

# Development of a Frailty Risk Score Model

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# Method

**Muscle Biopsy  
RNA-Seq Data**  
58,283 RNA transcripts  
80 Samples  
41 Male, 39 Female  
24 pre-frail (13 male, 11 female)  
26 young (13 male, 13 female),  
30 fit (15 male, 15 female)

*Data*



**Data Preprocessing**  
Map transcripts:  
35,835 genes  
Remove lowly-expressed  
genes (counts < 10):  
20,296 genes



**DE Analysis**  
LFC > 1 or LFC < -1,  
p < 0.05  
222 genes

*Feature Reduction*



**Recursive Feature  
Elimination**  
Estimator: Random Forest  
10-fold CV  
CV-Score = 0.785  
164 genes



**Minimum Redundancy  
Maximum Relevance  
(MRMR)**  
Top 5-10 genes

*Feature Selection*



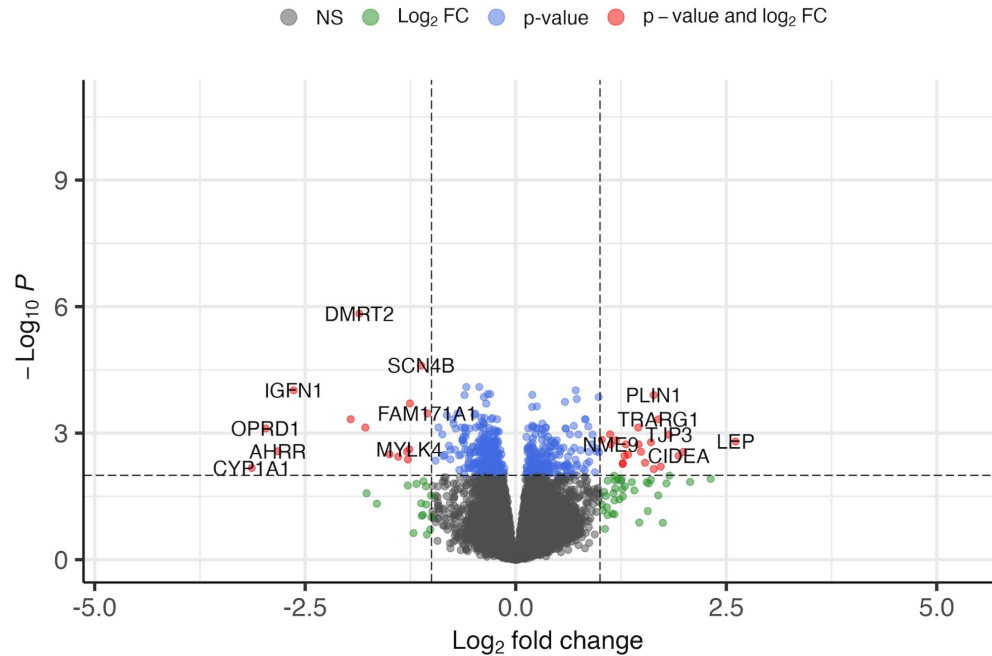
**Multinomial Logistic  
Regression Classifier**  
5 genes

*Model Development*

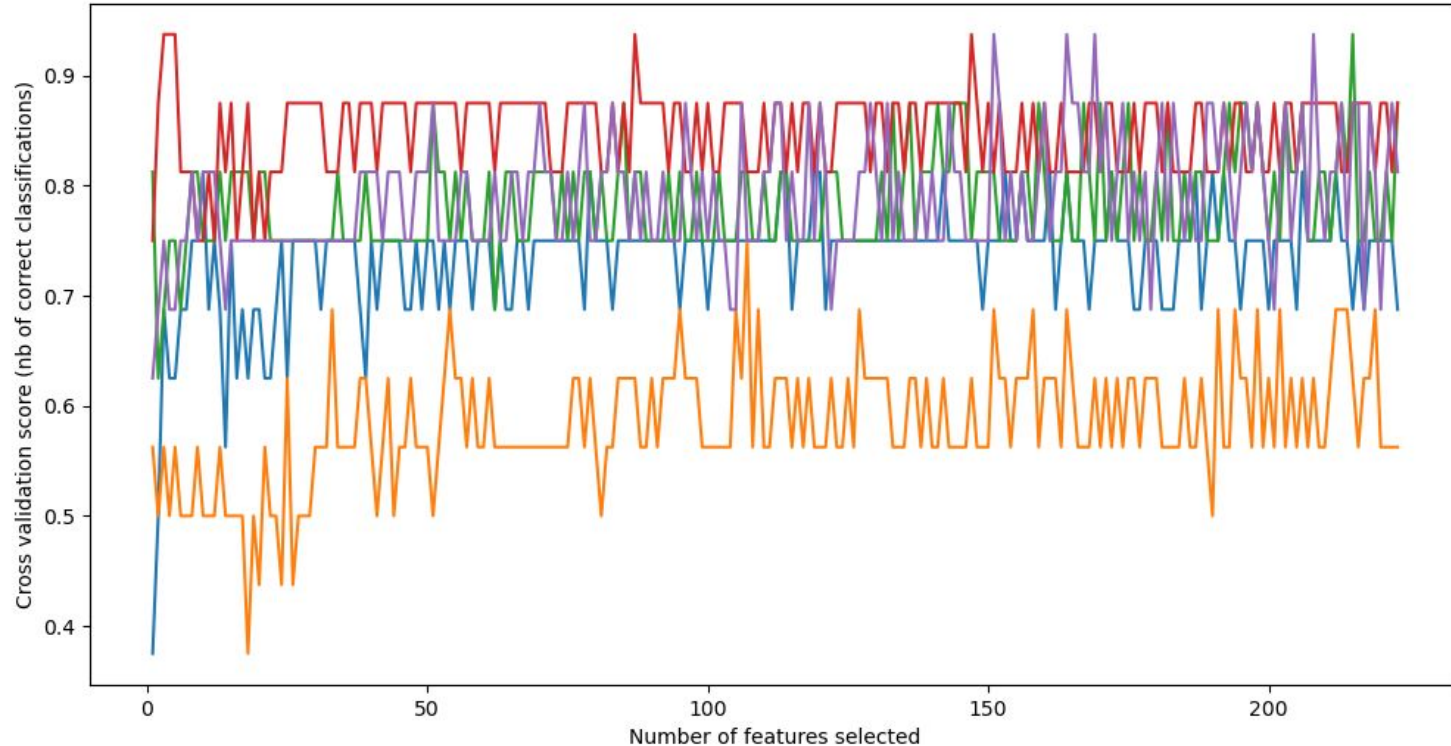
# DE Analysis

## Volcano plot

*EnhancedVolcano*



# Recursive Feature Elimination using Random Forest



# GO Pathways (Molecular Function)

164 Genes

	<a href="#">Homo sapiens</a> (REF)	<a href="#">upload_1</a> ( <a href="#">Hierarchy</a> ) <b>NEW!</b> (?)					
<a href="#">GO molecular function complete</a>	▲ #	#	<a href="#">expected</a>	<a href="#">Fold Enrichment</a>	<a href="#">+/-</a>	<a href="#">raw P value</a>	<a href="#">FDR</a>
<a href="#">protein tyrosine kinase activator activity</a>	<a href="#">34</a>	<a href="#">6</a>	.30	20.19	+	1.17E-06	5.92E-03
<a href="#">signaling receptor regulator activity</a>	<a href="#">567</a>	<a href="#">17</a>	4.96	3.43	+	1.38E-05	3.49E-02

# Minimum Redundancy Maximum Relevance (MRMR)

## Top 5 genes

- Accuracy = 0.9
- AUC = 0.884

<i>Predictors</i>	<i>Odds Ratios</i>	<b>frailty</b>	
		<i>CI</i>	<i>p</i>
(Intercept)	0.0007	0.0000 – 0.0262	<b>&lt;0.001</b>
HABP2	1.3626	1.0735 – 1.7295	<b>0.012</b>
MYBPHL	1.2475	0.6636 – 2.3452	0.487
TJP3	1.2777	1.0255 – 1.5918	<b>0.029</b>
TEX56P	5.8360	1.8895 – 18.0252	<b>0.003</b>
CCL14	1.2661	1.0500 – 1.5268	<b>0.014</b>
Observations	80		
R <sup>2</sup> / R <sup>2</sup> adjusted	0.676 / 0.655		

## Top 10 genes

- Accuracy = 0.95
- AUC = 0.942

<i>Predictors</i>	<i>Odds Ratios</i>	<b>frailty</b>	
		<i>CI</i>	<i>p</i>
(Intercept)	0.0000	0.0000 – 0.0119	<b>0.005</b>
EFNA5	0.9088	0.5795 – 1.4254	0.673
HABP2	1.5961	1.0245 – 2.4866	<b>0.039</b>
MYBPHL	1.2473	0.3812 – 4.0809	0.711
TJP3	1.2752	0.9091 – 1.7886	0.156
TEX56P	11.7245	1.1736 – 117.1343	<b>0.036</b>
ACRP1	1.2960	0.1127 – 14.9076	0.833
LRTM1	3.0851	0.6585 – 14.4552	0.150
CCL14	1.5228	1.0408 – 2.2280	<b>0.031</b>
SEMA3E	1.2113	0.7475 – 1.9629	0.431
PDF	1.3758	1.0092 – 1.8757	<b>0.044</b>
Observations	80		
R <sup>2</sup> / R <sup>2</sup> adjusted	0.815 / 0.795		

# Multinomial Logistic Regression Classifier

**Accuracy:** 0.95

**AUC:** 0.931

**Model Equation:**

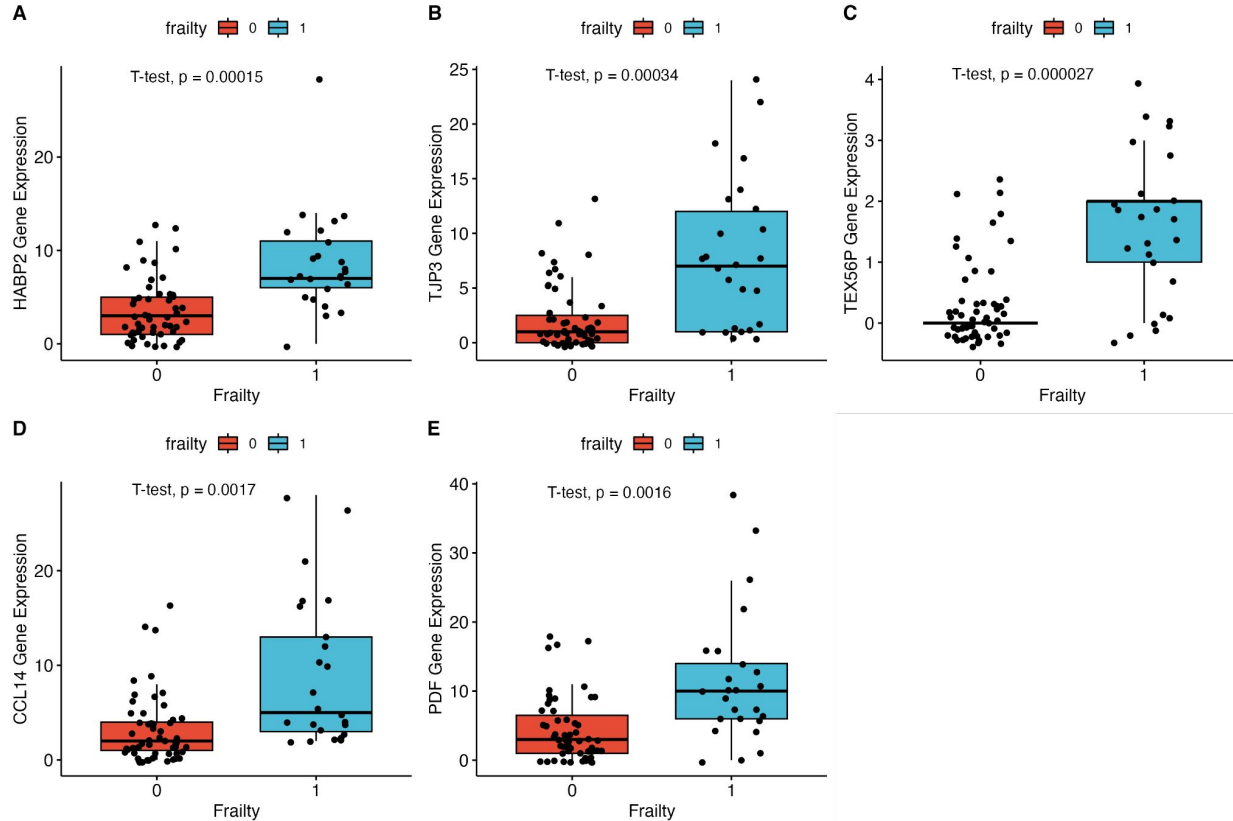
$LP = 0.000007422891 + (1.463481209314 * HABP2) + (1.432561618292 * TJP3) + (11.787795400887 * TEX56P) + (1.540721723569 * CCL14) + (1.324008646151 * PDF)$

**Frailty Risk Score** =  $1/(1+\exp(-LP))$

**Score Range:** [0,1.0]

<i>Predictors</i>	<i>Odds Ratios</i>	<b>frailty</b>	
		<i>CI</i>	<i>p</i>
(Intercept)	0.0000	0.0000 – 0.0107	<b>0.002</b>
HABP2	1.4635	1.0716 – 1.9986	<b>0.017</b>
TJP3	1.4326	1.0968 – 1.8712	<b>0.009</b>
TEX56P	11.7878	1.9031 – 73.0128	<b>0.009</b>
CCL14	1.5407	1.1132 – 2.1324	<b>0.010</b>
PDF	1.3240	1.0459 – 1.6760	<b>0.020</b>
Observations	80		
R <sup>2</sup> / R <sup>2</sup> adjusted	0.761 / 0.741		

# Gene Expression





# References

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