# PREDICTING TISSUE-SPECIFIC GENE EXPRESSION FROM BLOOD USING AI

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# INTRODUCTION

**Gene expression**

- Measured through RNA sequencing
- Indicates the “activation level” of genes in a tissue
- Used to understand disease mechanisms and assess the effectiveness and safety of treatments

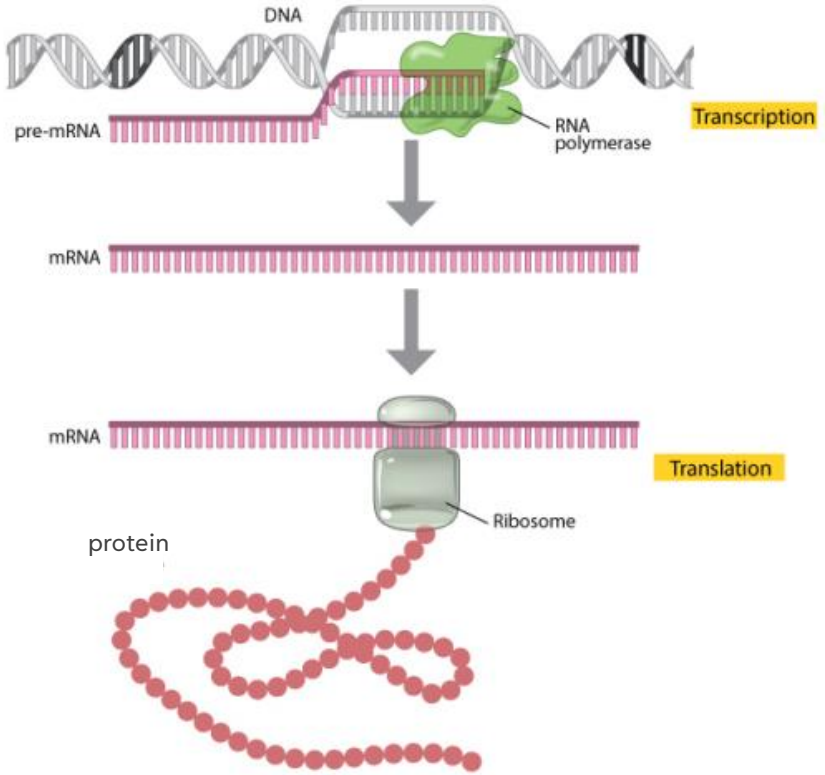
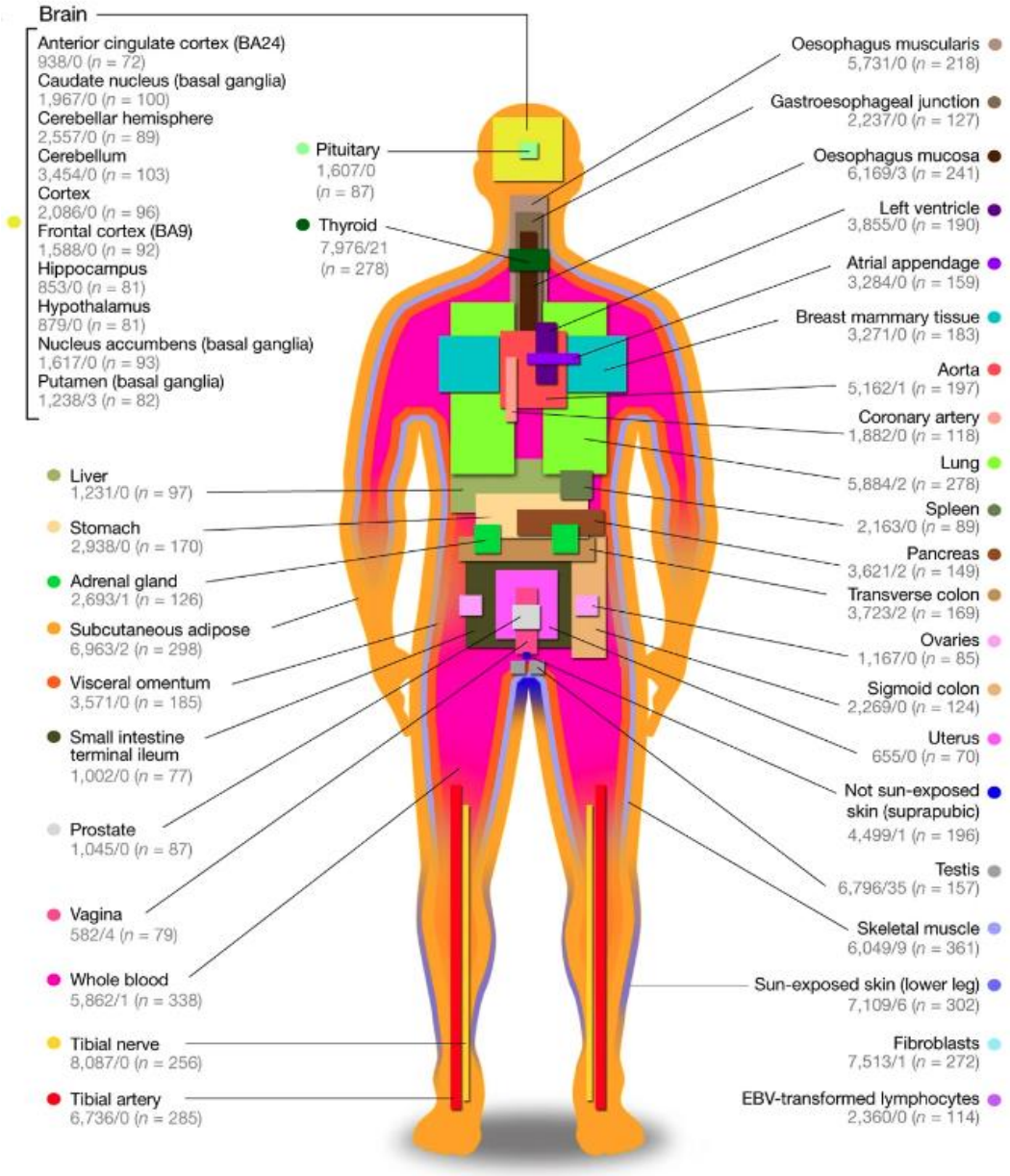



Image source: https://www.nature.com/




# DATA

The Genotype-Tissue Expression (GTEx)

Publicly available dataset containing gene expression of 54 post-mortem tissues from almost 1,000 individuals

Website: https://www.gtexportal.org/home/

Image source: https://www.researchgate.net/figure/Sample-and-data-types-in-the-GTEx-v8-study-A-Illustration-of-the-54-tissue-types_fig1_336246636

# PROBLEM

- Gene expression varies across tissues
- Obtaining samples from heart, lung, brain and other organs is often not possible

# GOAL

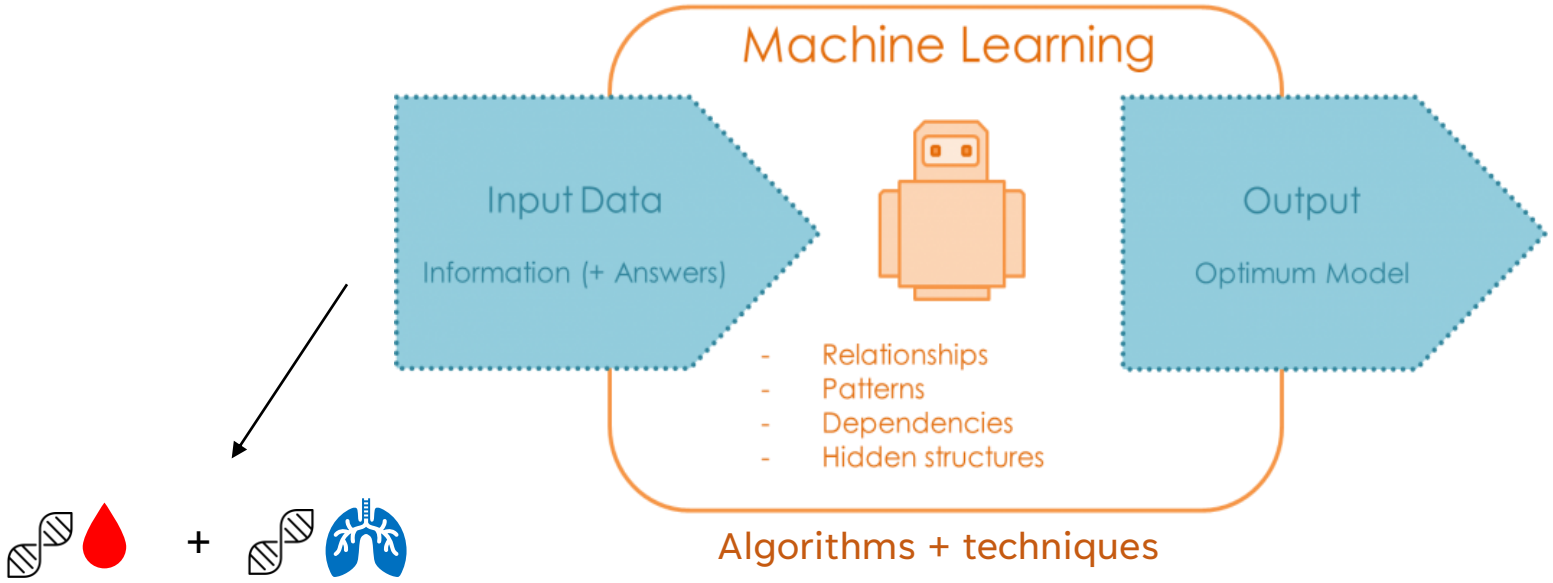
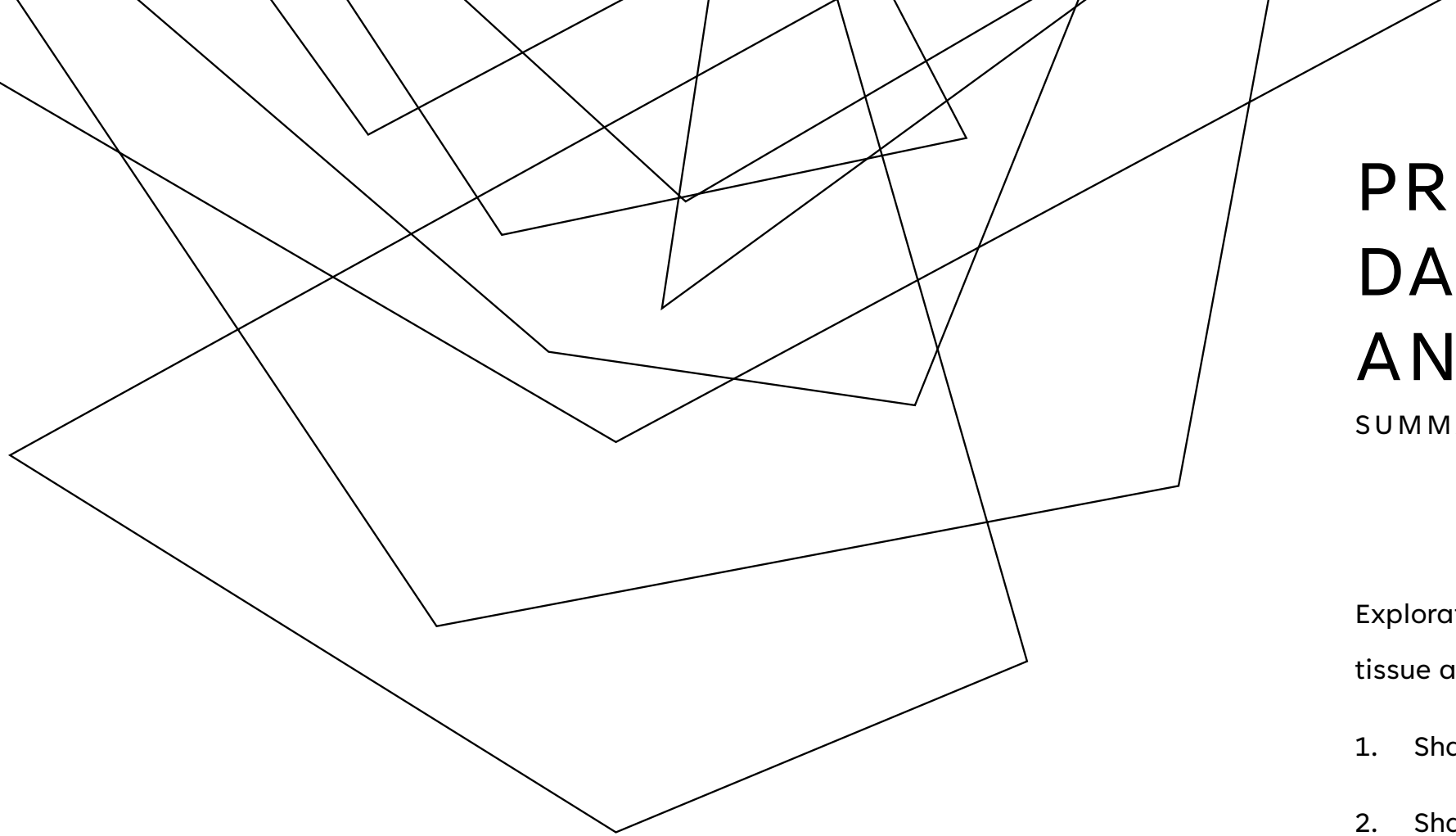



Image source: https://quantdare.com/

# DATA PRE-PROCESSING

| | NOC2L | KLHL17 | PLEKHN1 | HES4 | ISG15 | AGRN | C1orf159 |
|---|---|---|---|---|---|---|---|
| GTEX-111YS | 4.623645 | 1.9305234 | -0.757455296 | -2.04196059 | 3.202670 | 0.34305222 | 2.644519 |
| GTEX-1122O | 3.782539 | 1.2749997 | -2.178112437 | -0.37572051 | 3.300398 | 1.14820160 | 1.781592 |
| GTEX-1128S | 4.513360 | 3.5022390 | 0.886702570 | -0.07257490 | 2.585954 | 2.74835104 | 3.438855 |
| GTEX-117YW | 5.452794 | 3.5097032 | -0.361040851 | 1.20675685 | 4.961396 | 2.66612637 | 3.895245 |
| GTEX-11DXX | 3.375196 | 1.8264574 | -2.001951642 | -3.55957777 | 2.441123 | 0.46472915 | 1.706664 |
| GTEX-11DXZ | 4.473020 | 2.6155735 | -0.020073254 | 0.27319390 | 3.814766 | 2.14063671 | 2.751952 |
| GTEX-11EI6 | 4.503837 | 3.7731937 | -0.089162153 | 0.96350723 | 3.581990 | 1.66687554 | 3.257955 |
| GTEX-11EMC | 4.689939 | 2.7730465 | 1.233797566 | 2.48327357 | 6.018670 | 2.15817703 | 3.950064 |
| GTEX-11EQ9 | 3.966465 | 1.7293461 | -1.366626237 | -2.34489017 | 2.402989 | 1.00785226 | 2.256939 |
| GTEX-11GSP | 4.713622 | 3.0192610 | -0.137642769 | 1.52595816 | 4.664902 | 1.89930115 | 3.458261 |

| | NOC2L | KLHL17 | PLEKHN1 | HES4 | ISG15 | AGRN | C1orf159 |
|---|---|---|---|---|---|---|---|
| GTEX-111YS | 5.564605 | 3.605865 | -0.26752148 | 3.184108 | 3.877916 | 6.992831 | 3.997613 |
| GTEX-1122O | 5.874426 | 3.966150 | 0.51738596 | 3.422275 | 4.272583 | 7.030410 | 4.070818 |
| GTEX-1128S | 5.970547 | 4.392573 | 1.41139215 | 3.491767 | 4.466593 | 6.707747 | 4.035884 |
| GTEX-117YW | 5.166227 | 4.029355 | 1.74797744 | 5.045113 | 5.187642 | 7.266217 | 4.812552 |
| GTEX-11DXX | 5.958369 | 4.006143 | 0.23257945 | 2.753910 | 3.901730 | 7.207189 | 4.116435 |
| GTEX-11DXZ | 5.771633 | 4.627956 | 2.85381134 | 3.622749 | 5.236977 | 8.041496 | 4.574765 |
| GTEX-11EI6 | 5.211195 | 4.826346 | 1.46932243 | 4.520421 | 5.145422 | 7.703033 | 4.195147 |
| GTEX-11EMC | 5.748173 | 3.427566 | 1.95369092 | 4.087649 | 3.857217 | 6.868381 | 4.153474 |
| GTEX-11EQ9 | 6.000552 | 3.625458 | 0.79048291 | 2.635259 | 3.707483 | 6.842565 | 3.919237 |
| GTEX-11GSP | 6.049516 | 4.244247 | 1.64588696 | 5.739212 | 5.385897 | 7.577261 | 4.412140 |



# PRELIMINARY DATA ANALYSIS

SUMMARY OF PART 1

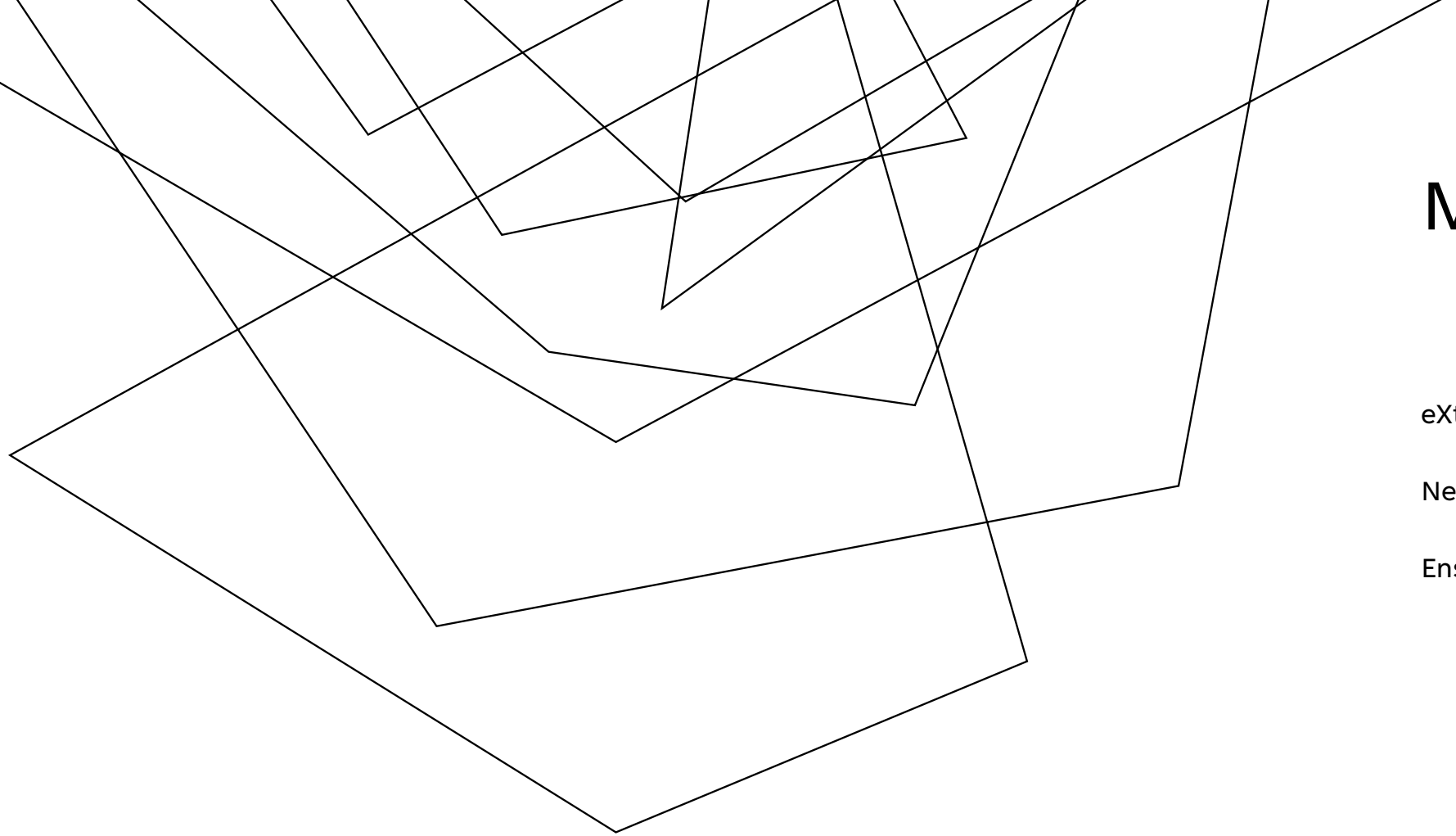
Exploration of **similarities** between each tissue and whole blood

1. Shared **donors**
2. Shared expressed **genes**
3. Gene expression **correlation**

# TISSUE SELECTION

Rank tissues based on the previously observed measures

| Subtissue | Donor Proportion | Donor Rank | Gene Proportion | Gene Rank | Mean Absolute Correlation | Correlation Rank | Average Rank |
|---|---|---|---|---|---|---|---|
| Lung | 0.619 | 8 | 0.983 | 2 | 0.227 | 7 | 5.67 |
| Adipose - Visceral (Omentum) | 0.585 | 10 | 0.966 | 11 | 0.196 | 10 | 10.33 |
| Spleen | 0.268 | 26 | 0.984 | 1 | 0.243 | 6 | 11 |
| Thyroid | 0.691 | 5 | 0.966 | 12 | 0.18 | 19 | 12 |
| Adipose - Subcutaneous | 0.71 | 4 | 0.956 | 18 | 0.171 | 22 | 14.67 |
| Esophagus - Muscularis | 0.56 | 12 | 0.944 | 25 | 0.205 | 9 | 15.33 |
| Breast - Mammary Tissue | 0.503 | 13 | 0.967 | 8 | 0.154 | 28 | 16.33 |
| Colon - Transverse | 0.448 | 17 | 0.97 | 5 | 0.157 | 27 | 16.33 |
| Esophagus - Mucosa | 0.6 | 9 | 0.958 | 15 | 0.162 | 26 | 16.67 |
| Nerve - Tibial | 0.668 | 6 | 0.955 | 19 | 0.164 | 25 | 16.67 |
| Artery - Aorta | 0.477 | 15 | 0.948 | 23 | 0.186 | 15 | 17.67 |
| Skin - Not Sun Exposed (Suprapubic) | 0.64 | 7 | 0.958 | 16 | 0.147 | 30 | 17.67 |
| Colon - Sigmoid | 0.415 | 18 | 0.954 | 20 | 0.182 | 17 | 18.33 |
| Adrenal Gland | 0.283 | 24 | 0.95 | 21 | 0.196 | 11 | 18.67 |
| Heart - Atrial Appendage | 0.457 | 16 | 0.943 | 27 | 0.191 | 13 | 18.67 |
| Esophagus - Gastroesophageal Junction | 0.409 | 19 | 0.943 | 26 | 0.194 | 12 | 19 |



# MODELS

eXtreme Gradient Boosting

Neural Network

Ensemble Model

# CROSS-VALIDATION

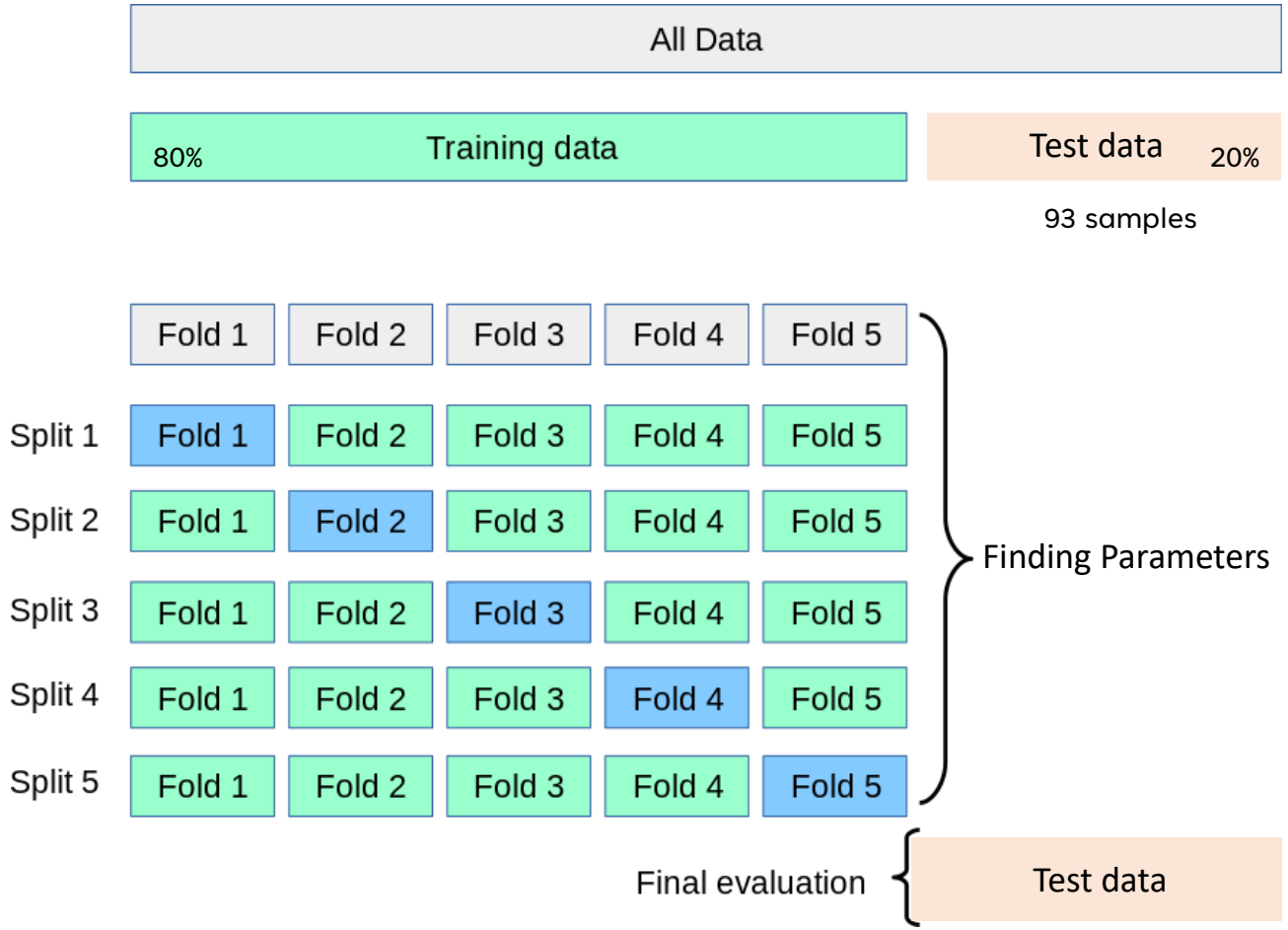





Image source: https://scikit-learn.org/stable/modules/cross_validation.html

# EXTREME GRADIENT BOOSTING (XGBOOST)

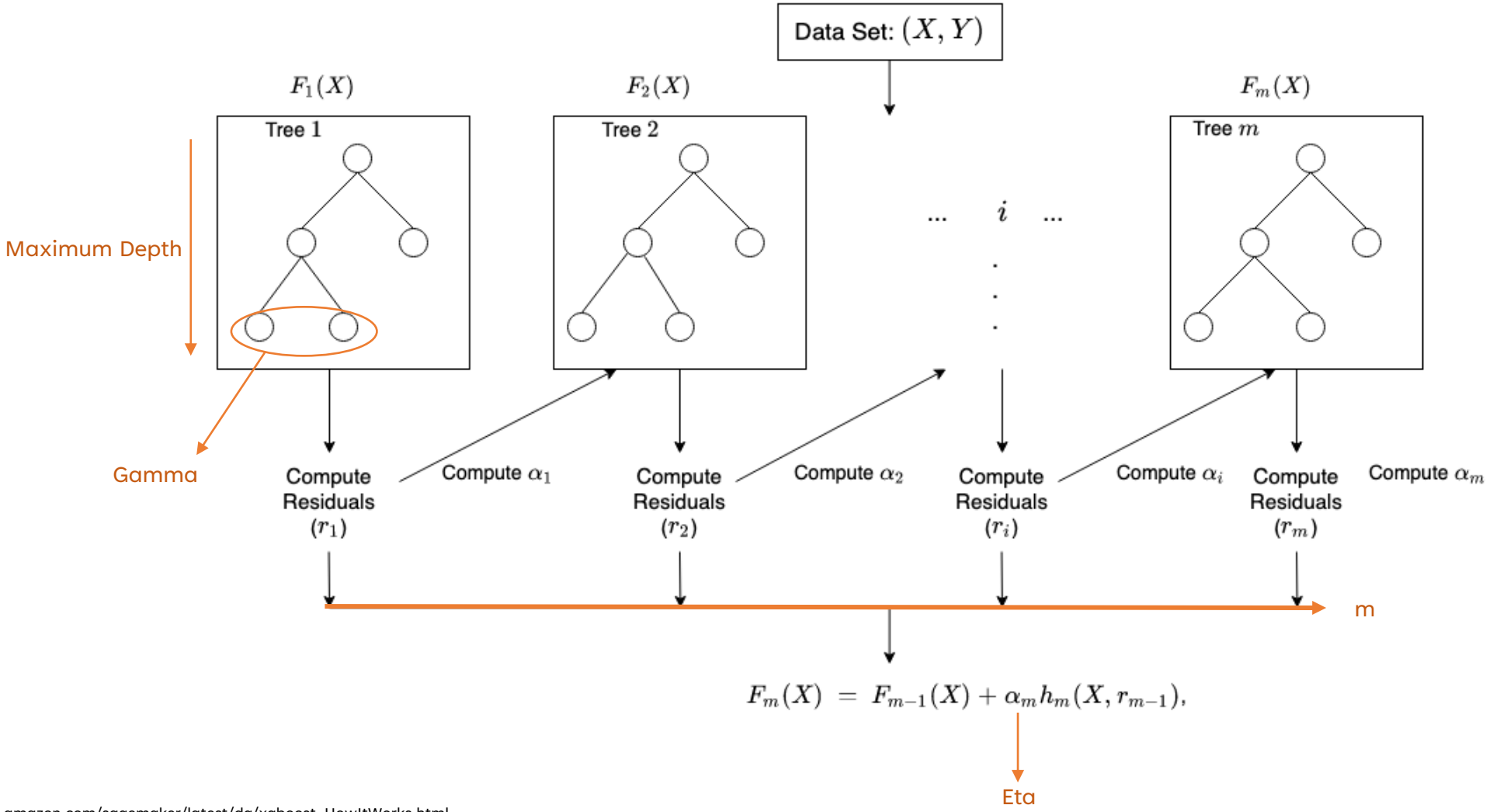
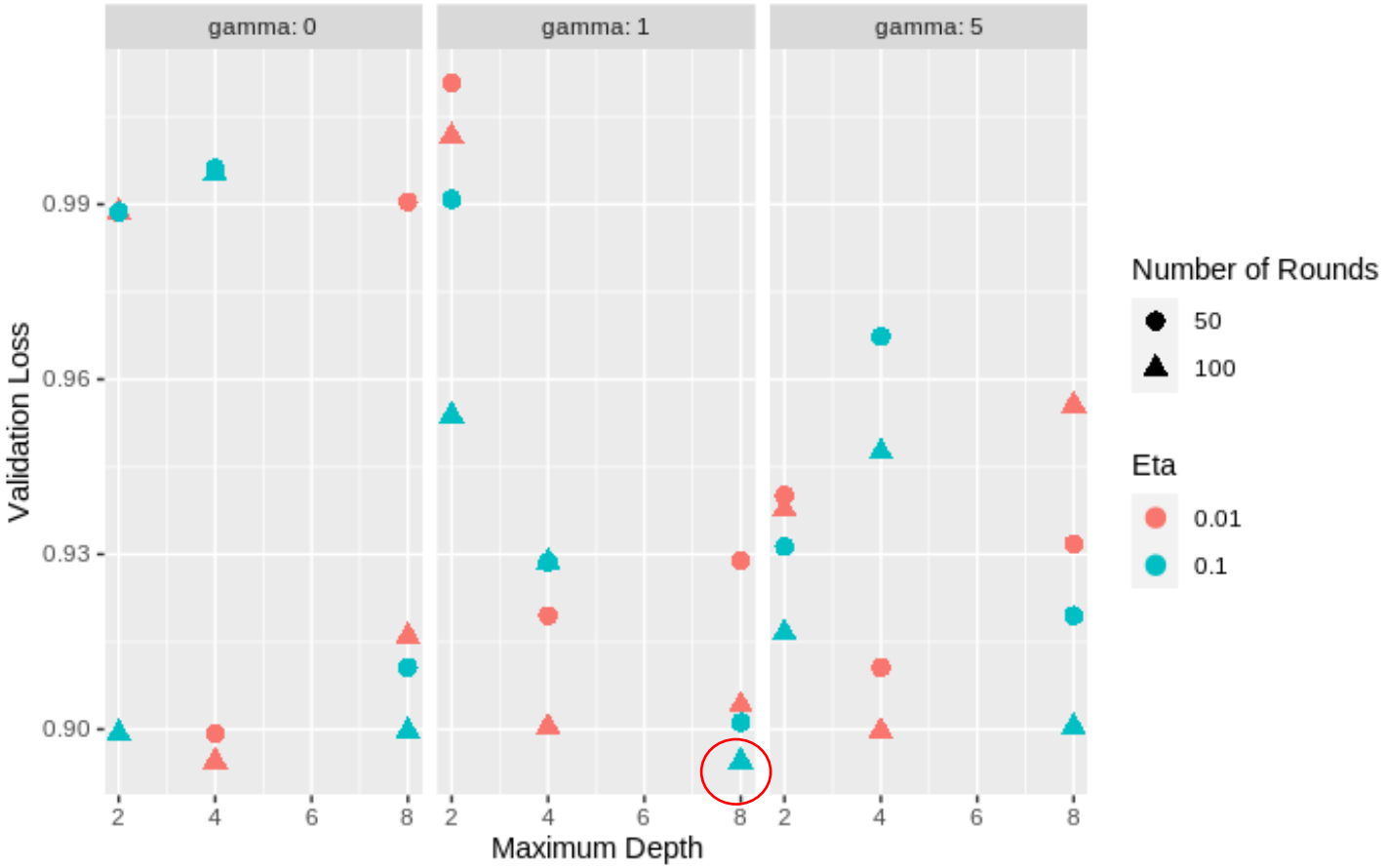



Image source: https://docs.aws.amazon.com/sagemaker/latest/dg/xgboost-HowItWorks.html

# HYPERPARAMETER TUNING

On 50 random genes

On gamma, maximum depth, eta, and number of rounds



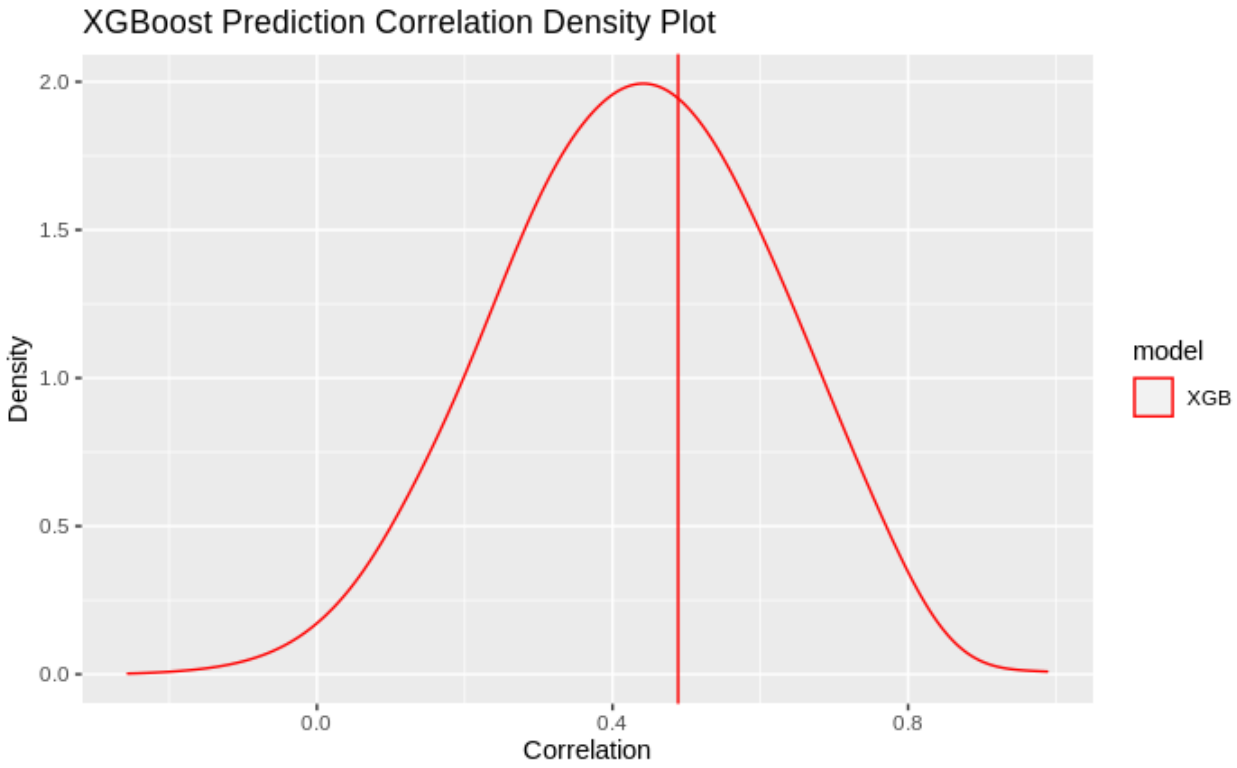

Loss Function

$$\text{MSE} = \frac{1}{n}\sum_{i=1}^{n}(y_i - \tilde{y}_i)^2$$

Best hyperparameter combination:
Gamma = 1
Maximum depth = 8
Eta = 0.1
Number of rounds = 100

# EVALUATION

Compute the correlation between each gene in the prediction and its true value




| Model | Median Correlation | |
|---|---|---|
| | Training | Test |
| XGBoost | 0.990975 | 0.4364047 |
| Neural Network | | |
| Ensemble | | |

# PERCEPTRON

SINGLE-LAYER NEURAL NETWORK

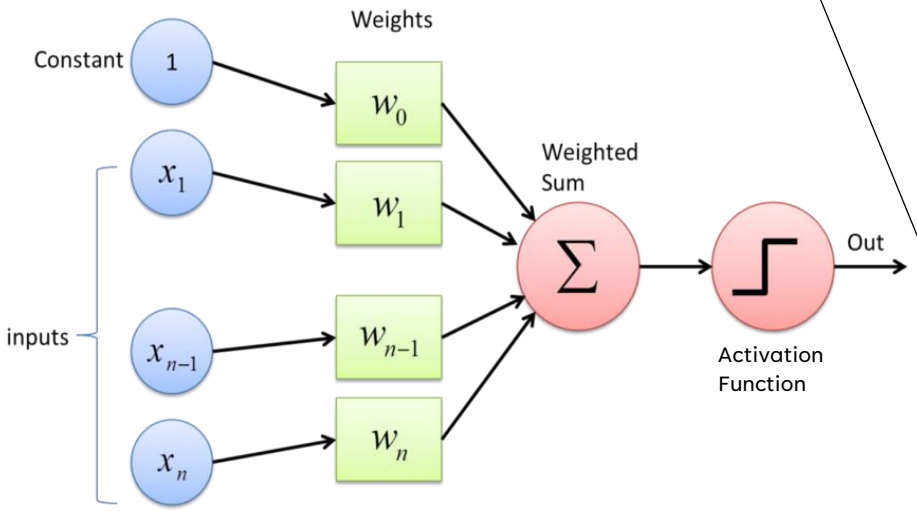



Image source: https://www.norwegiancreations.com/2019/04/introduction-to-neural-network/

# MULTILAYER PERCEPTRON

NEURAL NETWORK

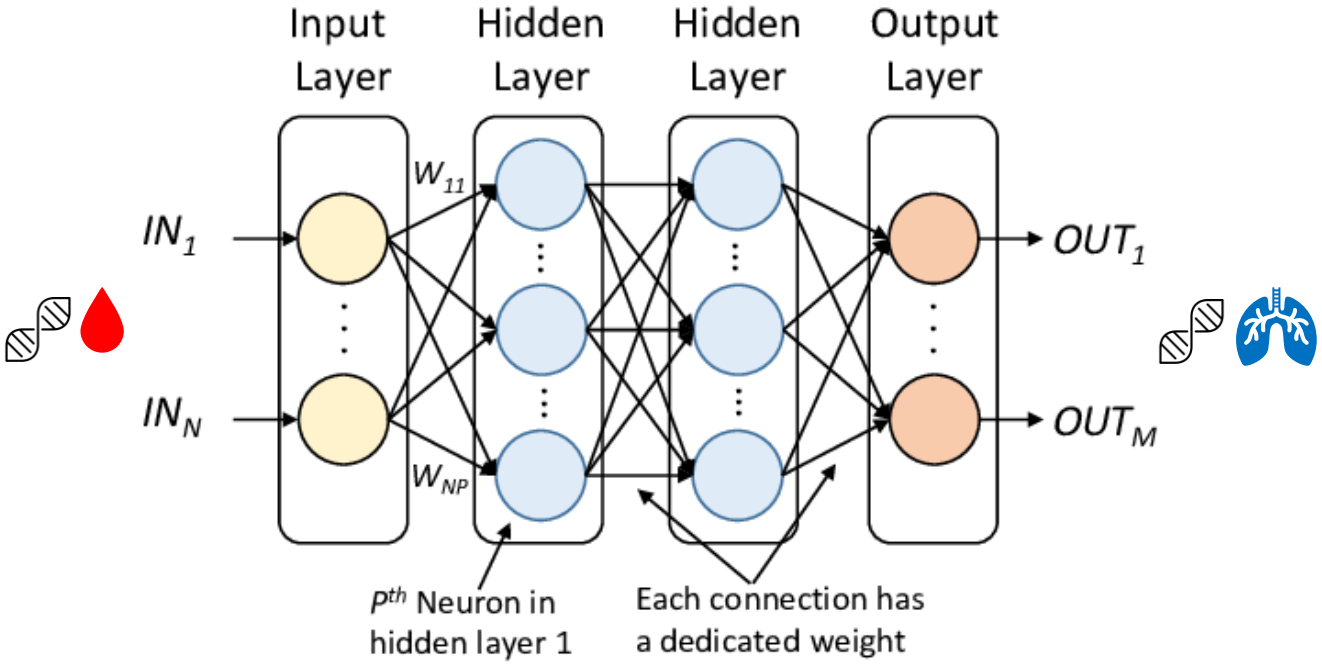
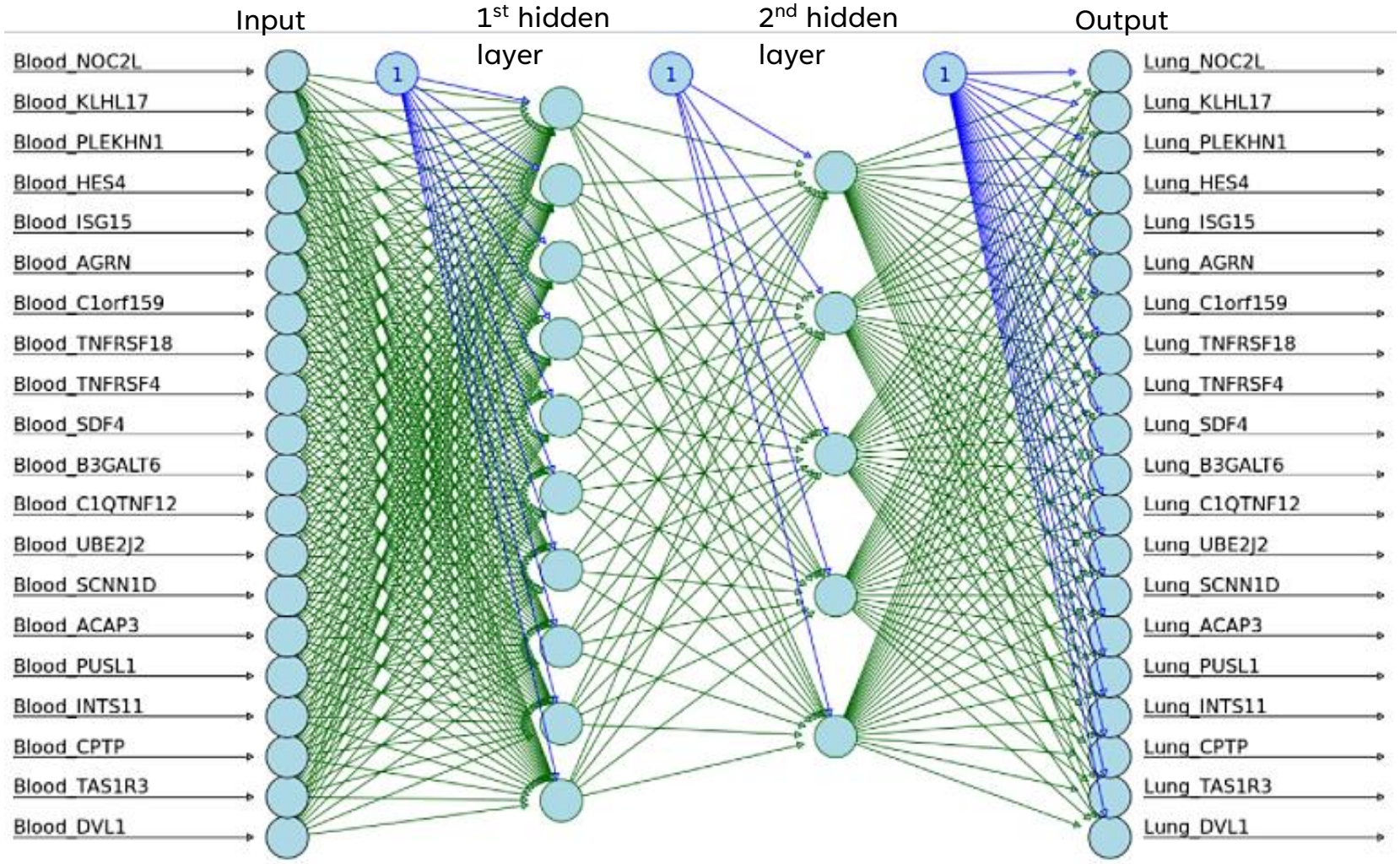


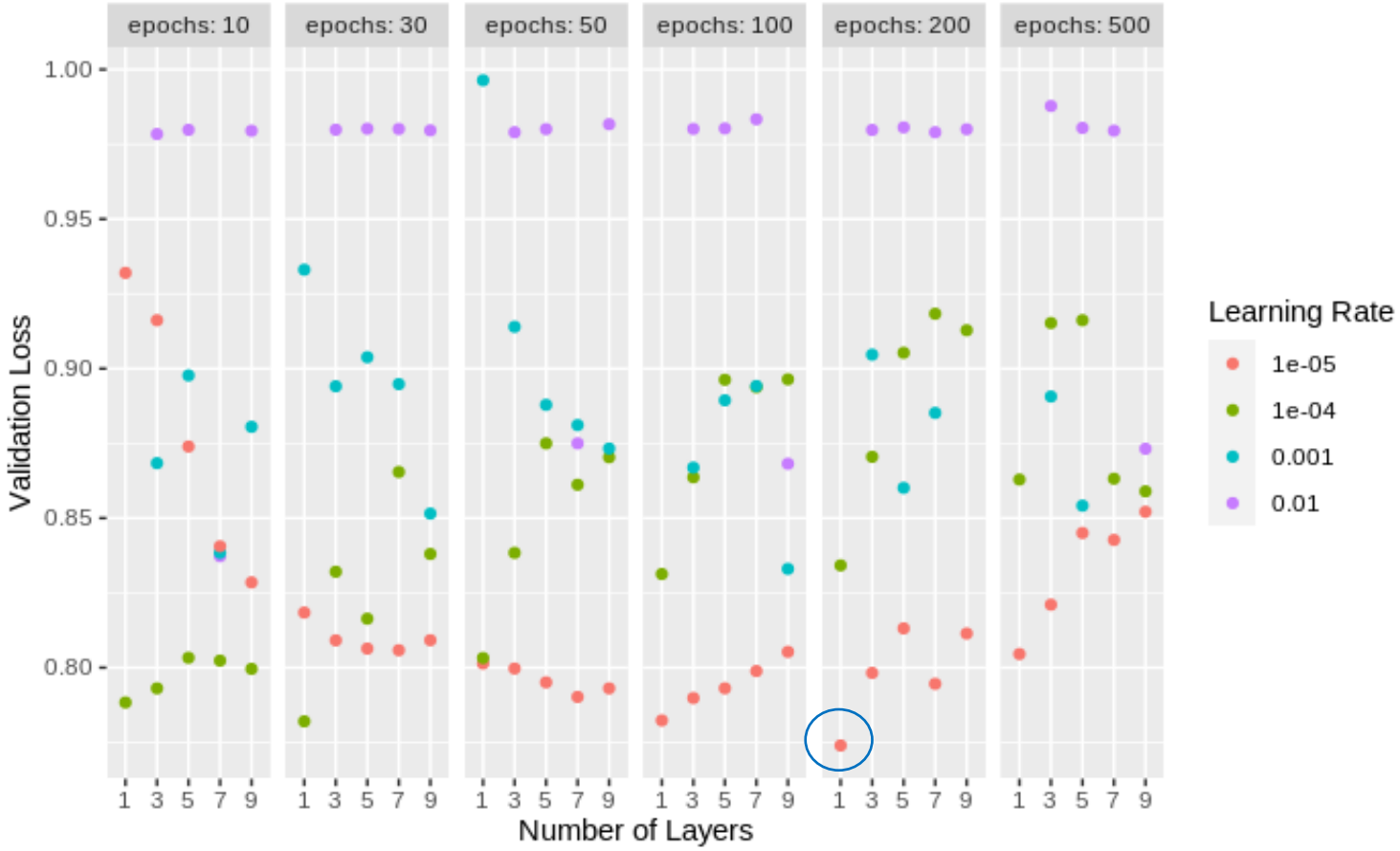

Image source: https://www.simplilearn.com/tutorials/deep-learning-tutorial/multilayer-perceptron

# NEURAL NETWORK ILLUSTRATION



# HYPERPARAMETER TUNING

On number of layers, learning rate, and number of epochs



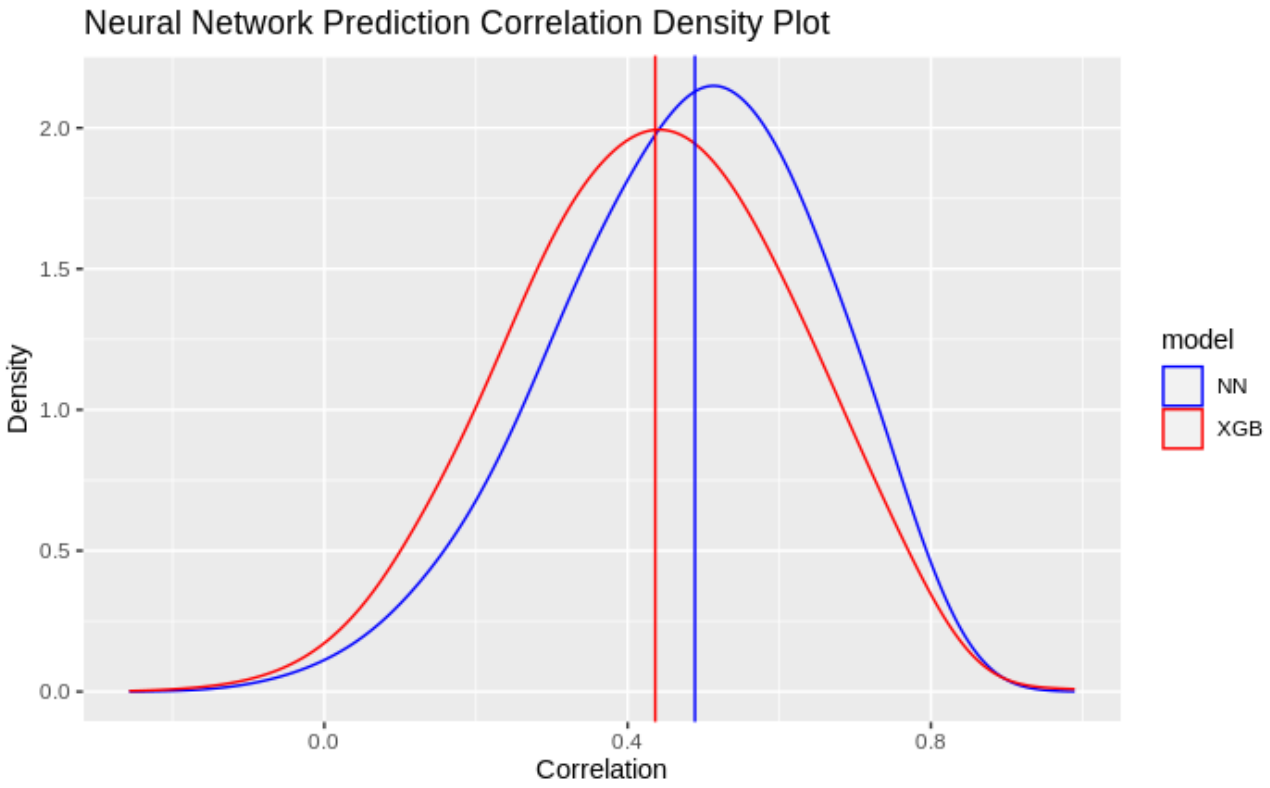

Loss Function

$$\text{MSE} = \frac{1}{n}\sum_{i=1}^{n}(y_i - \tilde{y}_i)^2$$

Best hyperparameter combination:
1 hidden layer of 100 units
Learning rate = $e^{-5}$
Epochs = 200

# EVALUATION

Compute the correlation between each gene in the prediction and its true value



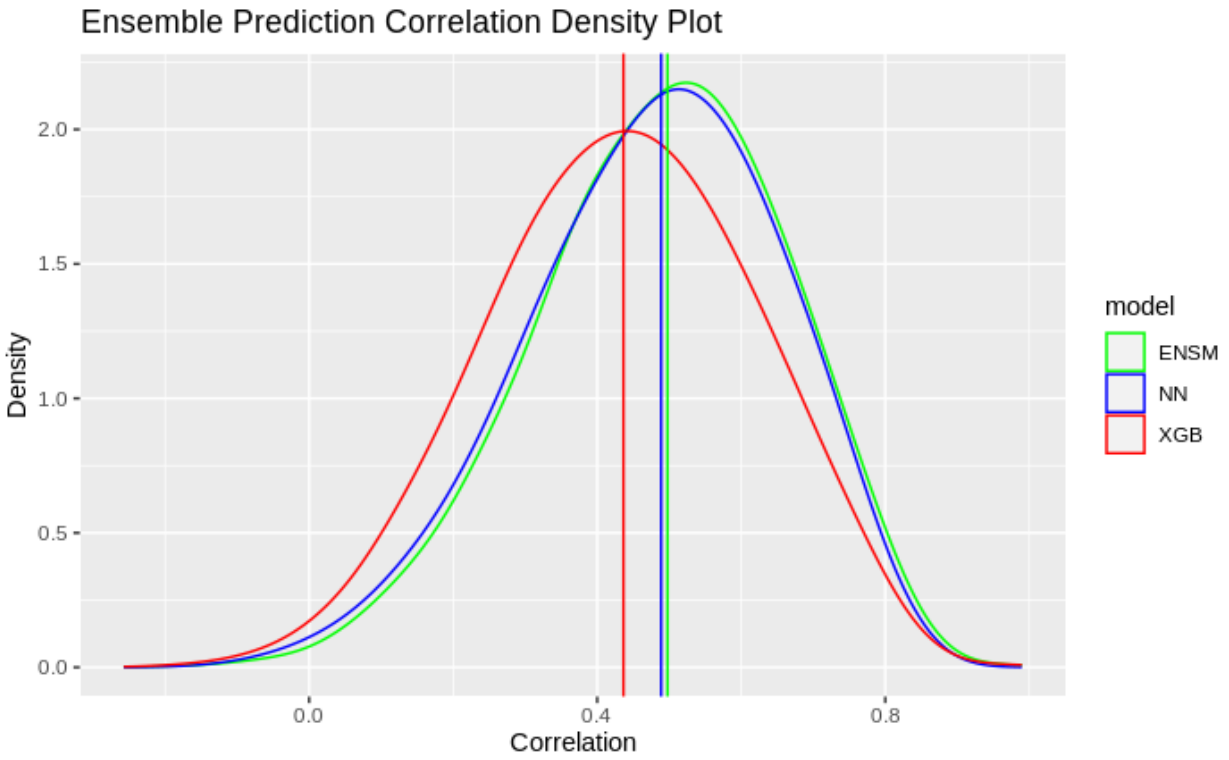

| Model | Median Correlation | |
|---|---|---|
| | Training | Test |
| XGBoost | 0.990975 | 0.4364047 |
| Neural Network | 0.6278658 | 0.4887672 |
| Ensemble | | |

# ENSEMBLE MODEL

$$ENSpred = \frac{1}{2}NNpred + \frac{1}{2}XGBpred = \frac{1}{2}\begin{bmatrix} \hat{y}_{11} & \cdots & \hat{y}_{1p} \\ \vdots & \ddots & \\ \hat{y}_{n1} & \cdots & \hat{y}_{np} \end{bmatrix} + \frac{1}{2}\begin{bmatrix} \hat{z}_{11} & \cdots & \hat{z}_{1p} \\ \vdots & \ddots & \\ \hat{z}_{n1} & \cdots & \hat{z}_{np} \end{bmatrix}$$

# EVALUATION

Compute the correlation for each gene in the prediction and the true value




| Model | Median Correlation | |
|---|---|---|
| | Training | Test |
| XGBoost | 0.990975 | 0.4364047 |
| Neural Network | 0.6278658 | 0.4887672 |
| Ensemble | 0.9205496 | 0.4976427 |

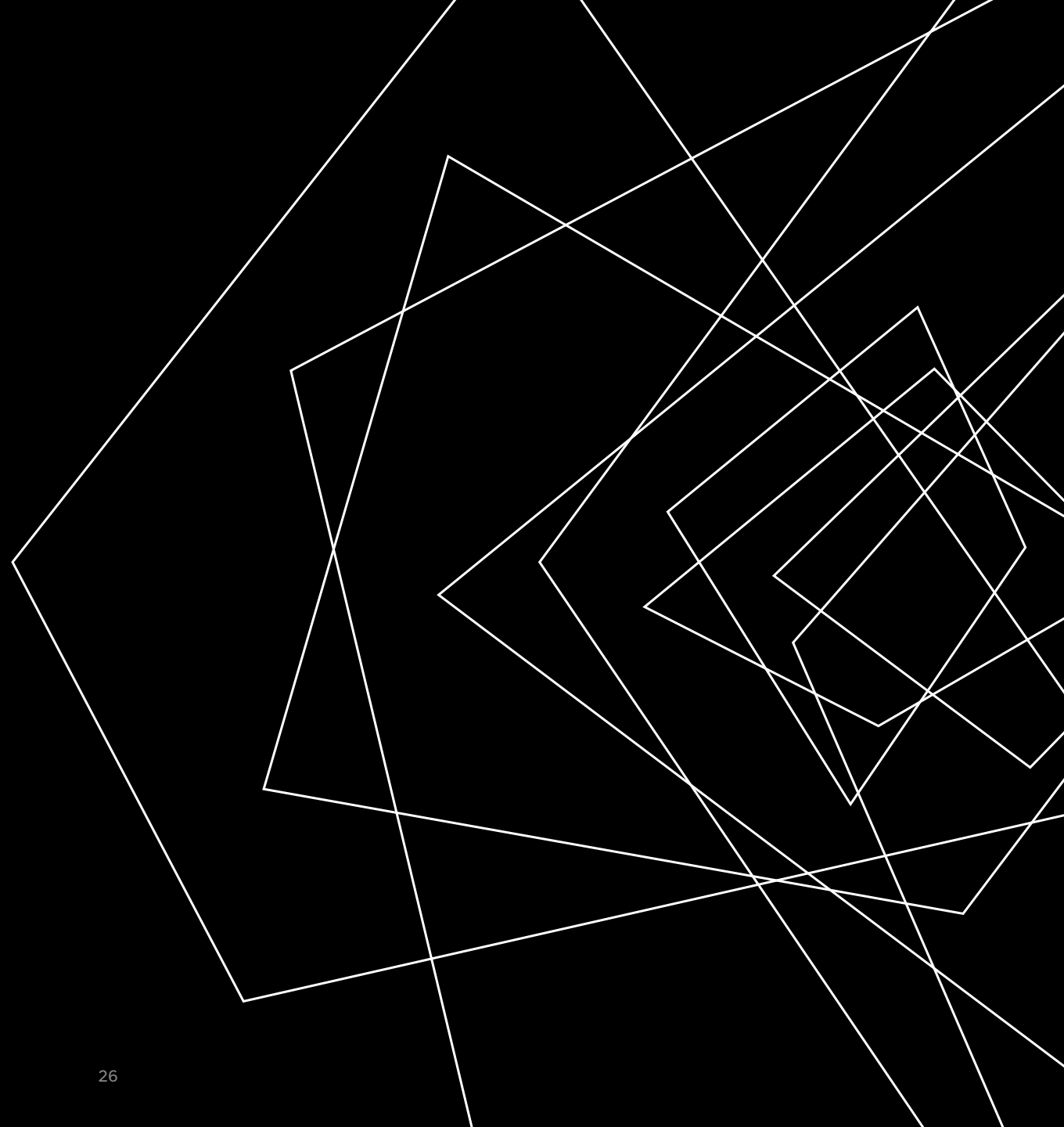
# FUTURE DIRECTIONS

Training the models on all other tissues, on the entire dataset

Stacking ensemble for improved prediction

Biological validation

Implementation of the web application



# WE WOULD LIKE TO EXTEND A HEARTFELT THANK YOU TO ALL OUR MENTORS INVOLVED IN THIS PROJECT!

Dr. Roberto Bonelli, CSL Research
Dr. Brendan Ansell, WEHI

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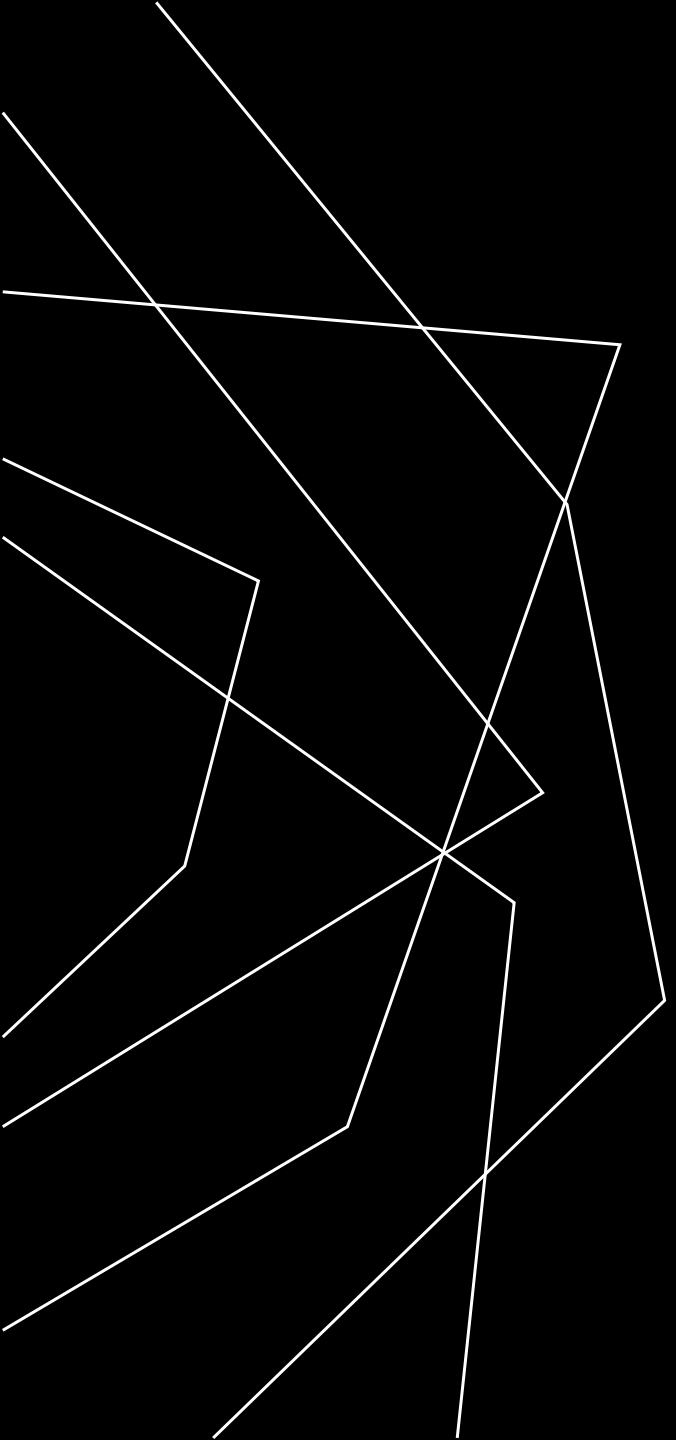
Dr. Monther Alhamdoosh, CSL Research
Dr. Melanie Bahlo, WEHI

Dr. Ziad Al Bkhetan, The University of Melbourne
Dr. Michael Kirley, The University of Melbourne



# THANK YOU