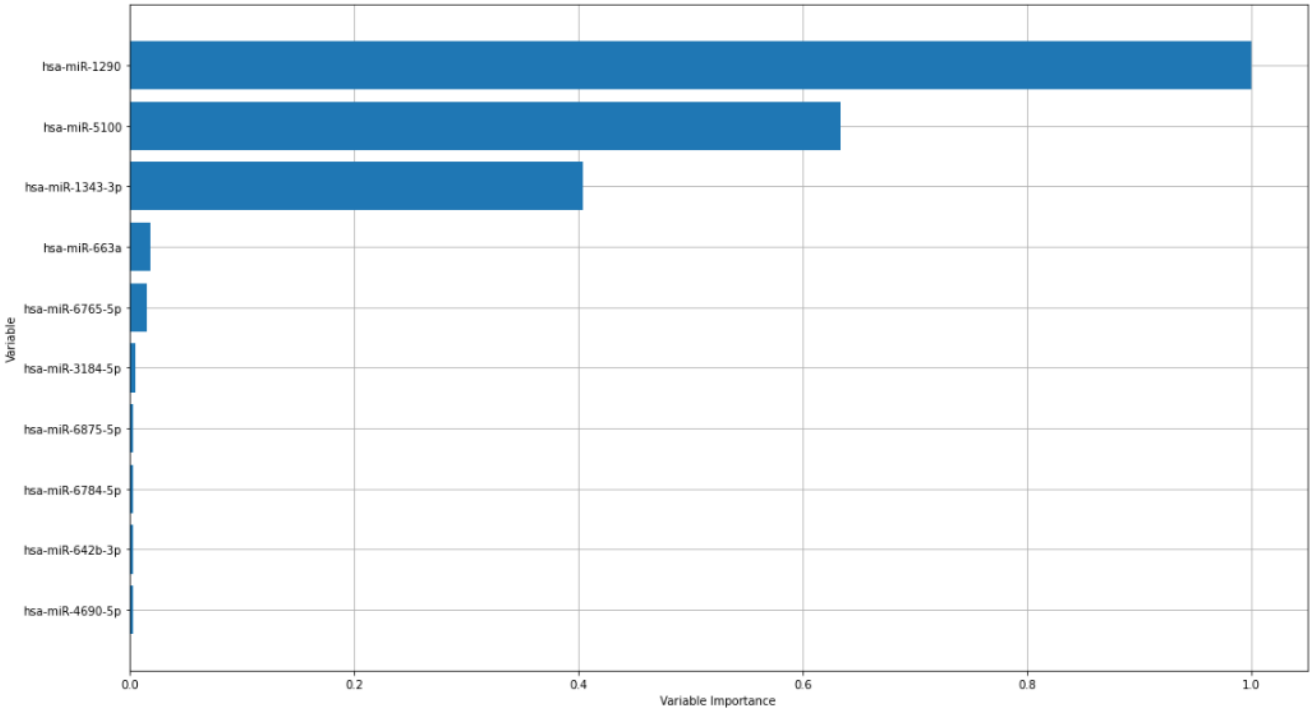

Fig. 9: Variable importance plot generated from lung cancer model. The top 2 miRNAs were used for pathway analysis

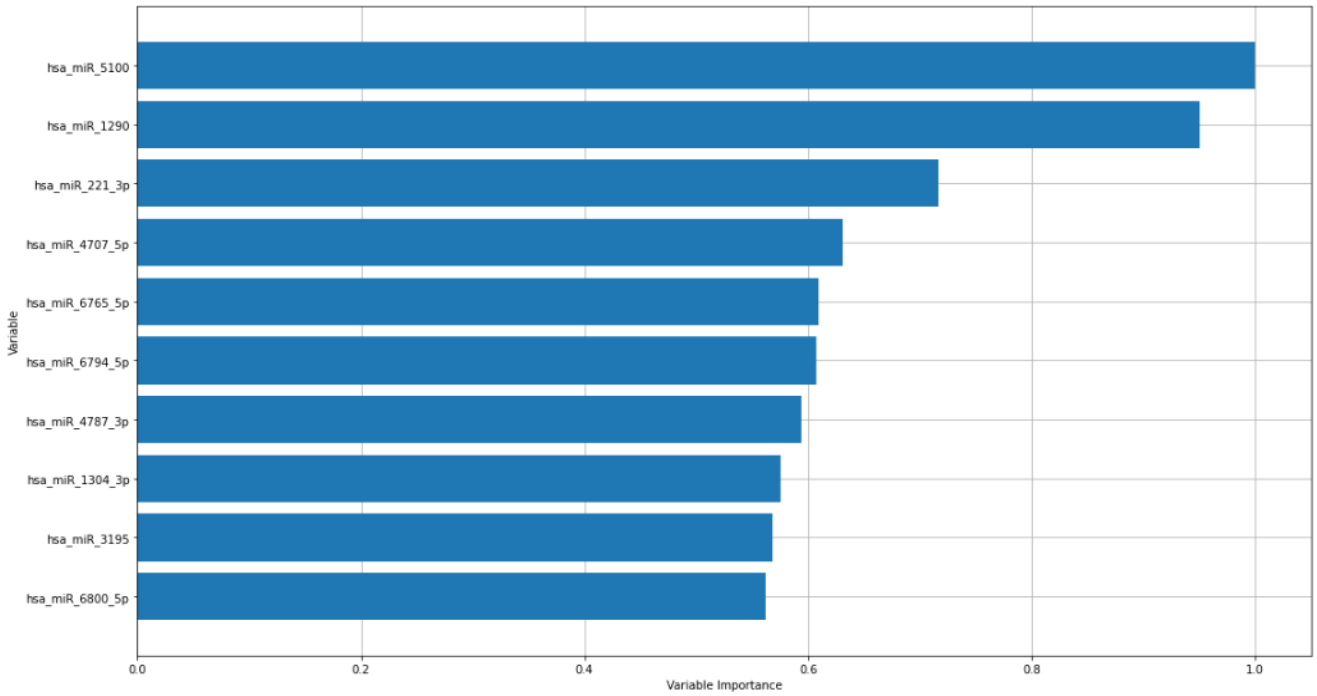

Fig. 10: Variable importance plot generated from esophageal cancer model

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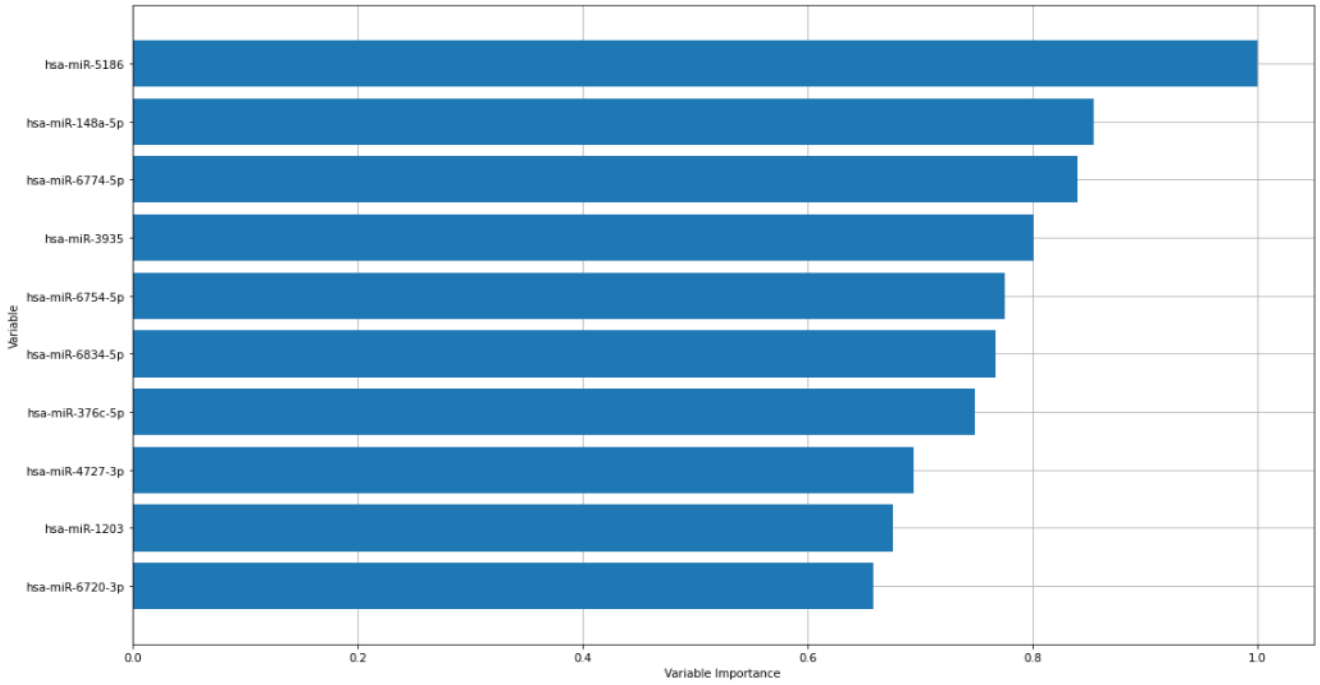

Fig. 11: Variable importance plot generated from gastric cancer model

The variable importance plots allowed us to identify the important miRNAs, and right after that we also obtained partial dependence plots. Variable importance plots were used for pathway analysis, which we performed on the top 2 miRNAs for the 3 different models.

Variable importance is calculated by comparing the relative importance, or how much a specific variable affects the outcome, of different miRNAs. This means that the miR at the top of each plot, or with the highest variable importance, are the main contributing miRNAs.

Some cancers had clear indications for which miRNAs were the top contributor, for example, miR-1290, miR-5100, and miR-1343-3p were the clear top 3 in lung cancer, as the remaining miRNAs on the leaderboard had significantly lower variable importance.

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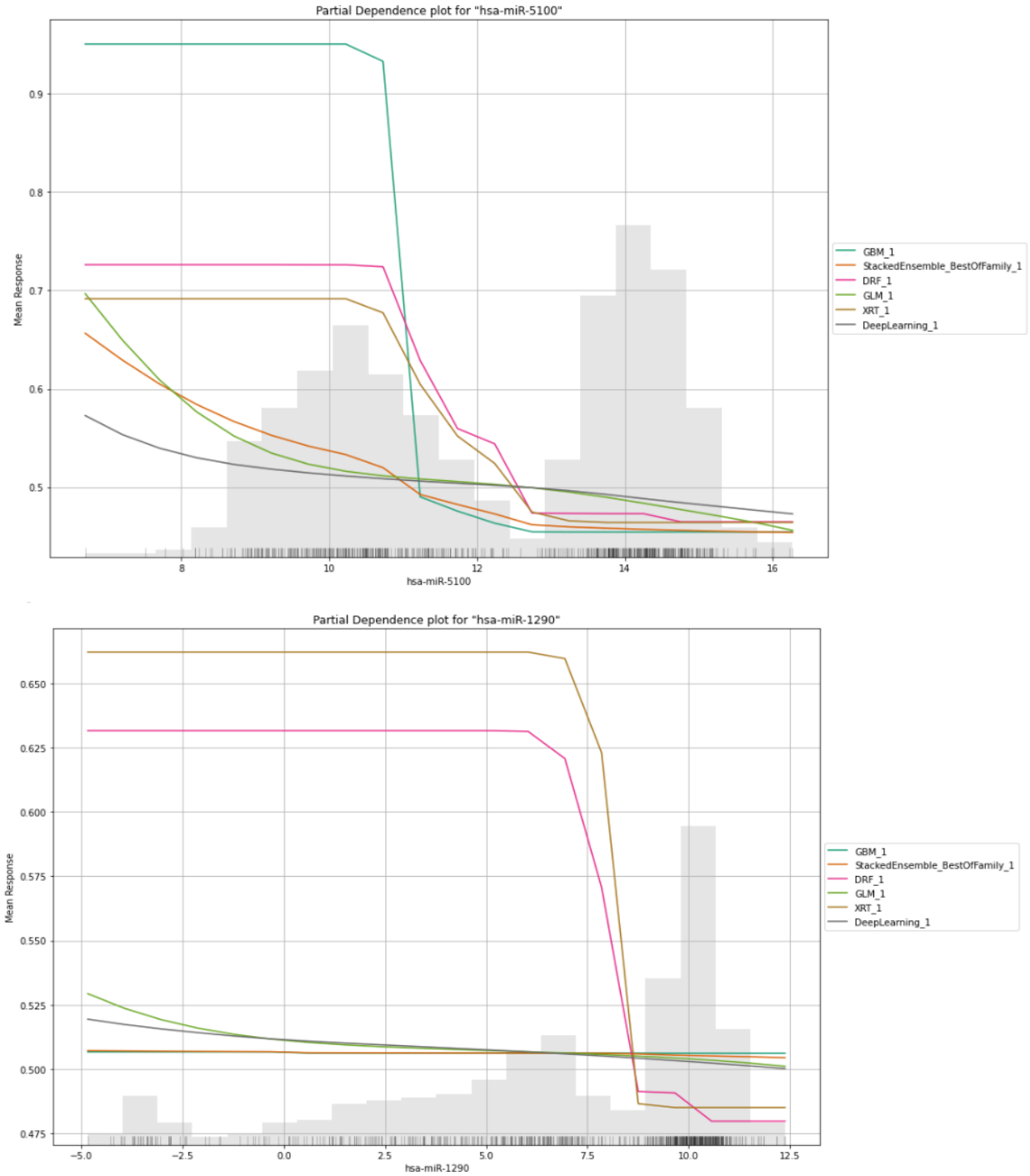

Fig. 12: Partial dependence plots for top 2 miRNAs in the lung cancer variable importance plot. Almost all of the different algorithms (different colored lines) have the same general trend, which further solidifies the plots. (whether they are overexpressed or underexpressed). In this plot, the higher expression of the miRNA leads to a lower mean response (y-axis), which means a higher frequency of cancer patients. The miRNA is overexpressed in cancer.

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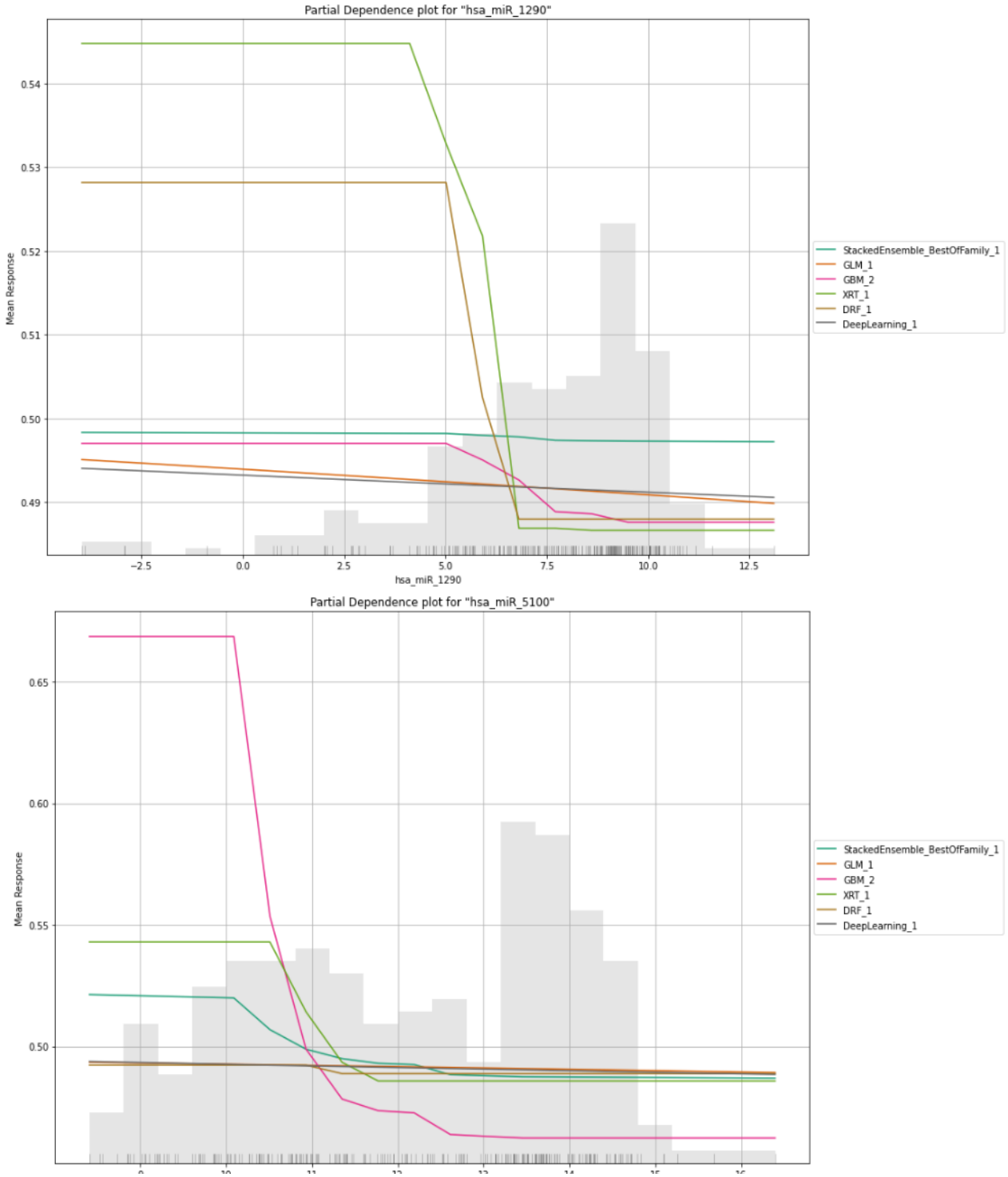

Fig. 13: Partial dependence plots for top 2 miRNAs in the esophageal cancer variable importance plot. A lower mean response (y-axis) means a higher frequency of cancer patients.

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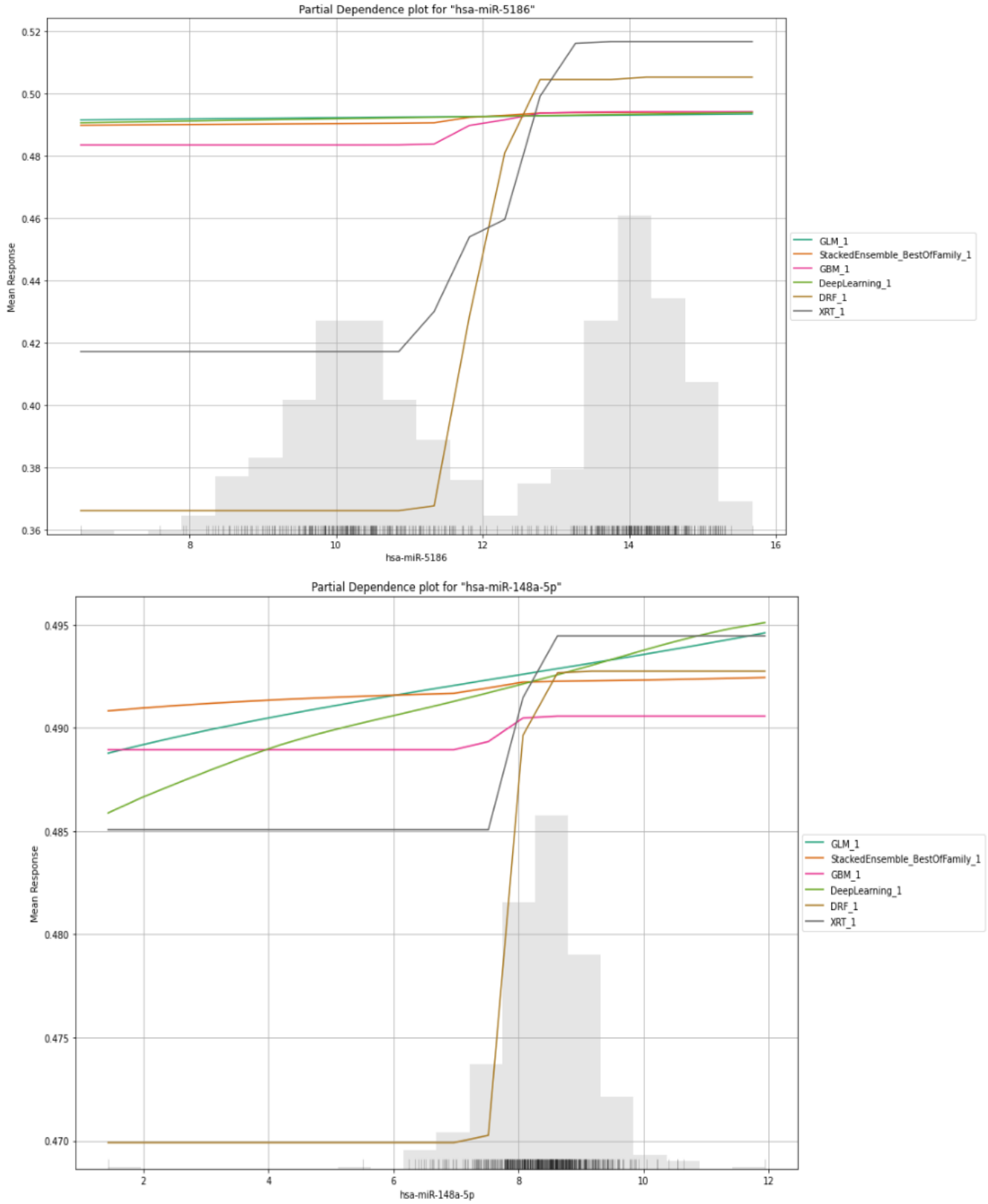

Fig. 14: Partial dependence plots for top 2 miRNAs in the gastric cancer variable importance plot. Contrary to the other miRNA plots, the mean response for the gastric cancer model reversed, meaning that as the expression of the miRNA increased, the frequency of cancer patients got higher.

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The partial dependence plots display above play a crucial role in the further development of this model. Partial dependence is a further extension of the variable importance plots, which displays the marginal effect of a single miRNA with variable levels of expression on the outcome of whether the patient has cancer or not. The partial dependence plot can also reveal the contour of the relationship, and its nature in terms of linear, exponential, or complex. The partial dependence plots also show the specific levels of expression in which cancer is most commonly found, which can be used for the further development of a therapeutic model.

After this, taking the top miRNAs, putting them into mirBase, and getting gene targets, we then found overlapping gene targets within the top 2 miRNAs and performed pathway analysis. Pathway analysis yielded certain high-entity pathways, which allowed us to generate these pathway plots (below).

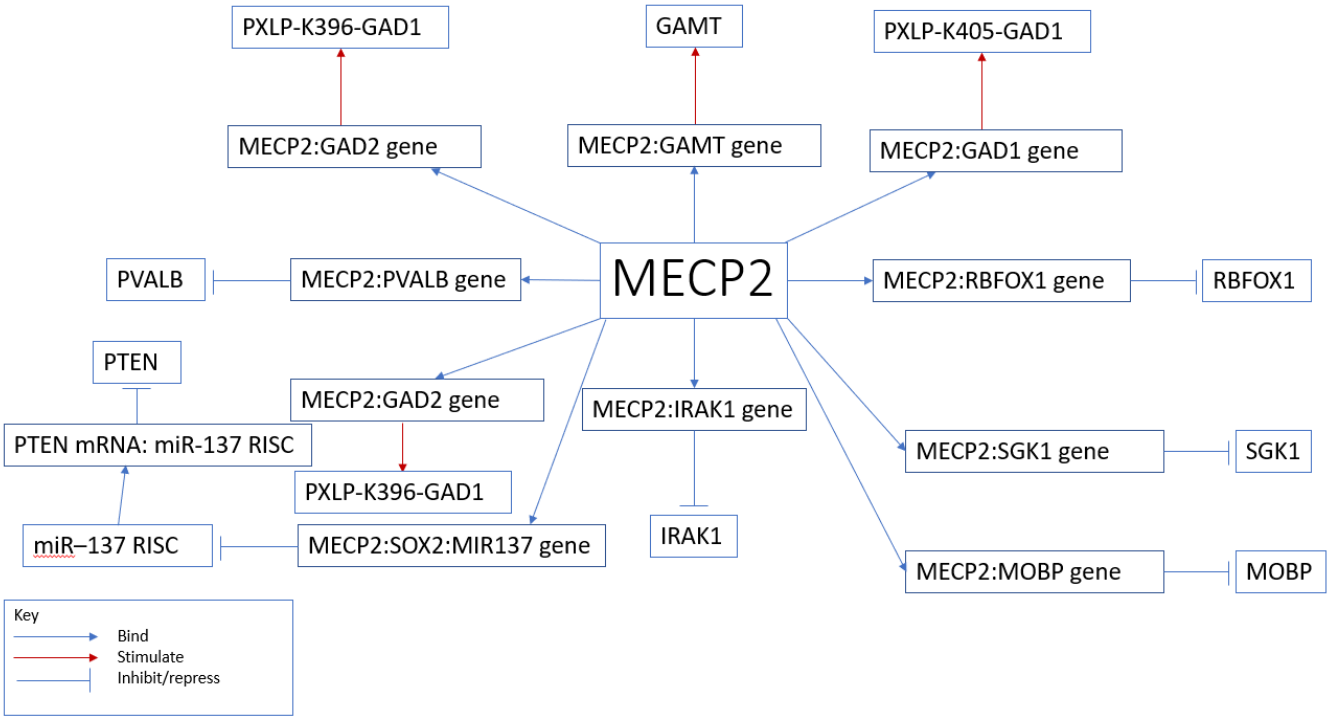

Fig. 15: The MECP2 pathway appeared multiple times with high entity counts in pathway analysis of gastric cancer. The graph depicts the gene targets that the miRNA contains, and their connection to the MECP2 pathway.

Pathway plots display the network of genes that a specific pathway promotes/inhibits. In this case, we chose MECP2 as it was recurring over multiple cancers. Looking at any gene here such as RBFOX1, which is downregulated in cancer, we can infer that since MECP2 inhibits RBFOX1, MECP2 is overexpressed in cancer.

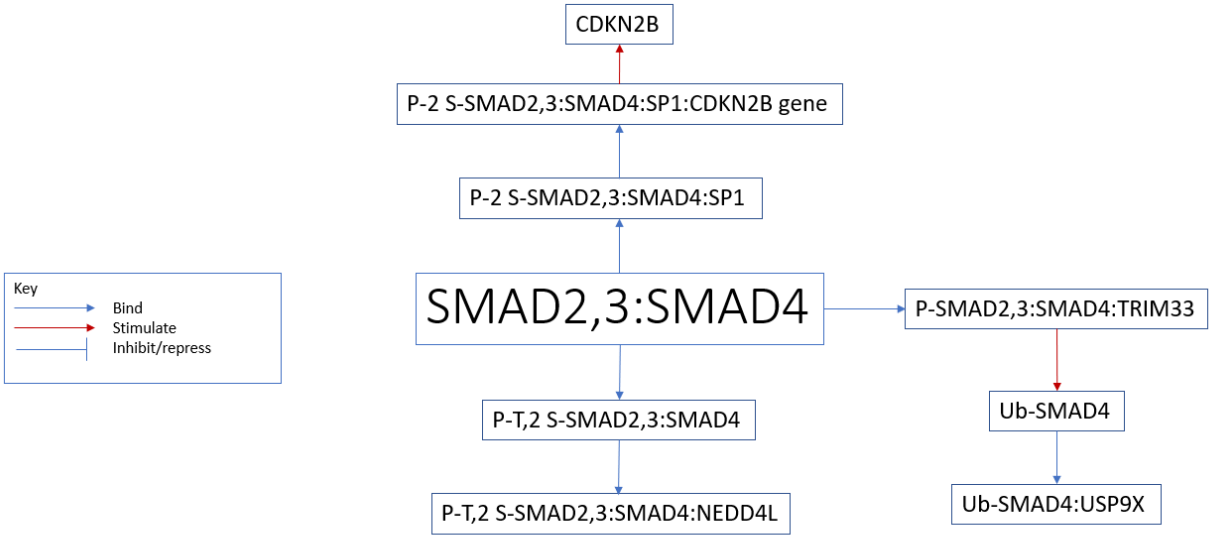

Fig. 16: The SMAD2,3:SMAD4 pathway appeared multiple times with high entity counts in pathway analysis of lung and esophageal cancer. The graph depicts the gene targets that the miRNA contains, and their connection to the pathway.

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CHAPTER FOUR

IMPLICATIONS AND CONCLUSION

A. Magnitude of impact

This model can be used side-by-side during health checkups because miRNA screening can take place as soon as blood samples are extracted. The impact of this could be significant for two main reasons. Firstly, in areas where access to healthcare is more limited, or inaccessible, a non-invasive and effective method will enable cancer to be diagnosed during health checks. Secondly, the early diagnosis of cancer is crucial to prevent the progression of symptoms, which would also in turn increase the survival rate. Although this method of testing still requires the patient to attend regular health checks, it is still a great increase in accessibility compared to those who do tests for cancer only. Waiting for symptoms to appear before seeking treatment is detrimental to chances of recovery, and recovering at later stages could cause permanent disabilities. Additionally, a less invasive method for cancer detection could motivate many who were deterred by the invasiveness of traditional cancer detection to partake in testing.

A single miRNA binds to many gene transcripts, therefore it is hard to elucidate the pathways that miRNAs regulate because of how many genes they regulate. Through our analysis, we were able to find miRNAs that have a shared relationship with cancer, in terms that they are linked to a similar cancer outcome. They may not both be over/underexpressed, but they are both linked to a cancer outcome, by then comparing the targets of these miRNAs, we can narrow down those which are in common. Performing a pathway analysis allows us to find novel pathways that are linked to these miRNAs.

B. Related works

An early published paper on machine learning combined with liquid biopsy techniques was published in 2018 by Jina Ko, in which they specifically investigate liquid biopsy-related diagnosis of pancreatic ductal adenocarcinoma (PDAC). In this experiment, they performed miRNA profiling of mice with PDAC and normal mice, with a dataset of only 84 mice in total. Overall, this paper serves as an introductory proof-of-concept of how machine learning can be used with miRNA profiling to identify cancer-inducing miRNAs. However, in this paper, limitations such as a small dataset (only 88% accuracy), one specific cancer, and non-human samples are taken into account as limitations for further development.

Developments after this can be seen from improvements to human samples with lung cancer in a research paper by Tobias Fehlmann in 2020, where the accuracy also increased to upwards of 97.7%, and the dataset ranged up to 3000 total samples. The limitation of this study is again that it is limited to one cancer, along with having suboptimal levels of accuracy.

The latest work published in December 2022 focuses primarily on breast cancer and the real-life applications of miRNA as non-invasive biomarkers.

C. Further study

In the future, a few immediate goals would be to implement a wider range of cancer types into the model. This would allow for wider coverage, as the current model is limited to esophageal, gastric, and lung cancer. While more cancers are included, diagnostic accuracy must remain the same, or even higher. Currently, the datasets are limited to below 5,500 data points for training, an increase in data would be beneficial to increasing diagnostic accuracy as well. On top of this, the model could potentially develop into a different field, also involving miRNAs, such as viral infections. Eventually, if the model's accuracy can be validated, it could be implemented as a tool for doctors to use alongside their own diagnostic abilities, to further refine the process of the detection of cancer among the population.

D. Conclusion

Overall, this project serves as a hypothetical model for a future diagnostic method for cancer treatment. A model with a high AUC of 0.99-1 was generated and consolidated to validate prediction results. This project demonstrates how machine learning can be integrated into hospitals for therapeutic usage, and how doctors can use this tool to diagnose cancer sufferers at an earlier stage, which could be greatly beneficial to increasing overall coverage of cancer treatment, and lowering treatment costs. Crucial statistics for the future development of a therapeutic model were obtained via partial dependence plots, along with leaderboard miRNAs indicative of cancer. An in-depth evaluation of potential targetted therapy along with specialized medicine was produced, giving a prediction of how realistic employing this diagnosis-treatment strategy truly is.

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