

## Milestone 2: Core results 01

Anders

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### Data

One clinical trials on breast cancer (advanced HR+/HER2- and HER2-E breast cancer) using two different drug combination; and a cohorts study (here used as test data set).

Both data set have mRNA expression of 771 genes at baseline (prior to treatment). This genes are specifically selected based on their potential roles in breast cancer pathology:

The gene set is divided into 25 sets of “signature genes”; which are thought to represent functional unities with respect to cancer biology. Often signaling pathways. Furthermore, 8 immune cells are represented with specific genes. These sets are substantially smaller than the signature genes; which I presume leads to some issue in modeling (as for clinical data too - see next sentence). In the domain knowledge part at the end 5 signature gene sets are used. Make sense to add more...

Additionally, both data-set contains clinical data; which up to now is not used in any models. If included they maybe should have a higher weight or be implemented differently from a sole gene. Maybe in a stacked ensemble model as signature.

### Responses in study -ish

#### Proliferation score

A score based on expression level of some of the genes. Range: -1.1366 to 0.8511

#### Risk of relapse score (ROR)

A combined score based on expression level of genes and some clinical findings. Range: -8.035678 to 75.13174 (only used in combination with proliferation score as described below)

#### Risk of relapse score with proliferation score (ROR\_Prolif)

A combined score of the two above. Range: 1 to 97 (1-100)

The two scores involving ROR also have categorical variants containing: low, medium, high (but not used...)

#### Progression free survival (PFS)

This is the outcome used in the clinical cohort. Here i have used correlation with the scores described above. Spearman can maybe be used. Another approach is to use the above scores to divide the patient in to two groups and see if the two groups show clearly separable PFS over time (basically look at the graphs). The differentiation into two groups is done based on best values from a ROC curve.

### Trail

Two treatments which differ with respect to drug combination - Target: ribociclib and endocrine therapy (letrozole) - Chemotherapy: doxorubicin, cyclophosphamide and paclitaxel. approx. 50 patients in each group.

Endpoints: proliferation score, ROR score, combined ROR and prolifer

## Cohort

The primary objective of this study is to compare two cdk4/6 targeted drugs (Palbociclib, n=36; Abemaciclib, n=3 in combination with endocrine therapy (tamoxifen, fulvestrant or aromatase inhibitors, I think?)

Endpoints: progression free survival (months), OS?, and status of the two former (dont know what that means)

## Major goal

1. Find best model to predict outcome of cancer treatment with genetic profile as predictive features
2. Features selection in order to understand cancer biology

## Major challenges

Preliminary experiments (on trail 1) showed instability in prediction and feature selection between bootstrap samples of Lasso. I believe this is a classical problem of high-dim data?

## Approch

Test all thinkable models in a search for superior models

## Evaluation of models

Two levels of evaluation is considered:

### 1. Relative comparison of the different models

1000 bootstrap models are fitted and then evaluated on the original sample. This gives a relative comparison of the various models with respect to data very similar to the given data set. Correlation, MSE and frequency of selected features is compared.

### 2. Expected outcome of future patients

3 strategies are considered:

1. Repeated cross-validations (200 rep, 5-fold)
2. Bootstrap models with 0.632 (or 0.632?) adjustment (Not done)
3. Use the cohort as test data-set (Challenge: This trail have different responses)

## RESULTS

### Features tested:

6 genes

771 genes

node values of mech model

residuals of mech model

## Responses tested:

proliferation score

combined score including proliferation and ROR

## Models tested:

Lasso

Ridge

Elastic Net

Boosting with stumps as base learner

(- mboost)

- xgboost

PCA on subsets of genes

Stacking using different features in the base models

Sparse group lasso (not done)

Iterative learning (ongoing)

Post Lasso (not done)

## Results of individual modles:

### Lasso - Bootstrap

6 genes -> proliferation score

```
## number of models fitted: 1000
```

```
## Fraction of model fits with no selected genes: 0.182
```

```
##
```

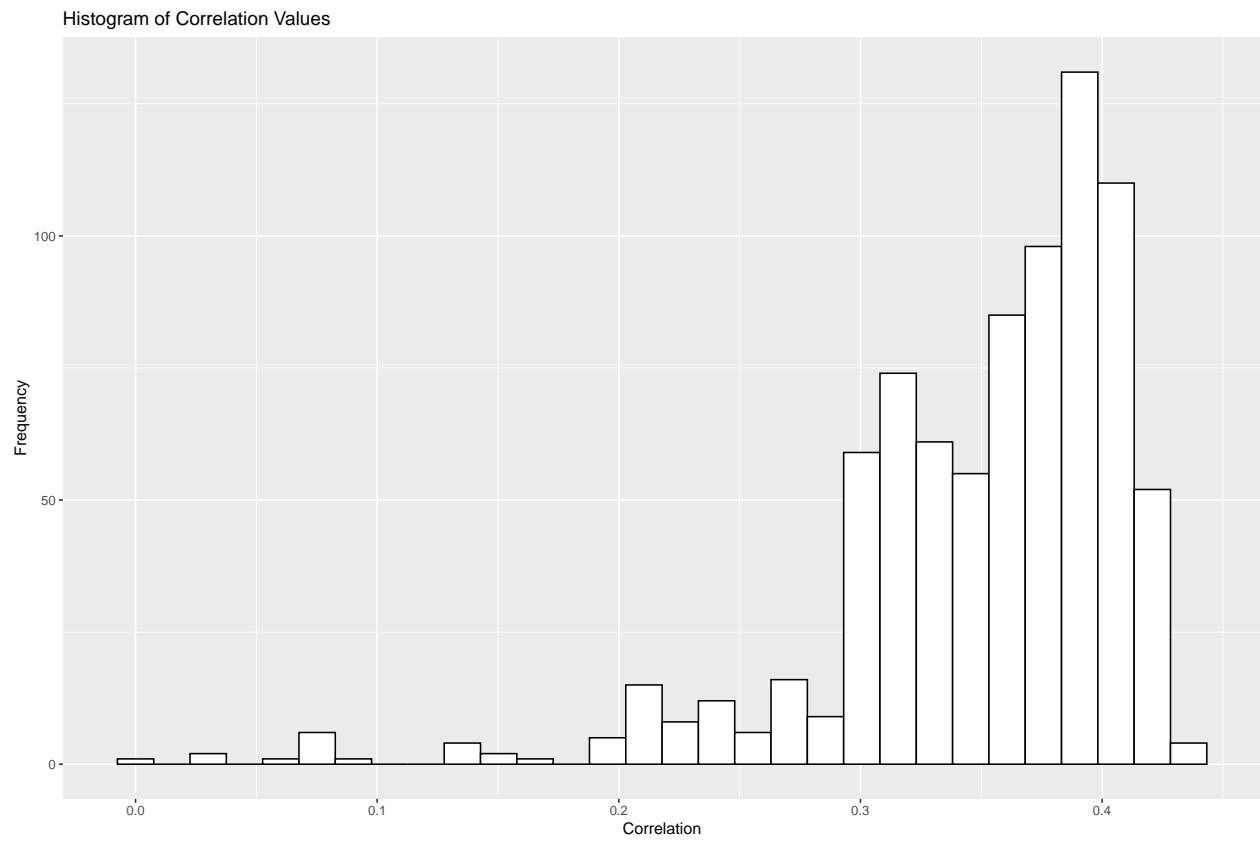
```
## CORRELATIONS RESULTS
```

```
## Mean: 0.3498379
```

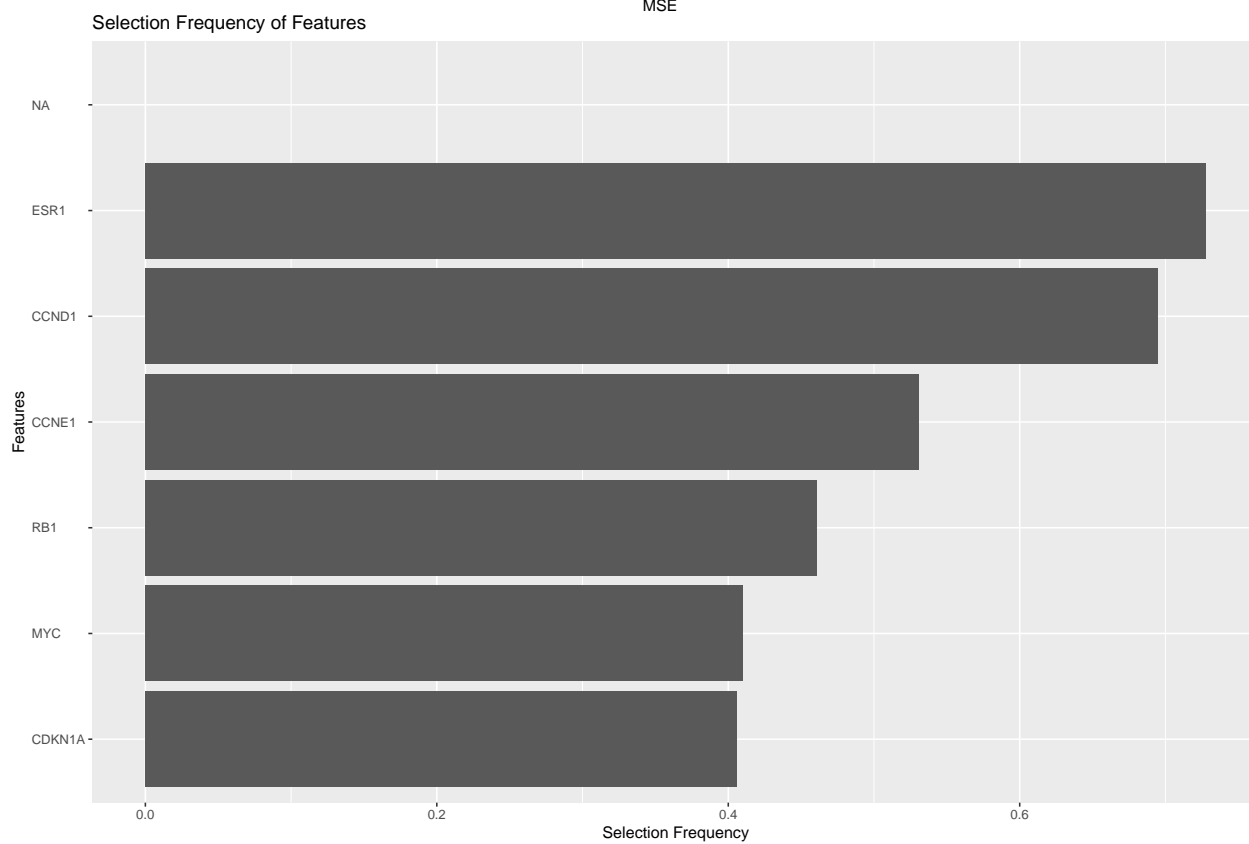
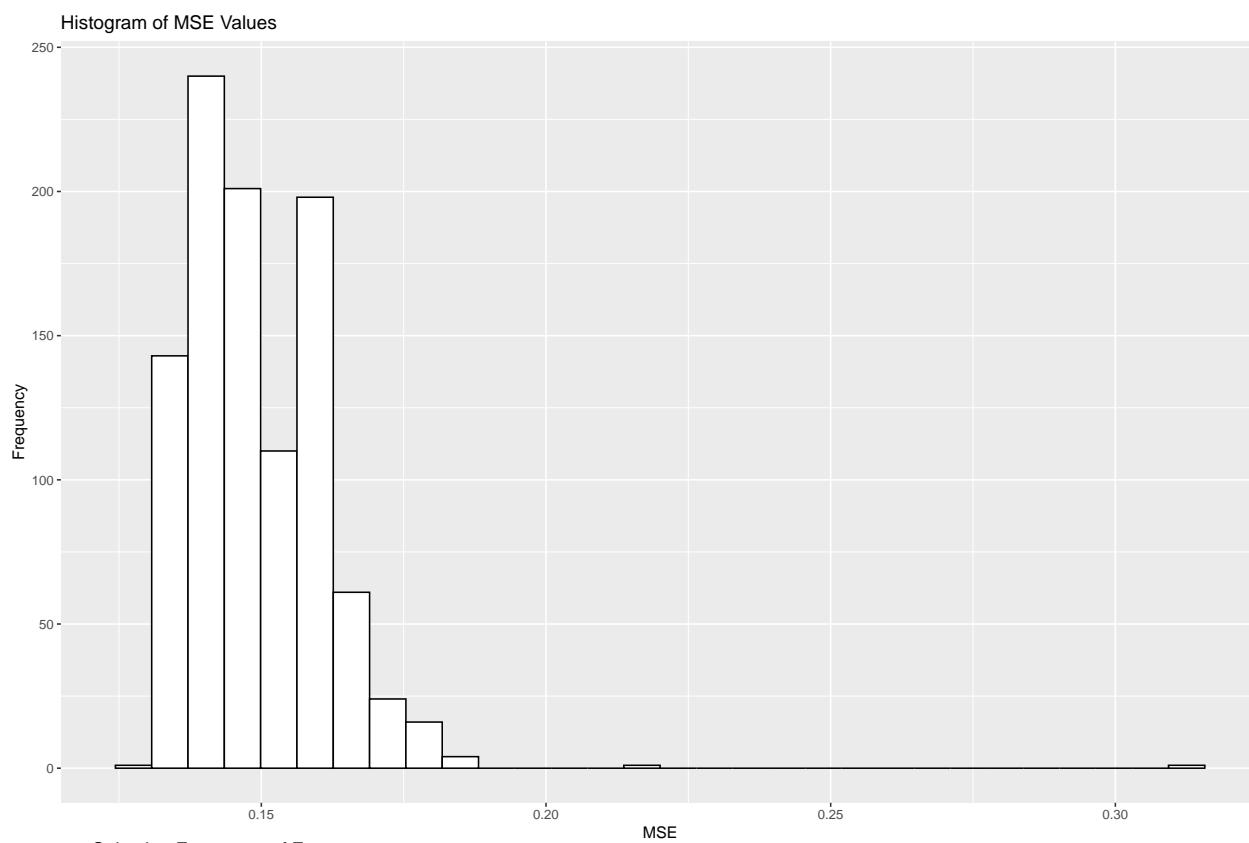
```
## Median: 0.3672243
```

```
## Variance: 0.003984261
```

```
## st.dev.: 0.063121
```



```
## MSE RESULTS
## Mean: 0.1492302
## Median: 0.1469228
## Variance: 0.0001550247
## st.dev.: 0.01245089
```

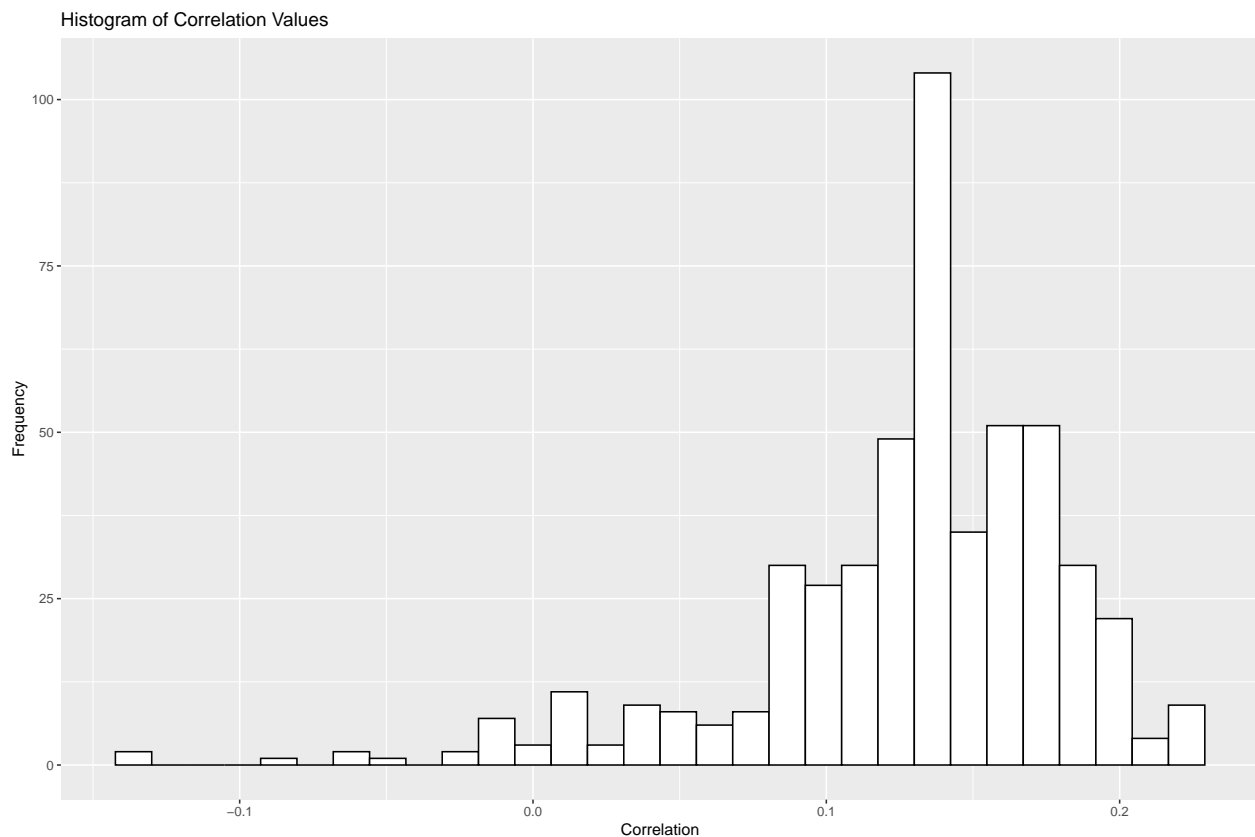


##

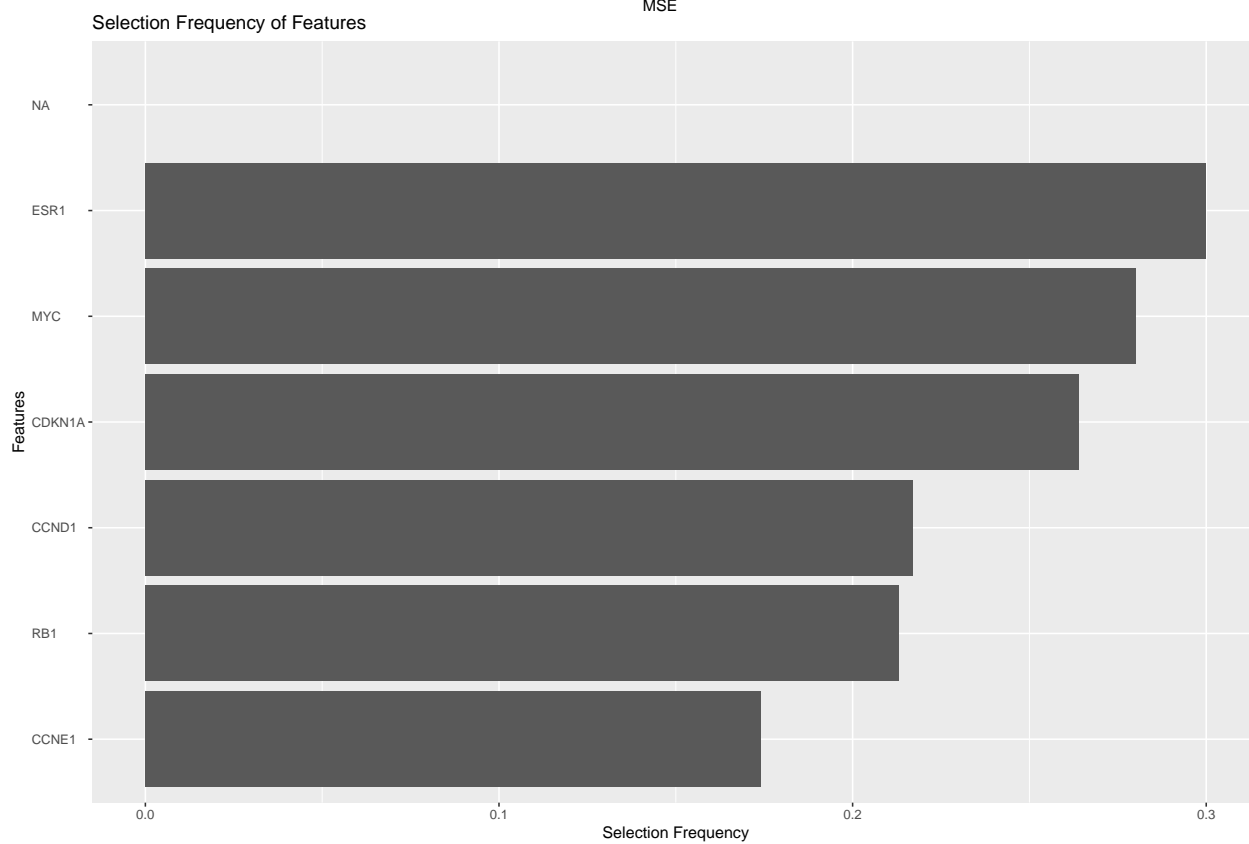
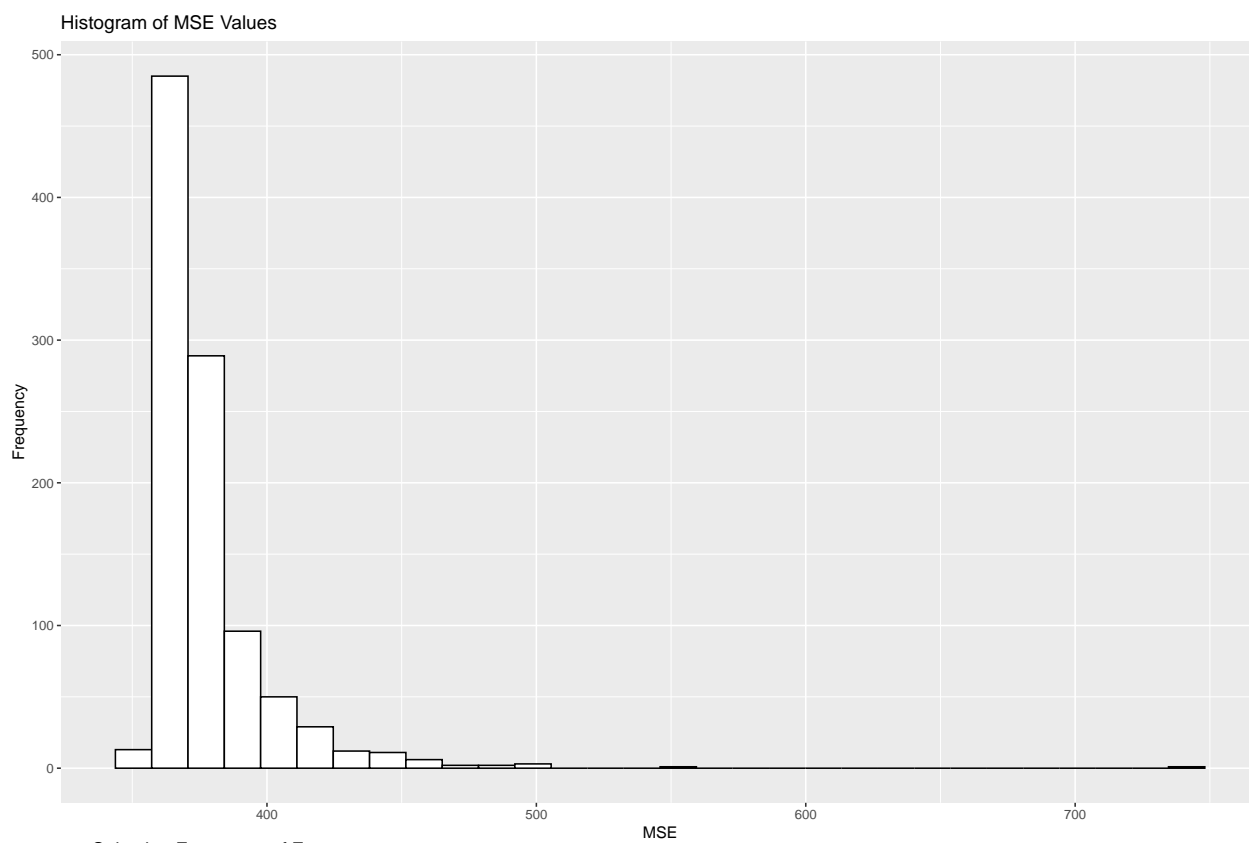
```
## Features selected 50% or more times:
## CCND1 CCNE1 ESR1
## Top 20 featruess:
## [1] "ESR1" "CCND1" "CCNE1" "RB1" "MYC" "CDKN1A" NA NA
## [9] NA NA NA NA NA NA NA NA
## [17] NA NA NA NA
```

**6 genes -> ROR\_proliferation score**

```
## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0.495
##
## CORRELATIONS RESULTS
## Mean: 0.1282306
## Median: 0.1311715
## Variance: 0.00285293
## st.dev.: 0.05341282
```



```
## MSE RESULTS
## Mean: 378.094
## Median: 370.7201
## Variance: 549.4448
## st.dev.: 23.44024
```



##

```
## Features selected 50% or more times:
```

```
##
```

```
## Top 20 featrues:
```

```
## [1] "ESR1"  "MYC"   "CDKN1A" "CCND1" "RB1"   "CCNE1" NA      NA
## [9] NA      NA      NA      NA      NA      NA      NA      NA
## [17] NA      NA      NA      NA
```

```
771 genes -> proliferation score
```

```
## number of models fitted: 1000
```

```
## Fraction of model fits with no selected genes: 0.002
```

```
##
```

```
## CORRELATIONS RESULTS
```

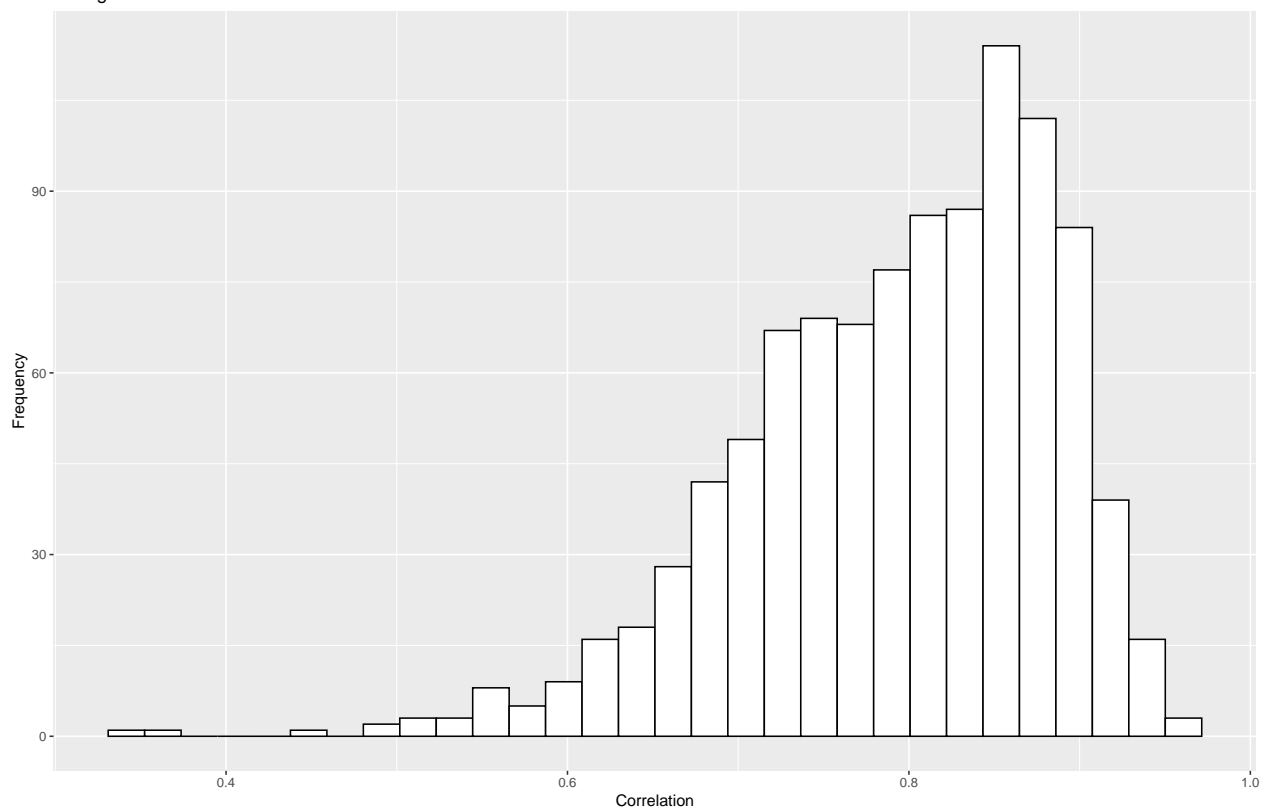
```
## Mean: 0.7941413
```

```
## Median: 0.8101886
```

```
## Variance: 0.008119272
```

```
## st.dev.: 0.090107
```

Histogram of Correlation Values



```
## MSE RESULTS
```

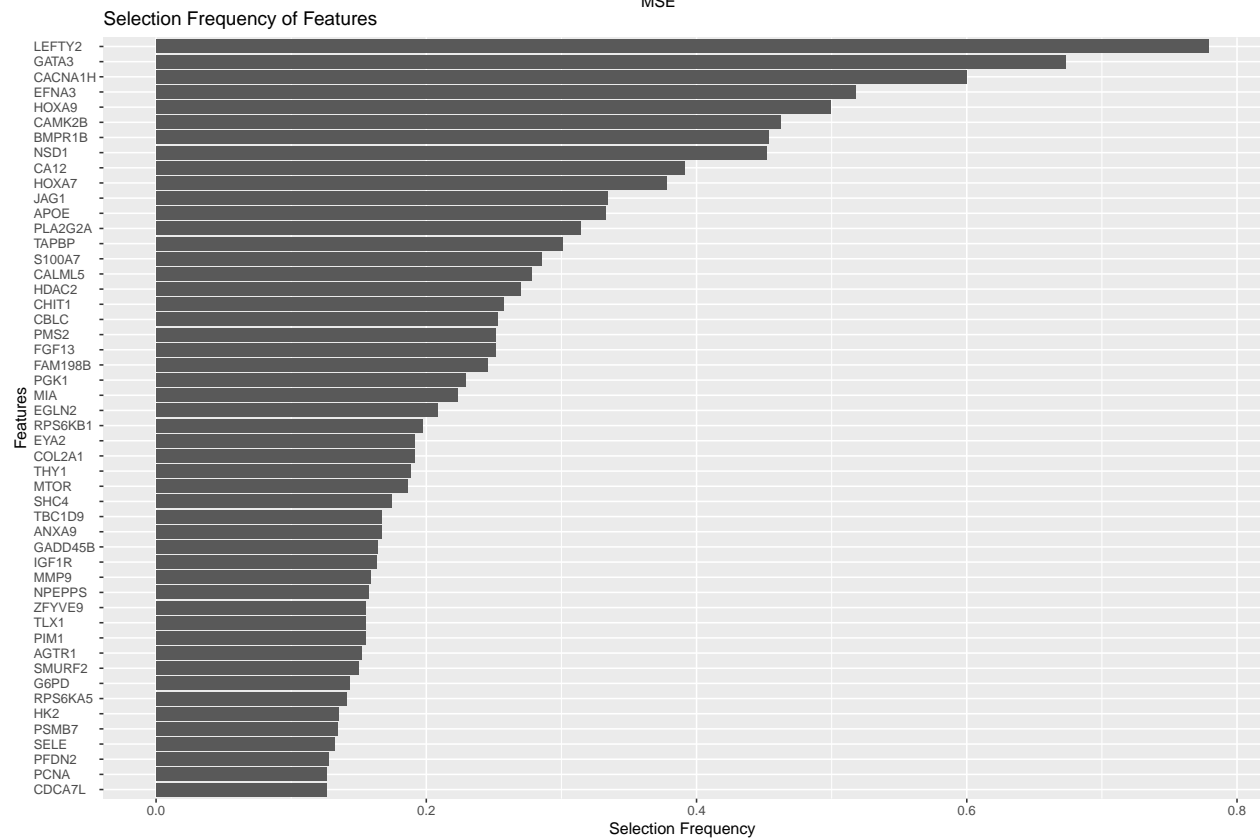
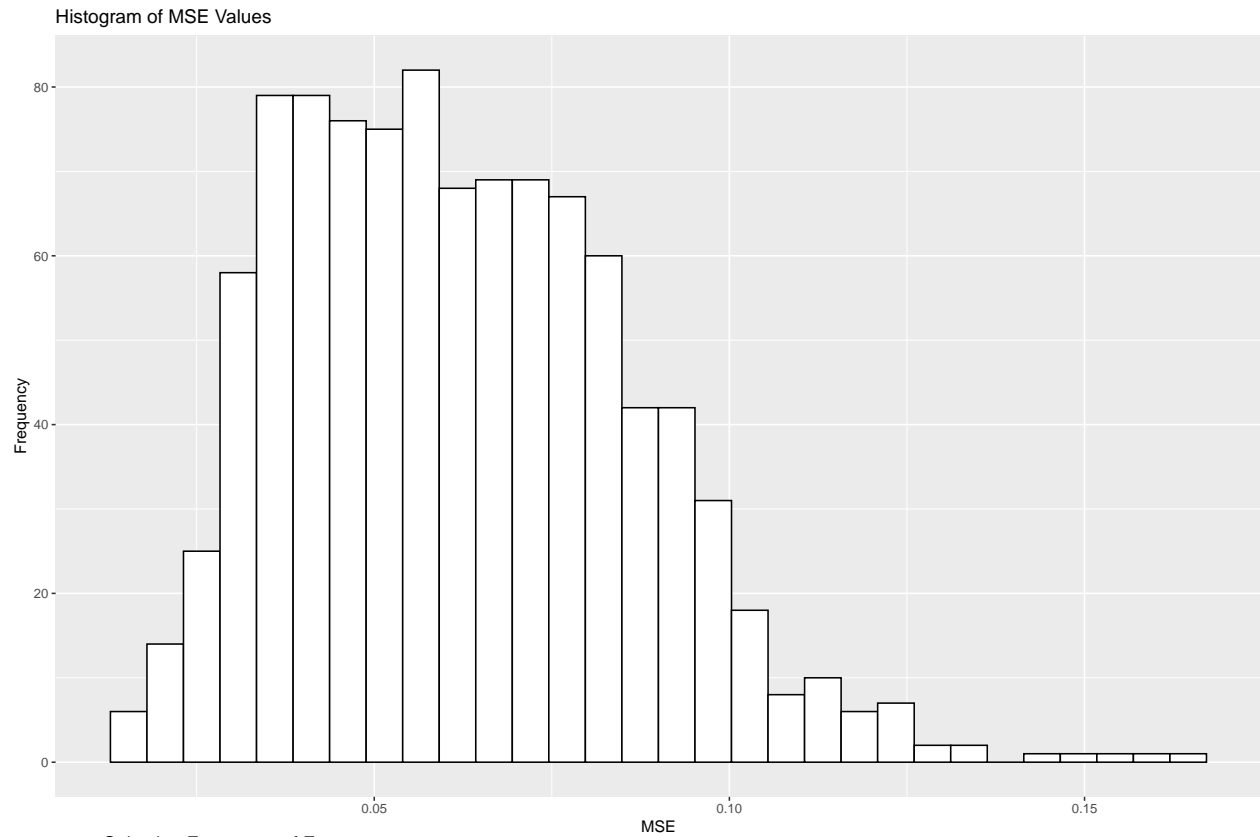
```
## Mean: 0.06209131
```

```
## Median: 0.0598495
```

```
## Variance: 0.0005751012
```

```
## st.dev.: 0.02398127
```



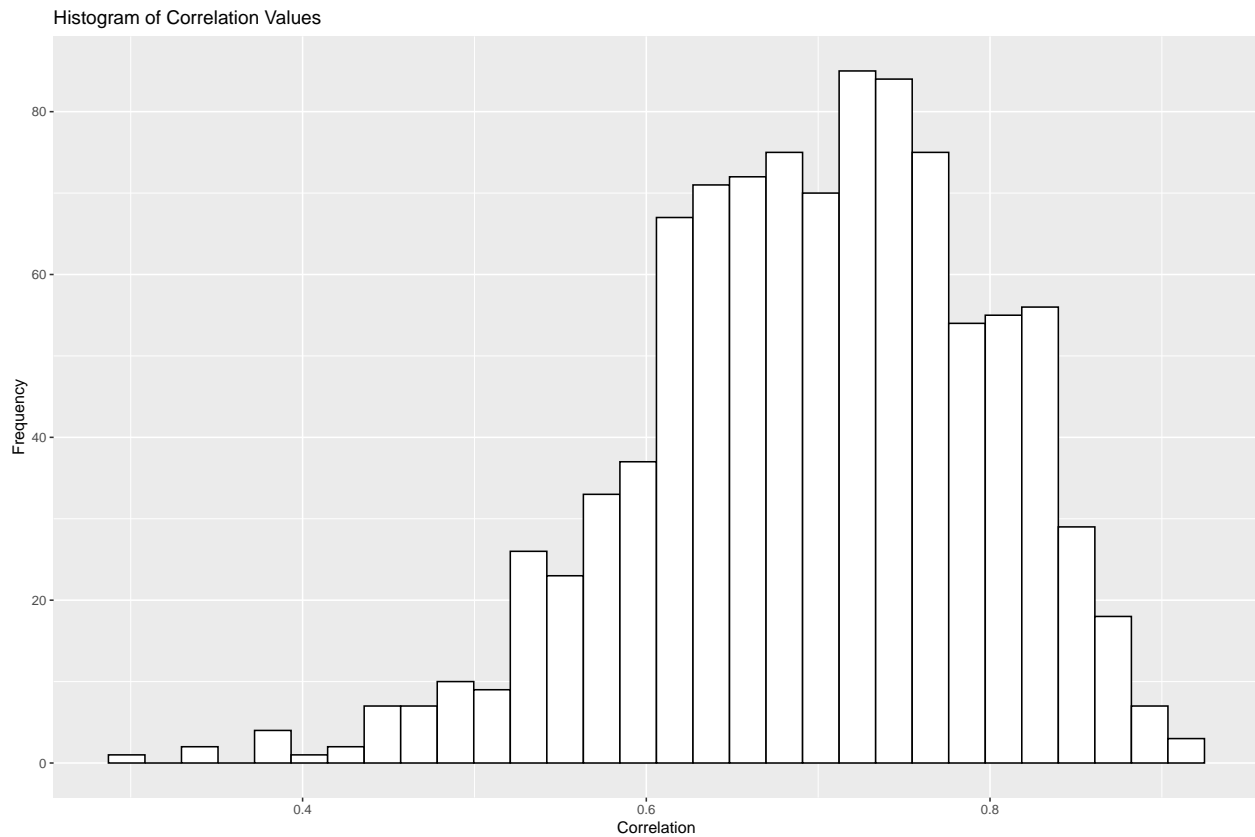


##

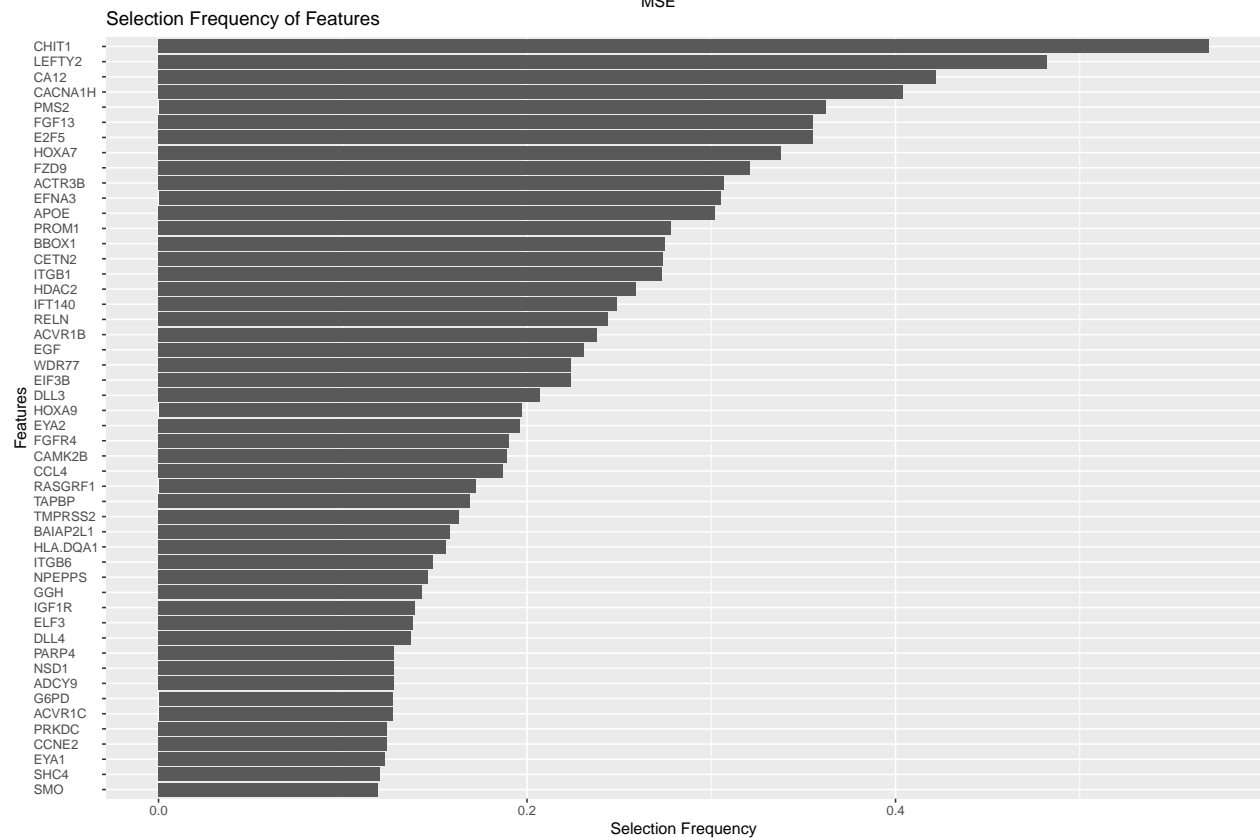
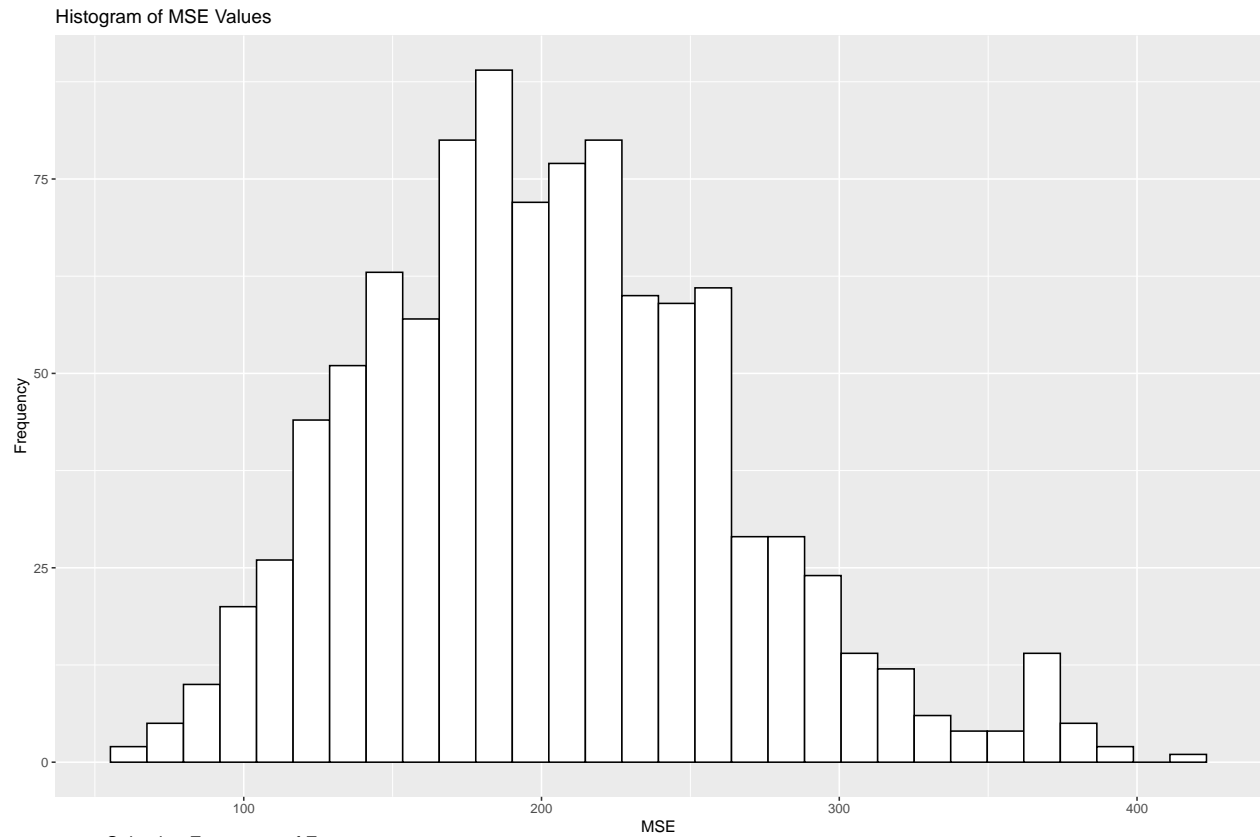
```
## Features selected 50% or more times:
## CACNA1H EFNA3 GATA3 LEFTY2
## Top 20 featrues:
## [1] "LEFTY2" "GATA3" "CACNA1H" "EFNA3" "HOXA9" "CAMK2B" "BMPR1B"
## [8] "NSD1" "CA12" "HOXA7" "JAG1" "APOE" "PLA2G2A" "TAPBP"
## [15] "S100A7" "CALML5" "HDAC2" "CHIT1" "CBLC" "FGF13"
```

### 771 genes -> ROR-proliferation score

```
## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0.017
##
## CORRELATIONS RESULTS
## Mean: 0.6968101
## Median: 0.7035889
## Variance: 0.009901439
## st.dev.: 0.09950598
```



```
## MSE RESULTS
## Mean: 203.408
## Median: 198.455
## Variance: 3763.666
## st.dev.: 61.34872
```



##

```
## Features selected 50% or more times:
```

```
## CHIT1
```

```
## Top 20 featrues:
```

```
## [1] "CHIT1" "LEFTY2" "CA12" "CACNA1H" "PMS2" "E2F5" "FGF13"
```

```
## [8] "HOXA7" "FZD9" "ACTR3B" "EFNA3" "APOE" "PROM1" "BBOX1"
```

```
## [15] "CETN2" "ITGB1" "HDAC2" "IFT140" "RELN" "ACVR1B"
```

```
node values -> proliferation score
```

```
## number of models fitted: 1000
```

```
## Fraction of model fits with no selected genes: 0.053
```

```
##
```

```
## CORRELATIONS RESULTS
```

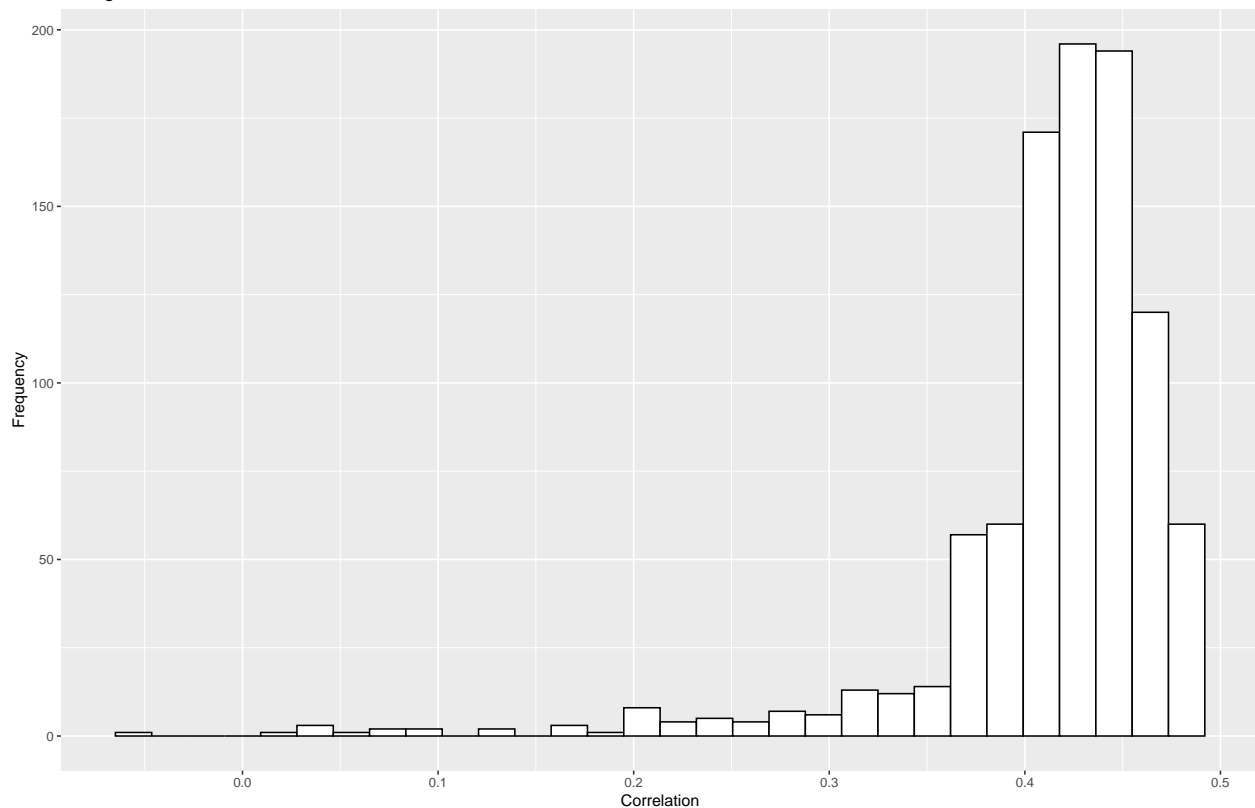
```
## Mean: 0.414496
```

```
## Median: 0.4275114
```

```
## Variance: 0.00413092
```

```
## st.dev.: 0.06427223
```

```
Histogram of Correlation Values
```



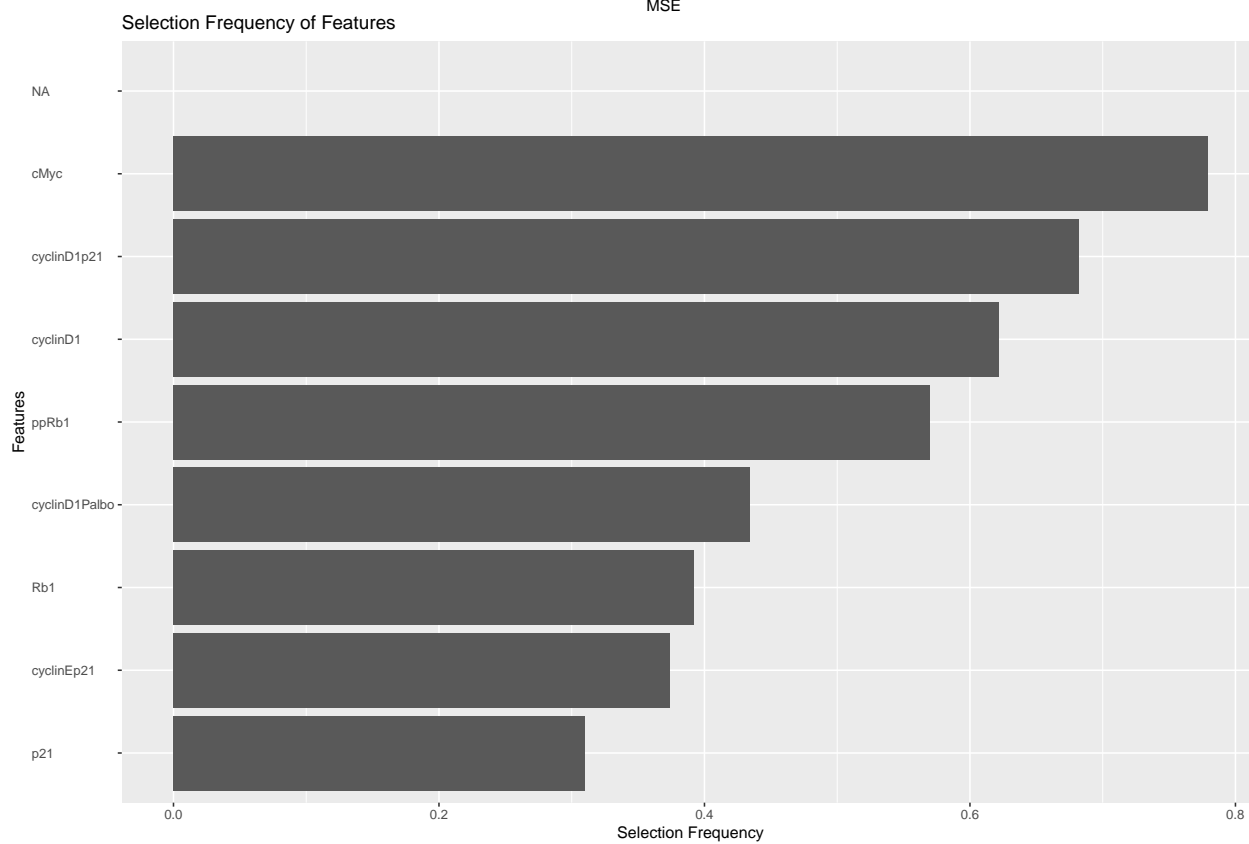
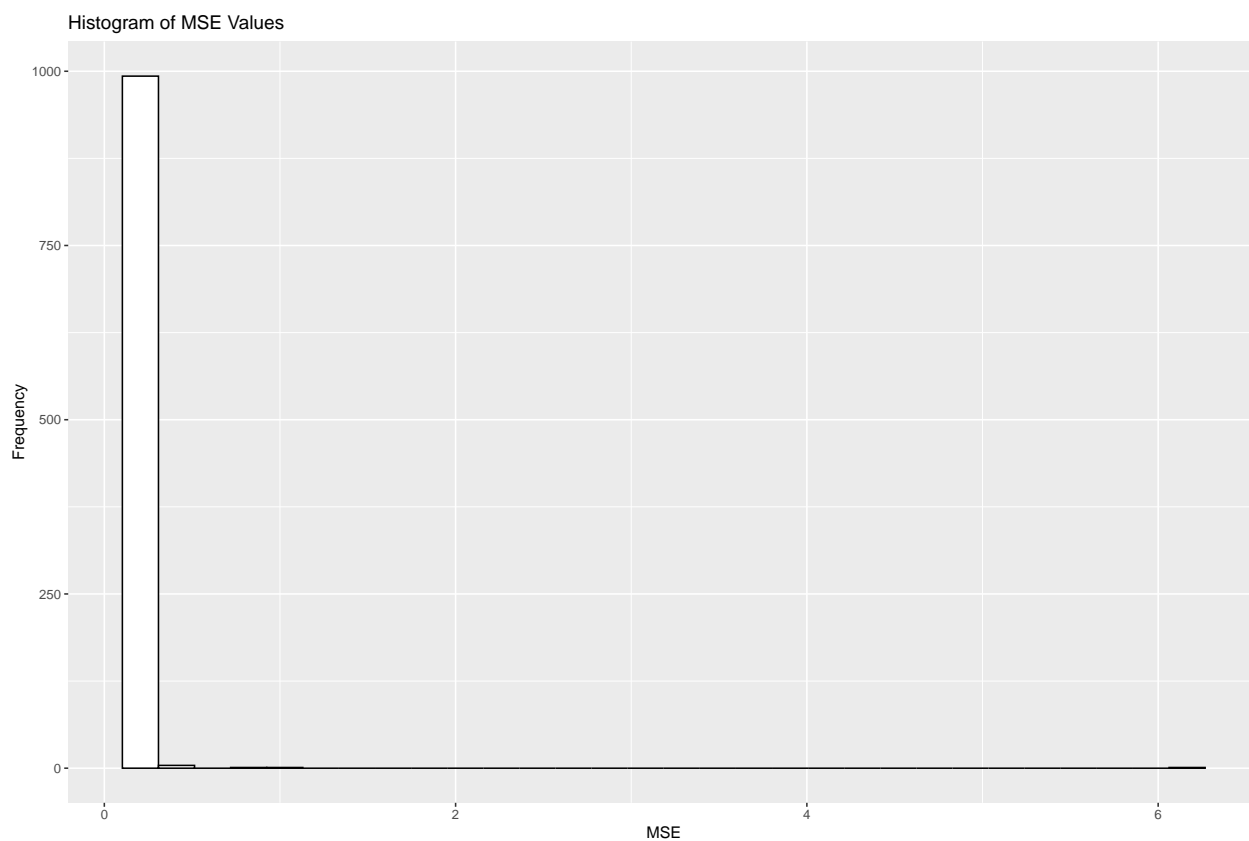
```
## MSE RESULTS
```

```
## Mean: 0.1479731
```

```
## Median: 0.1355805
```

```
## Variance: 0.03673469
```

```
## st.dev.: 0.191663
```

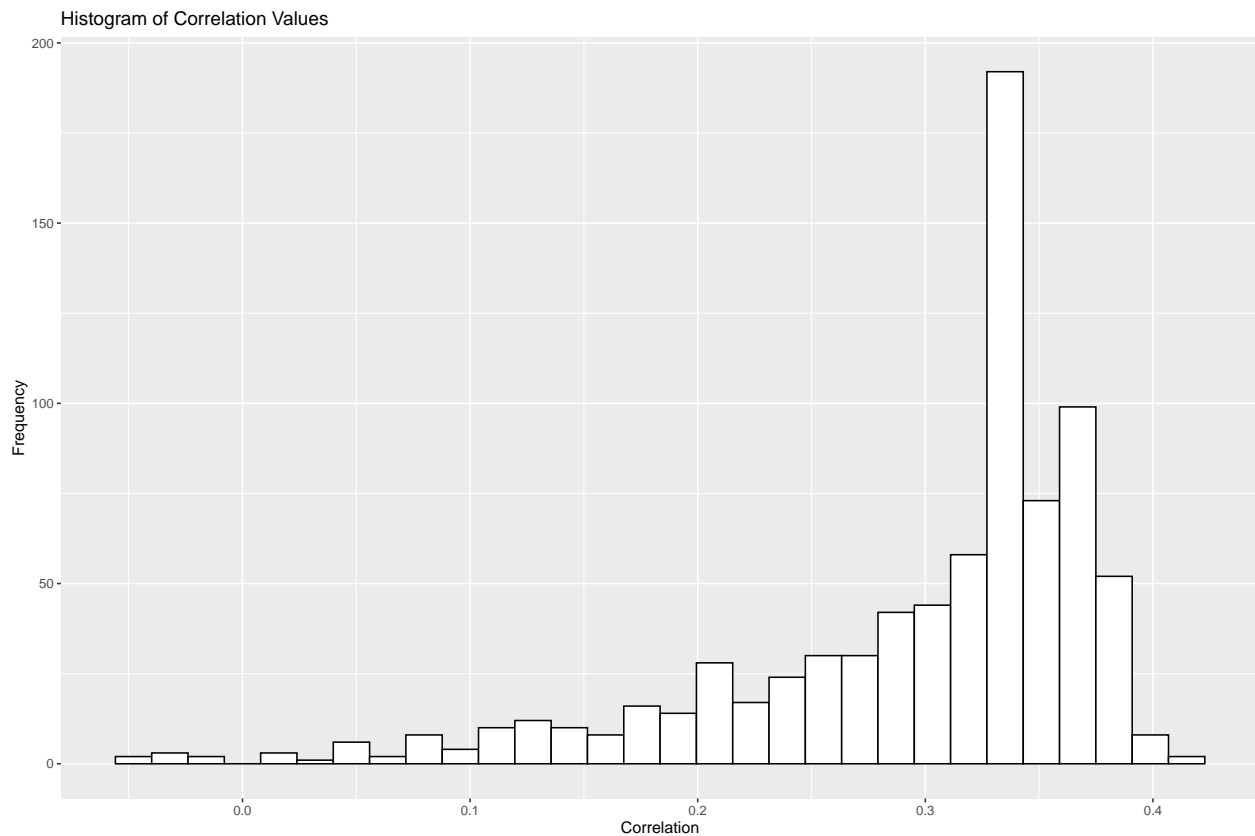


##

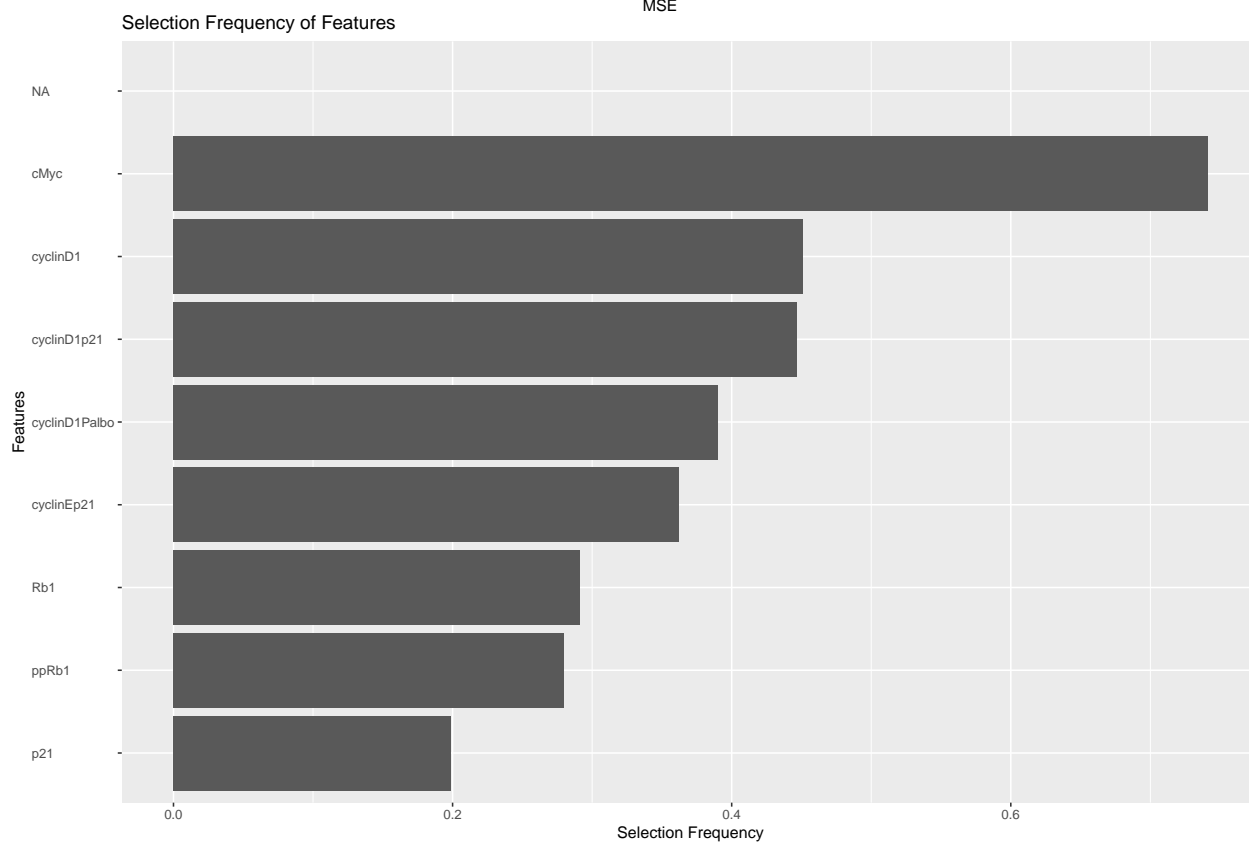
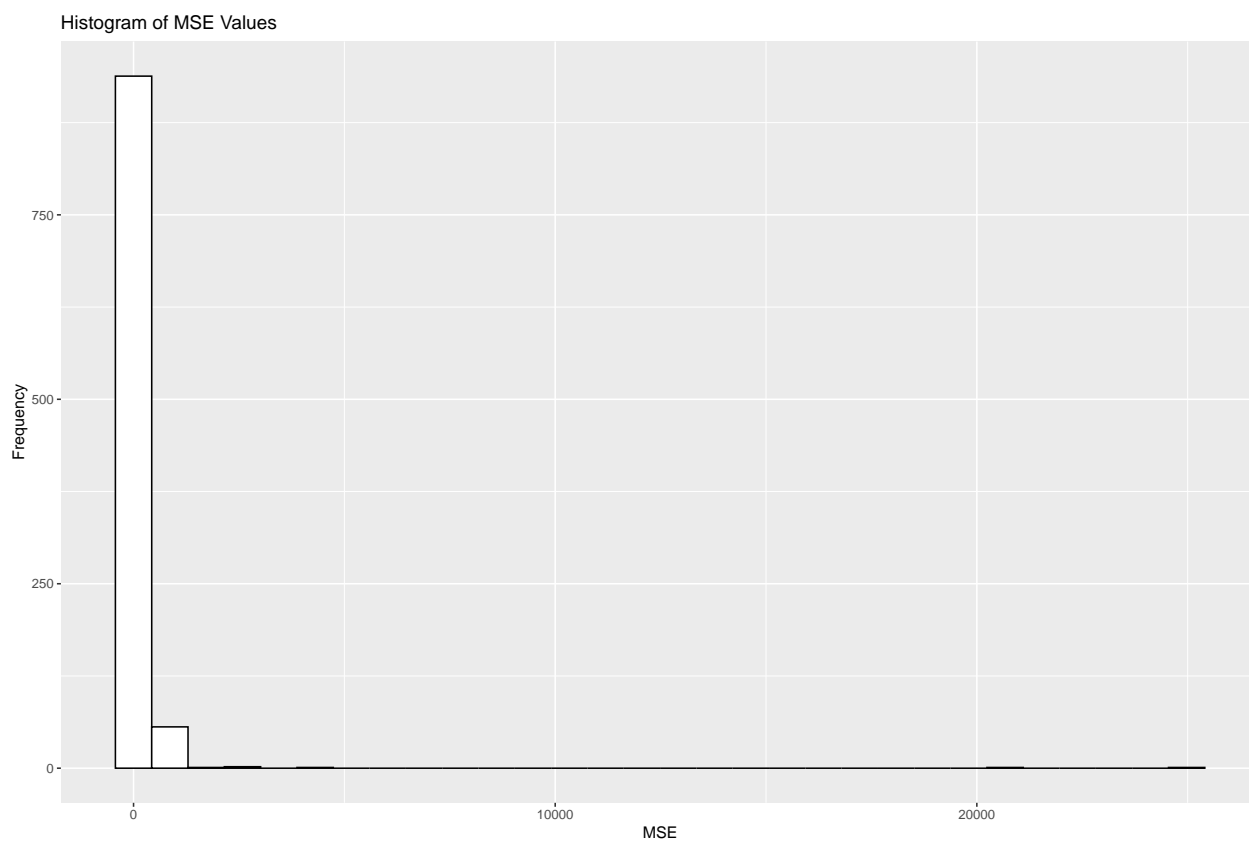
```
## Features selected 50% or more times:
## cyclinD1 cyclinD1p21 cMyc ppRb1
## Top 20 featrues:
## [1] "cMyc"          "cyclinD1p21"  "cyclinD1"     "ppRb1"
## [5] "cyclinD1Palbo" "Rb1"          "cyclinEp21"   "p21"
## [9] NA              NA              NA              NA
## [13] NA              NA              NA              NA
## [17] NA              NA              NA              NA
```

node values -> ROR-proliferation score

```
## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0.2
##
## CORRELATIONS RESULTS
## Mean: 0.2964169
## Median: 0.3317433
## Variance: 0.006900552
## st.dev.: 0.08306956
```



```
## MSE RESULTS
## Mean: 417.6667
## Median: 353.8176
## Variance: 1054857
## st.dev.: 1027.062
```

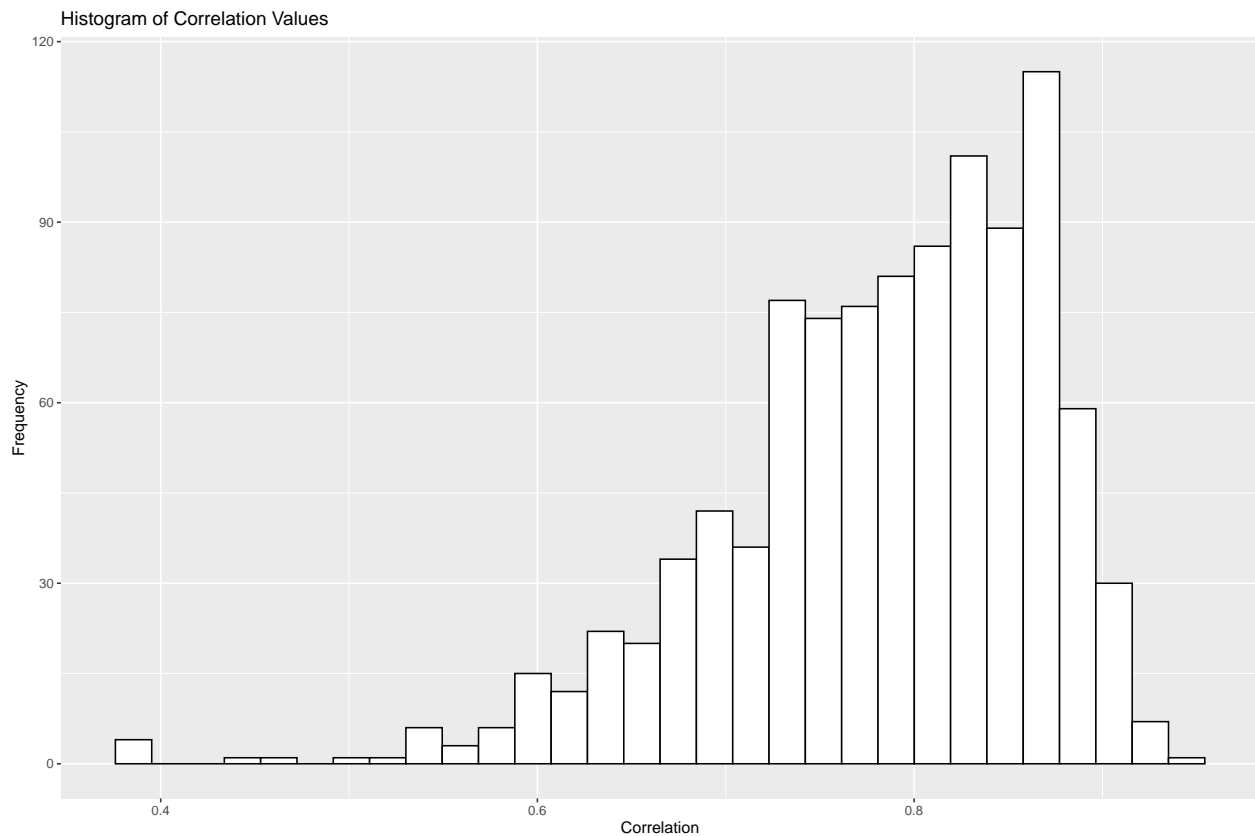


##

```
## Features selected 50% or more times:
## cMyc
## Top 20 featrues:
## [1] "cMyc"          "cyclinD1"      "cyclinD1p21"   "cyclinD1Palbo"
## [5] "cyclinEp21"    "Rb1"           "ppRb1"         "p21"
## [9] NA              NA              NA              NA
## [13] NA             NA              NA              NA
## [17] NA             NA              NA              NA
```

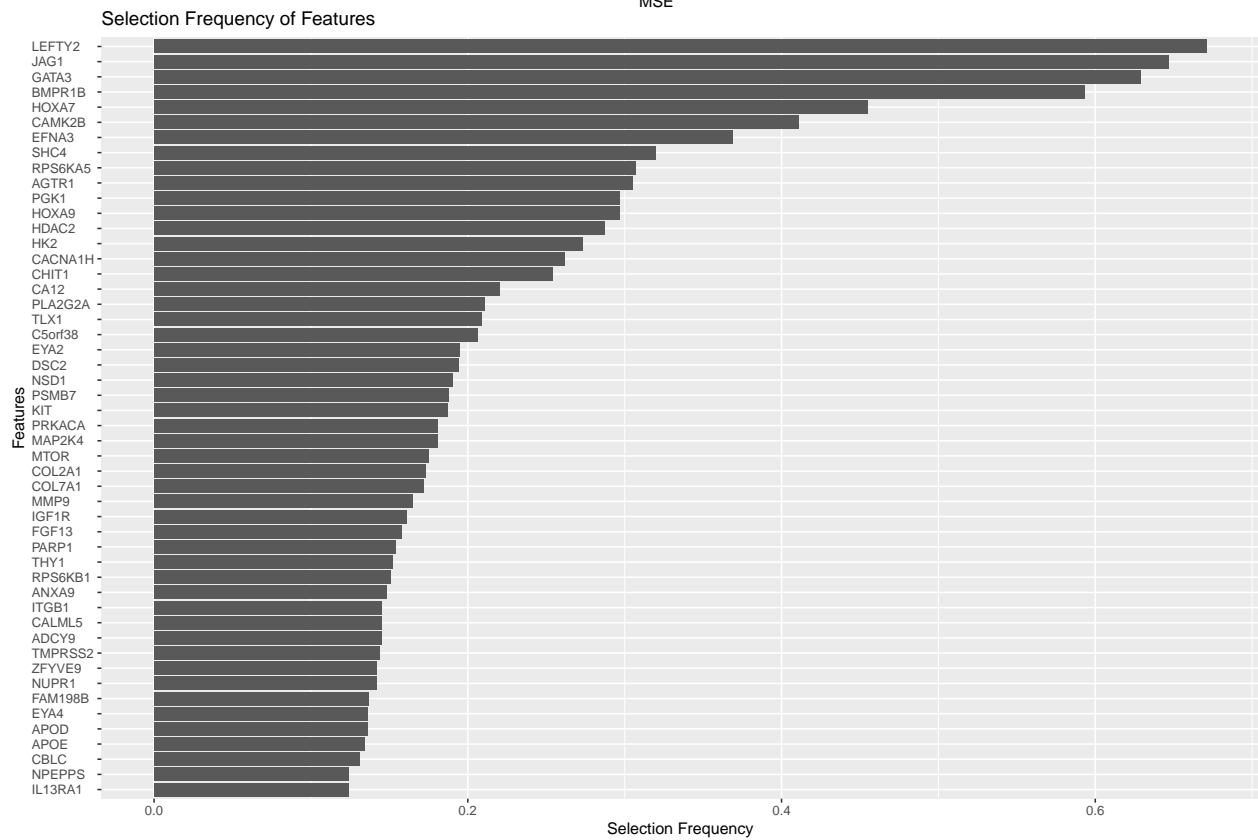
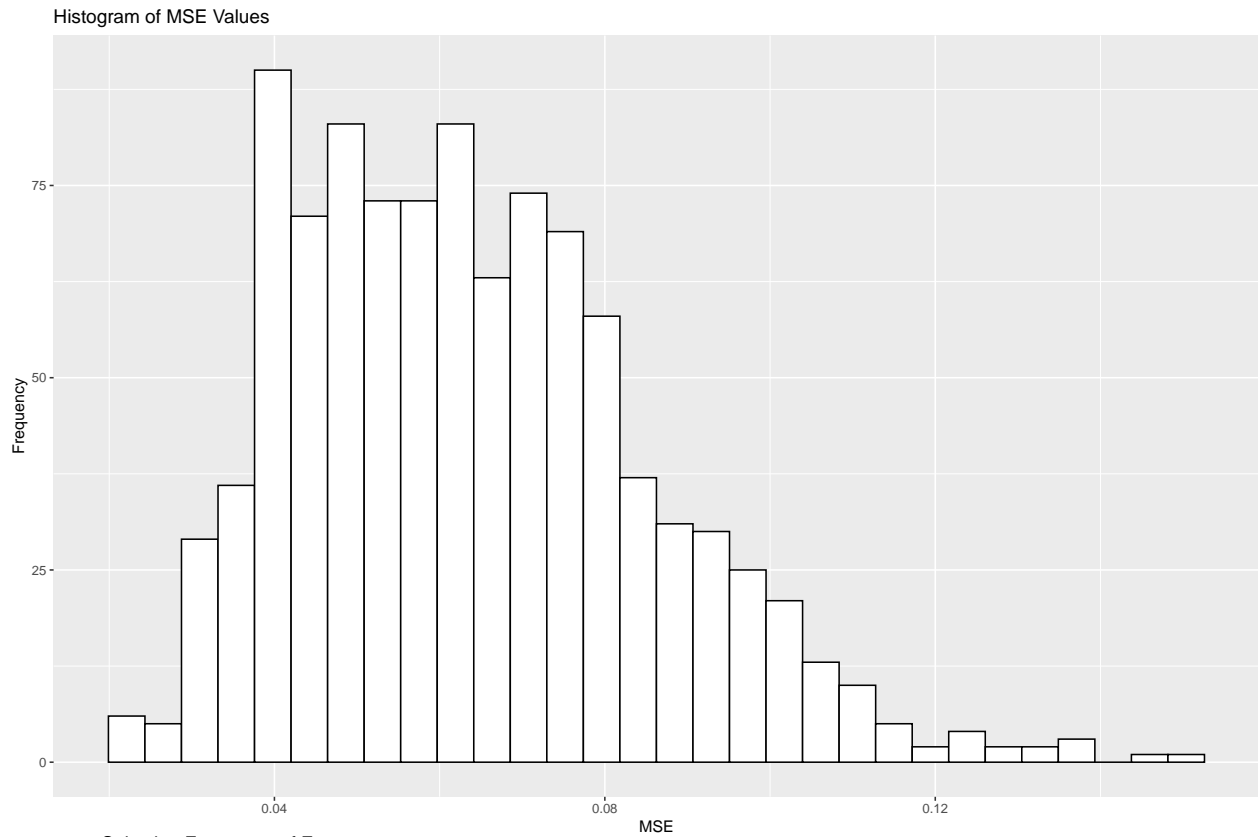
**Mechanistic + Residuals -> proliferation score (additive)**

```
## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0
##
## CORRELATIONS RESULTS
## Mean: 0.7835808
## Median: 0.7962129
## Variance: 0.007298891
## st.dev.: 0.08543355
```



```
## MSE RESULTS
## Mean: 0.06384841
## Median: 0.06161072
## Variance: 0.0004577716
## st.dev.: 0.0213956
```



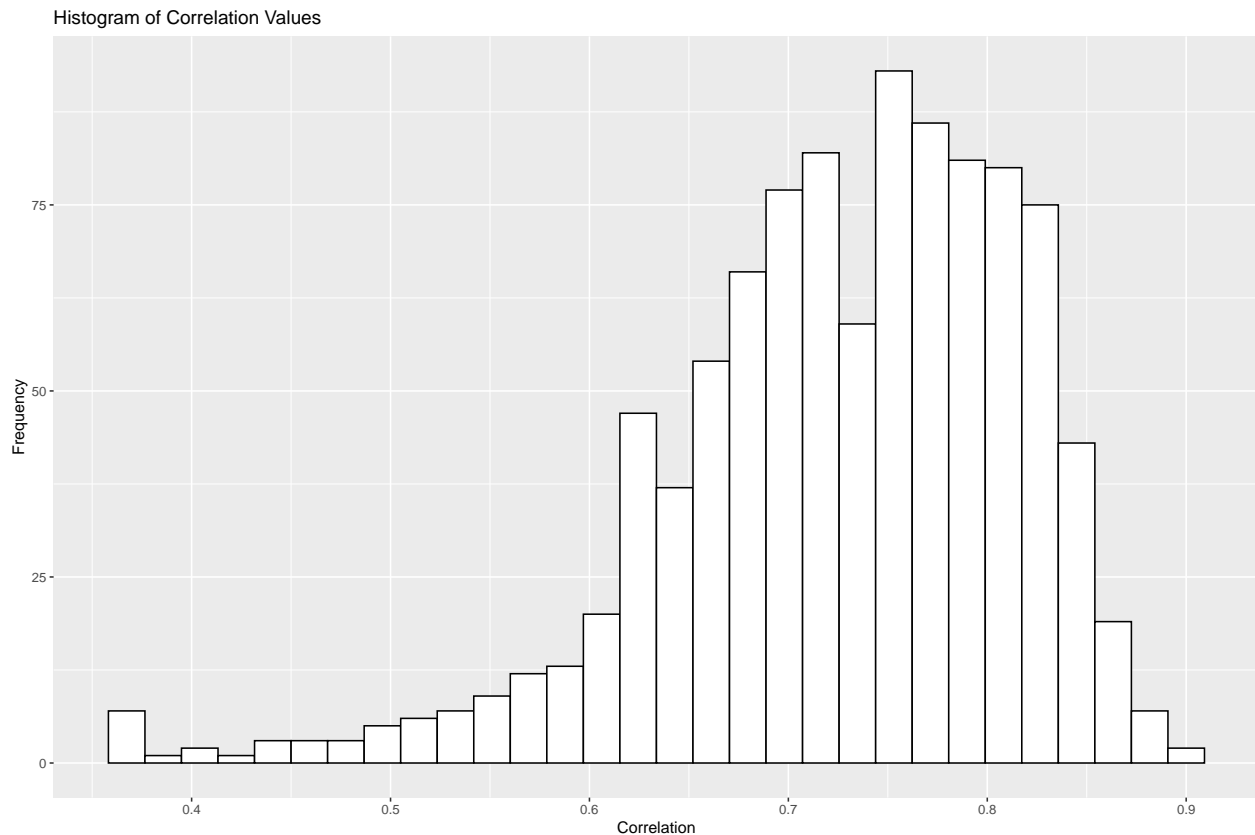


##

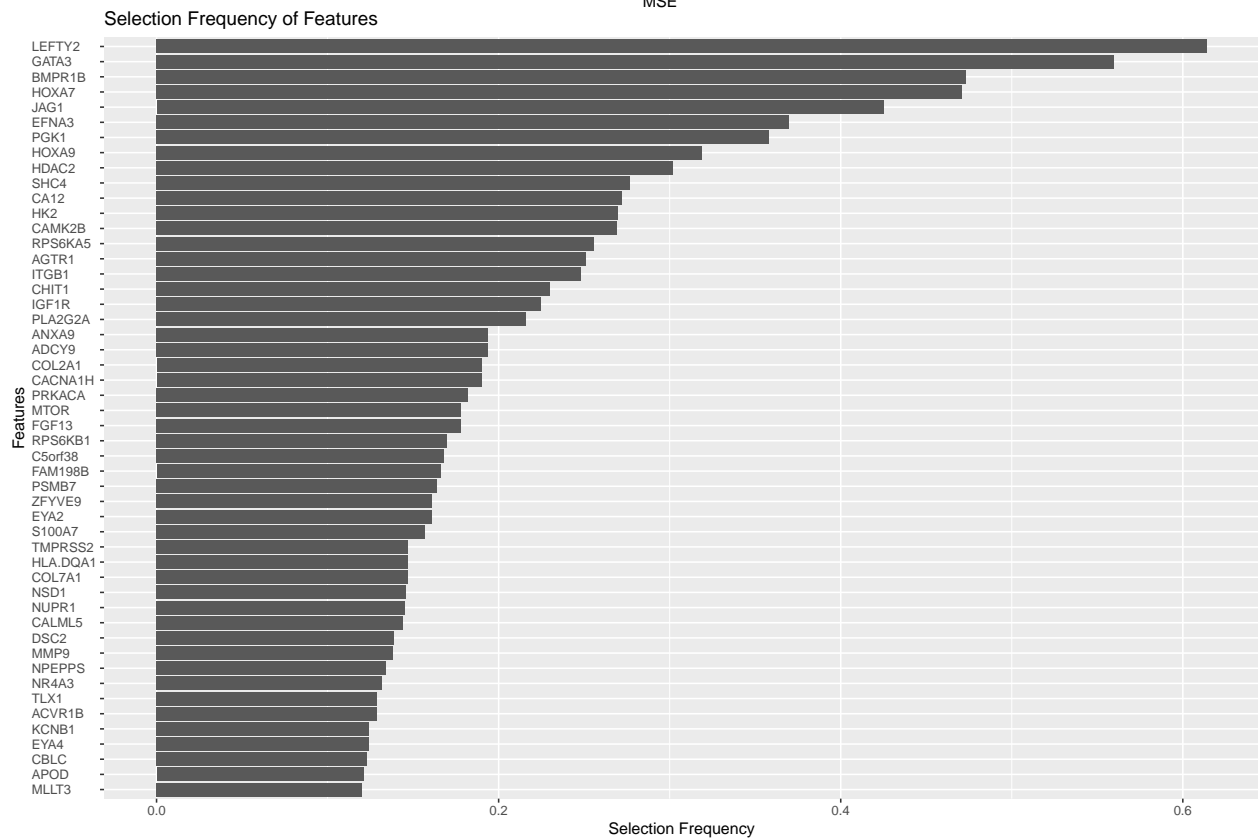
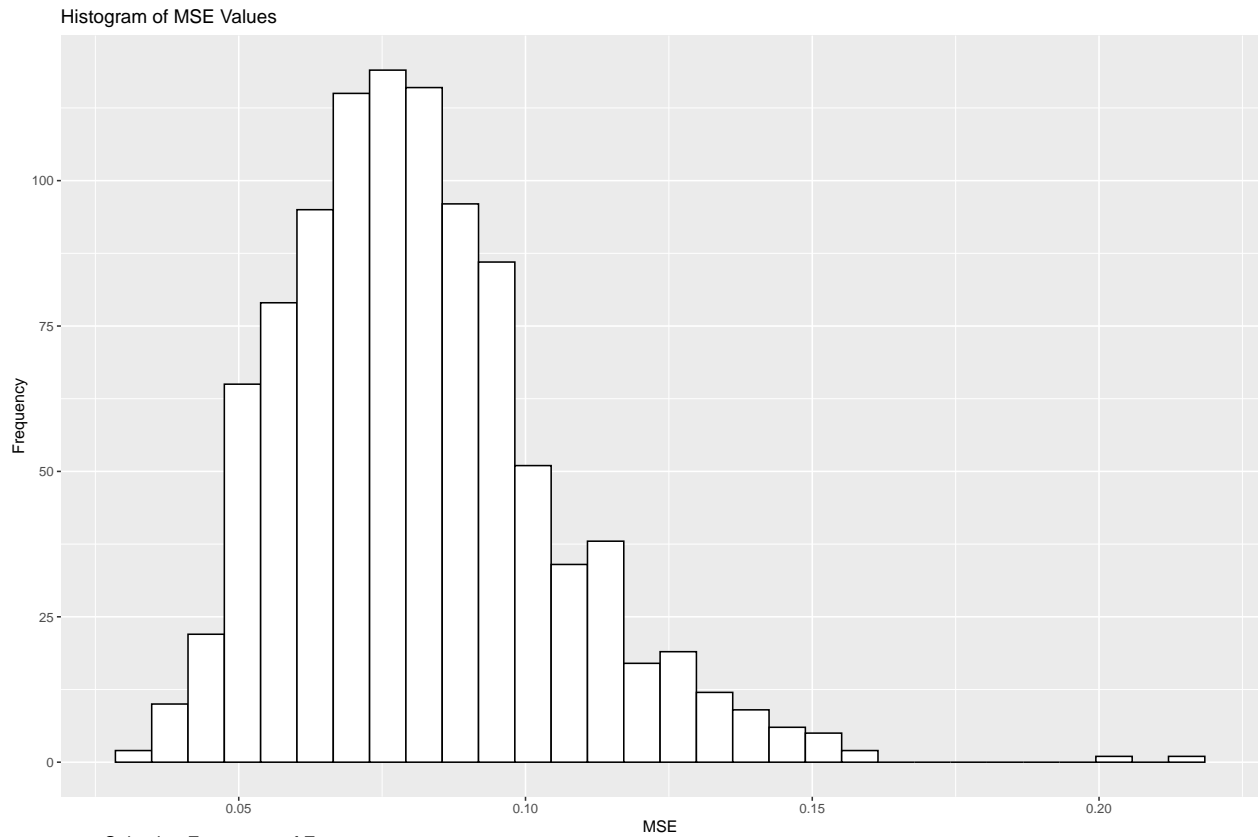
```
## Features selected 50% or more times:
## BMPR1B GATA3 JAG1 LEFTY2
## Top 20 featrues:
## [1] "LEFTY2" "JAG1" "GATA3" "BMPR1B" "HOXA7" "CAMK2B" "EFNA3"
## [8] "SHC4" "RPS6KA5" "AGTR1" "HOXA9" "PGK1" "HDAC2" "HK2"
## [15] "CACNA1H" "CHIT1" "CA12" "PLA2G2A" "TLX1" "C5orf38"
```

**Mechanistic + Residuals -> proliferation score (multiplicative)**

```
## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0
##
## CORRELATIONS RESULTS
## Mean: 0.7266736
## Median: 0.739984
## Variance: 0.008014481
## st.dev.: 0.08952363
```



```
## MSE RESULTS
## Mean: 0.0813415
## Median: 0.07892236
## Variance: 0.0005355891
## st.dev.: 0.0231428
```

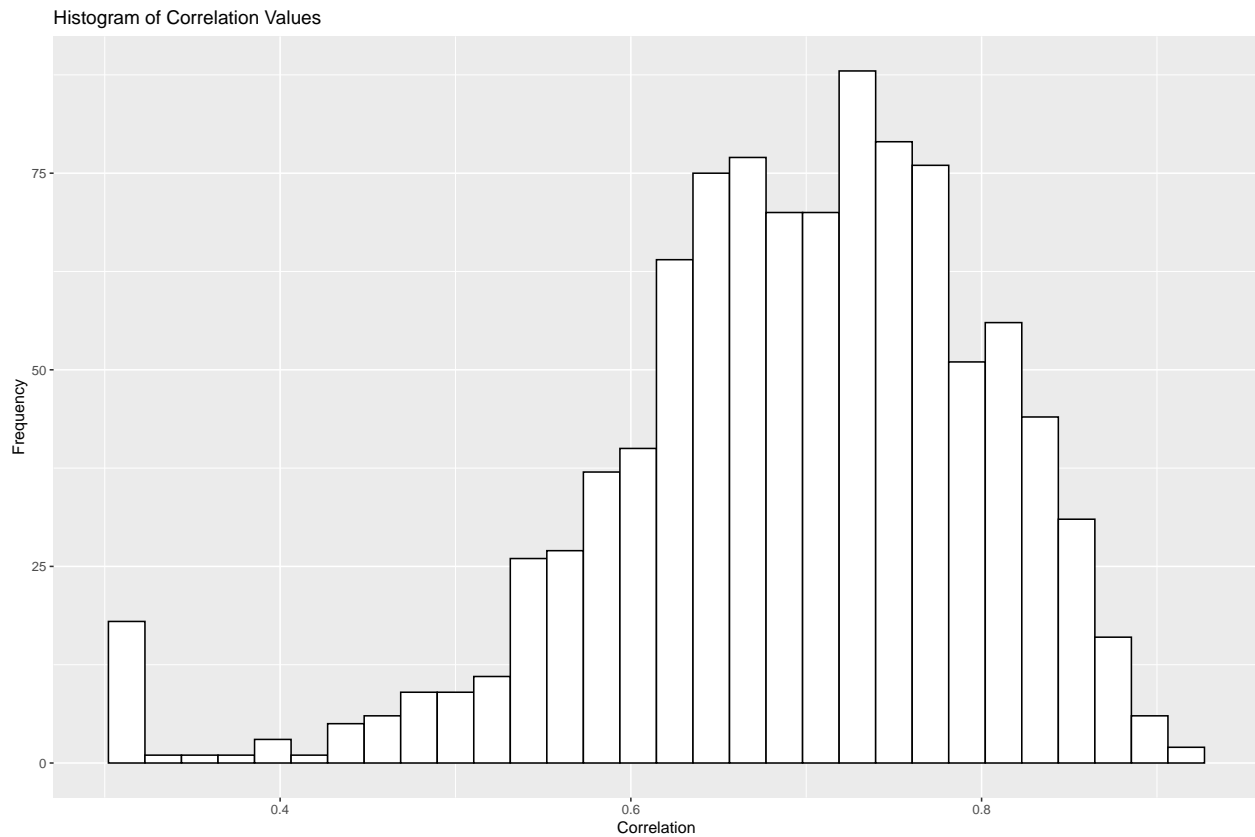


##

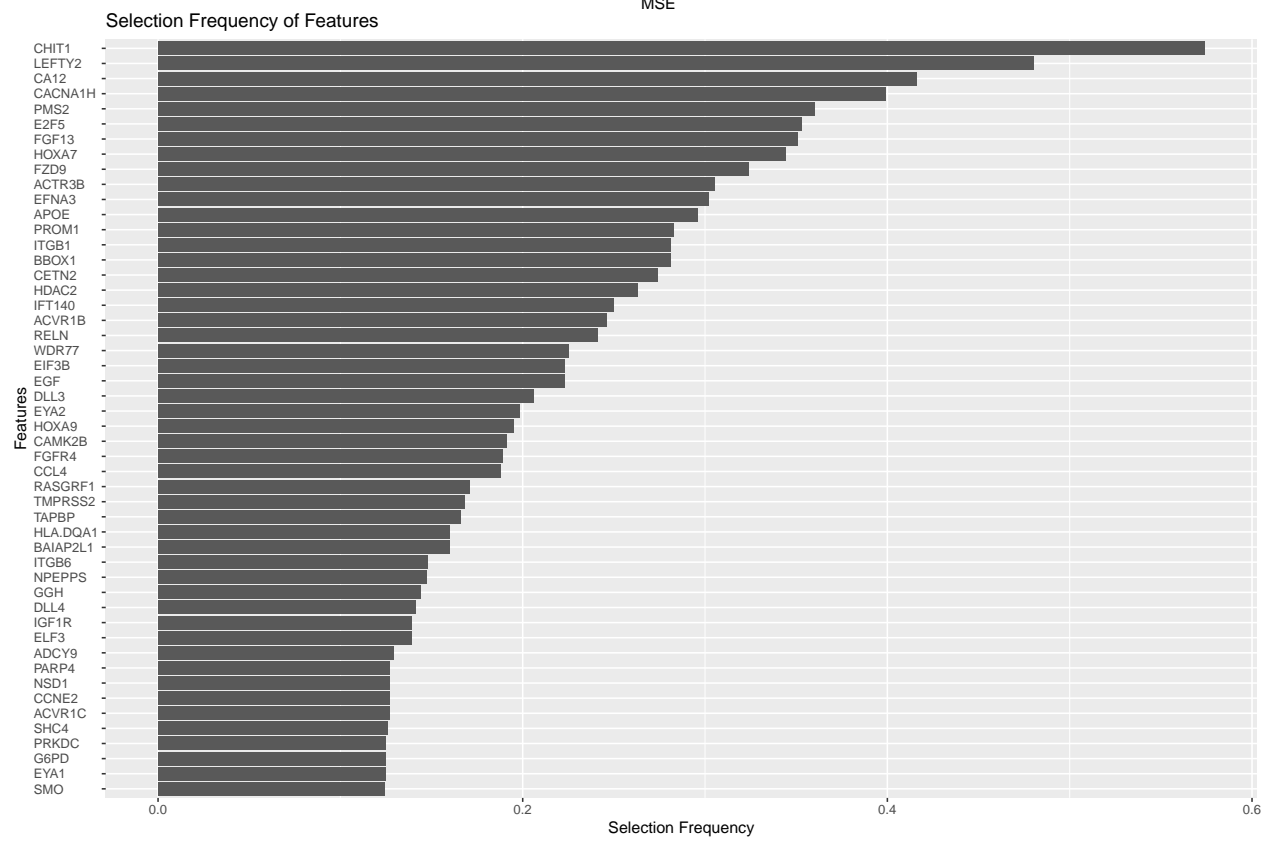
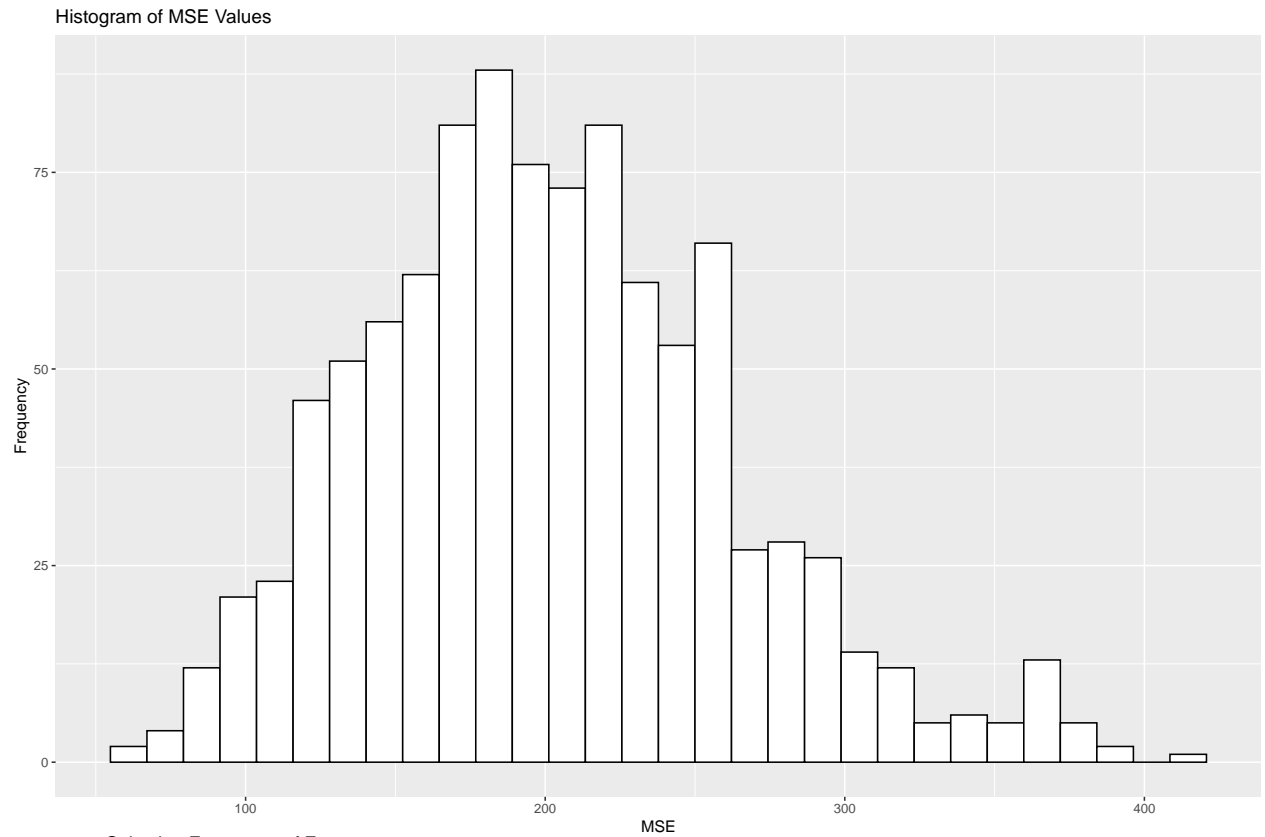
```
## Features selected 50% or more times:
## GATA3 LEFTY2
## Top 20 featrues:
## [1] "LEFTY2" "GATA3" "BMPR1B" "HOXA7" "JAG1" "EFNA3" "PGK1"
## [8] "HOXA9" "HDAC2" "SHC4" "CA12" "HK2" "CAMK2B" "RPS6KA5"
## [15] "AGTR1" "ITGB1" "CHIT1" "IGF1R" "PLA2G2A" "ADCY9"
```

**Mechnaistic + Residuals -> ROR-proliferation score (additive)**

```
## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0
##
## CORRELATIONS RESULTS
## Mean: 0.6925953
## Median: 0.7037142
## Variance: 0.01193153
## st.dev.: 0.1092315
```



```
## MSE RESULTS
## Mean: 202.3235
## Median: 197.4845
## Variance: 3726.169
## st.dev.: 61.04236
```

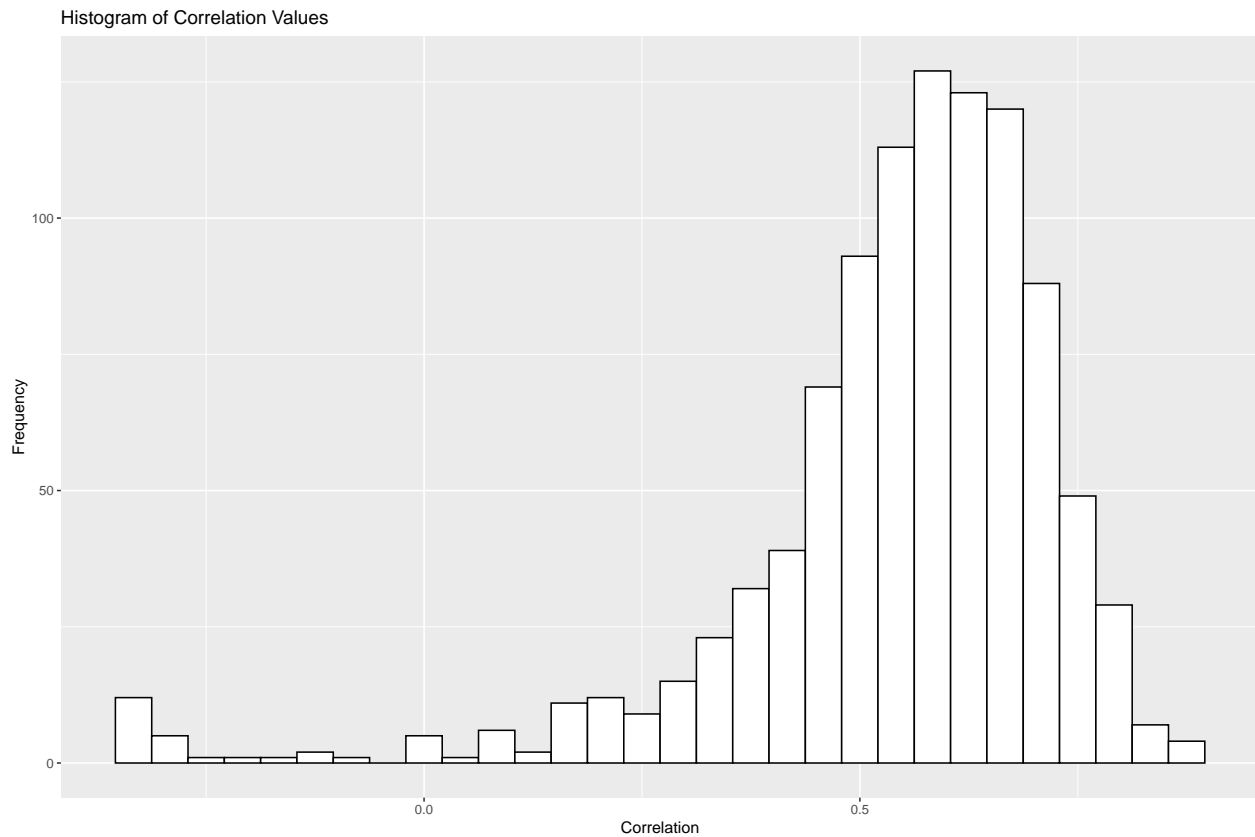


##

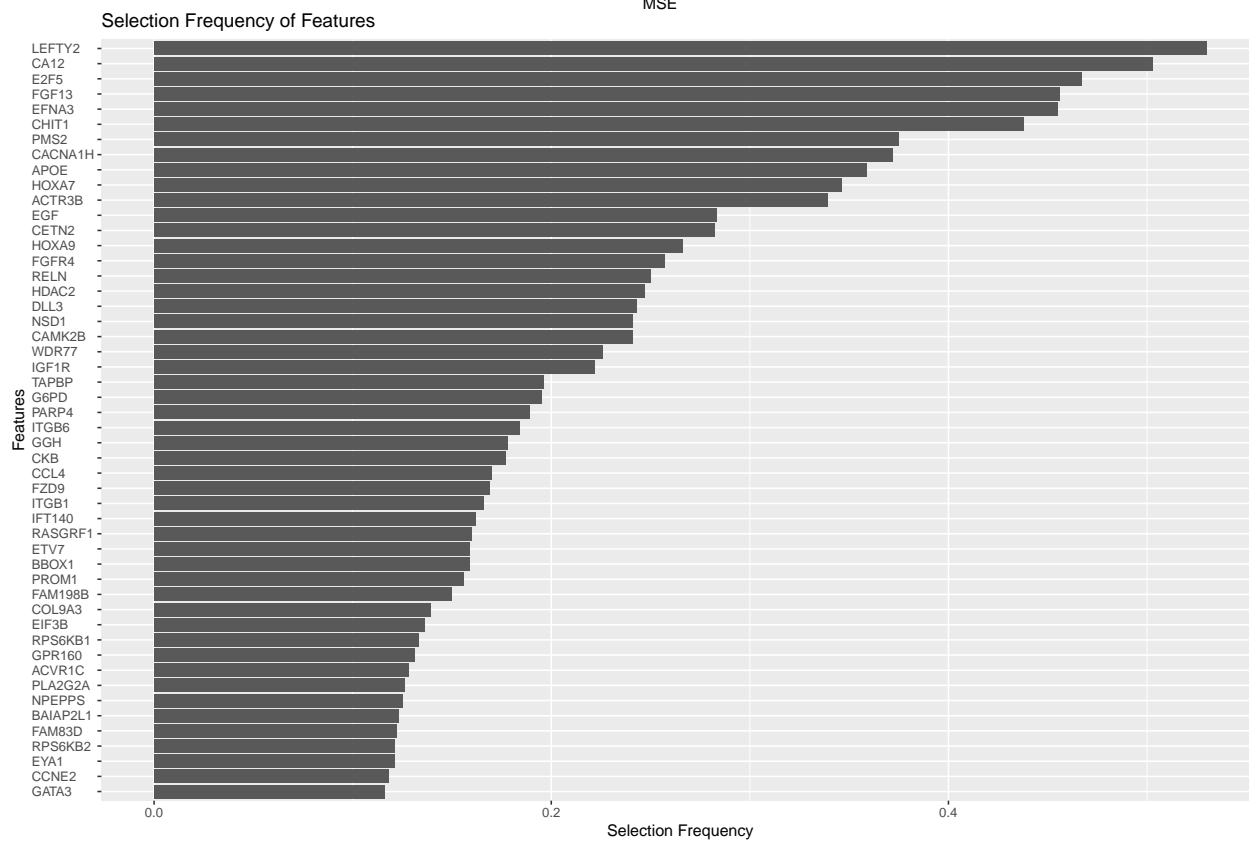
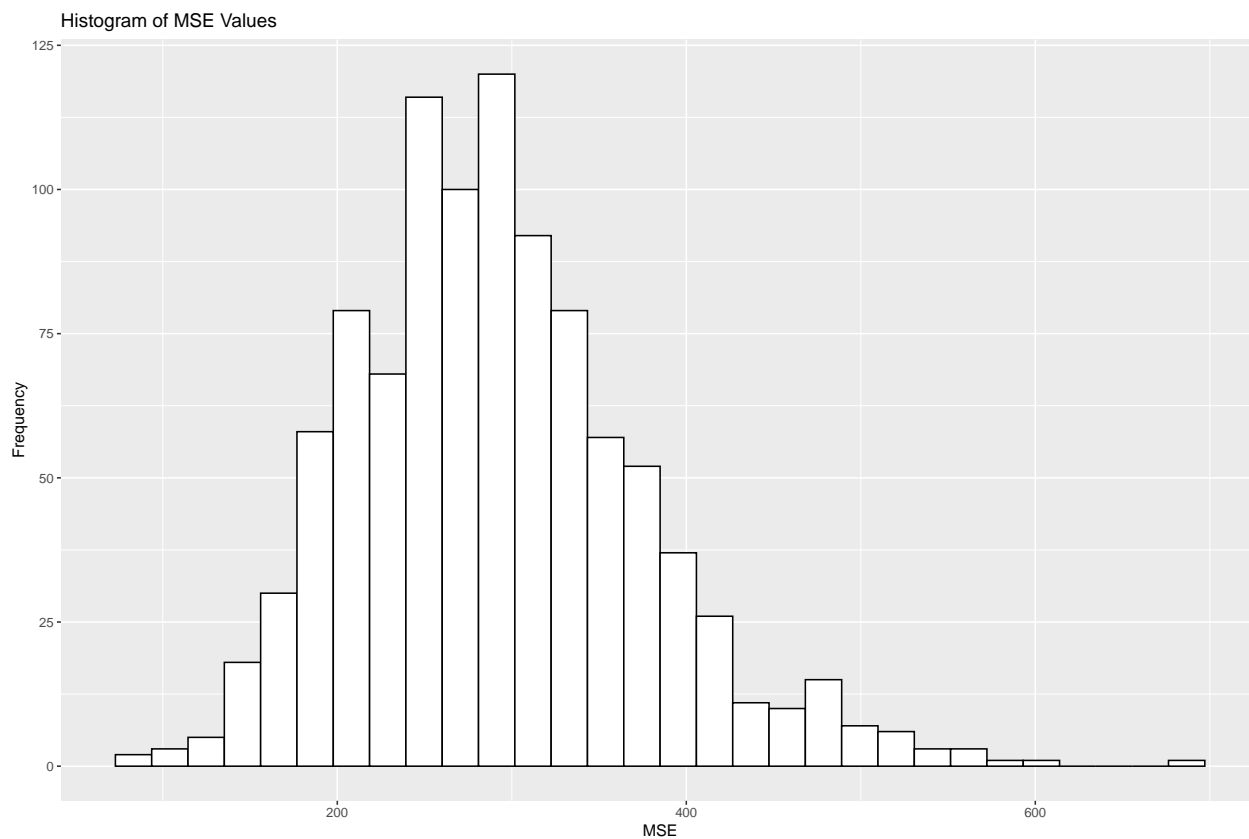
```
## Features selected 50% or more times:
## CHIT1
## Top 20 featrues:
## [1] "CHIT1"    "LEFTY2"   "CA12"     "CACNA1H"  "PMS2"     "E2F5"     "FGF13"
## [8] "HOXA7"    "FZD9"     "ACTR3B"   "EFNA3"    "APOE"     "PROM1"    "BBOX1"
## [15] "ITGB1"    "CETN2"    "HDAC2"    "IFT140"   "ACVR1B"   "RELN"
```

**Mechnaistic + Residuals -> ROR-proliferation score (multiplicative)**

```
## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0
##
## CORRELATIONS RESULTS
## Mean: 0.5427757
## Median: 0.5790305
## Variance: 0.03640698
## st.dev.: 0.1908061
```



```
## MSE RESULTS
## Mean: 291.0186
## Median: 284.2399
## Variance: 6854.567
## st.dev.: 82.79231
```



##

```
## Features selected 50% or more times:
## CA12 LEFTY2
## Top 20 featrues:
## [1] "LEFTY2" "CA12" "E2F5" "FGF13" "EFNA3" "CHIT1" "PMS2"
## [8] "CACNA1H" "APOE" "HOXA7" "ACTR3B" "EGF" "CETN2" "HOXA9"
## [15] "FGFR4" "RELN" "HDAC2" "DLL3" "CAMK2B" "NSD1"
```

#### Summery results: lasso proliferation score (bootstrap)

Model	cor_mean	sd_cor	MSE_mean	MSE_sd
lasso 6 genes	0.3498379	0.0631210	0.1492302	0.0124509
lasso 771 genes	0.7941413	0.0901070	0.0620913	0.0239813
Nodes	0.4144960	0.0642722	0.1479731	0.1916630
Residual additive	0.7835808	0.0854335	0.0638484	0.0213956
Residual multiplicative	0.7266736	0.0895236	0.0813415	0.0231428

#### Summery results: lasso ROR+proliferation score (bootstrap)

Model	cor_mean	sd_cor	MSE_mean	MSE_sd
lasso 6 genes	0.1282306	0.0534128	378.0940	23.44024
lasso 771 genes	0.6968101	0.0995060	203.4080	61.34872
Nodes	0.2964169	0.0830696	417.6667	1027.06231
Residual additive	0.6925953	0.1092315	202.3235	61.04236
Residual multiplicative	0.5427757	0.1908061	291.0186	82.79231

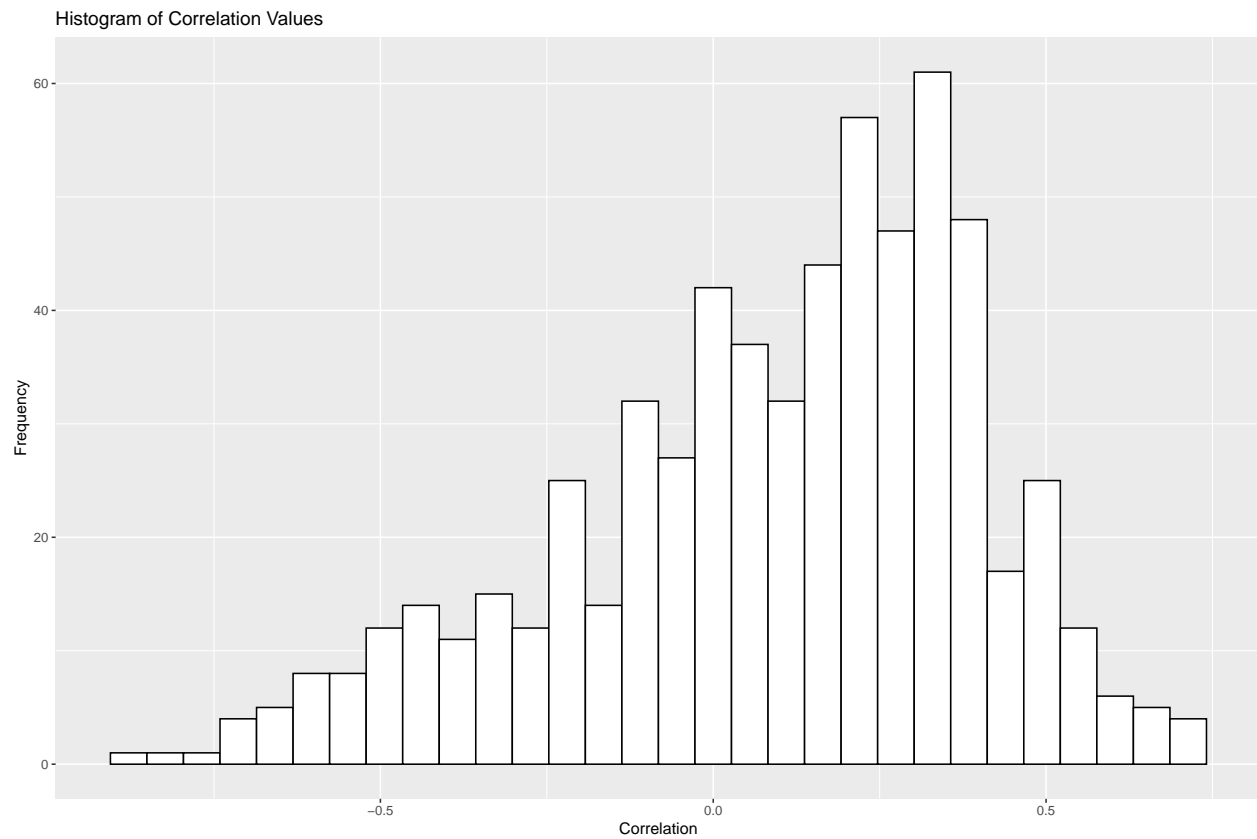
### Lasso - Repeated cross-validation

200 repeats of five fold cross-validation

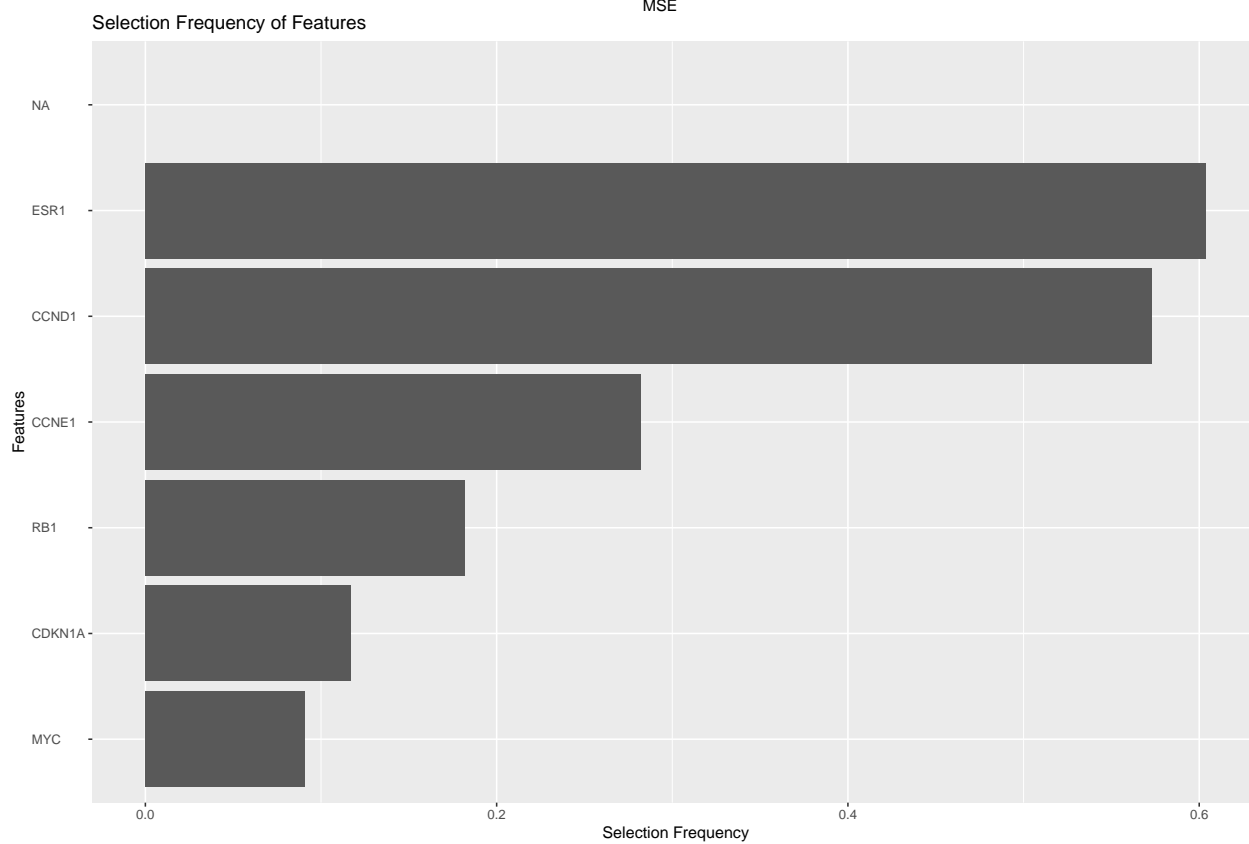
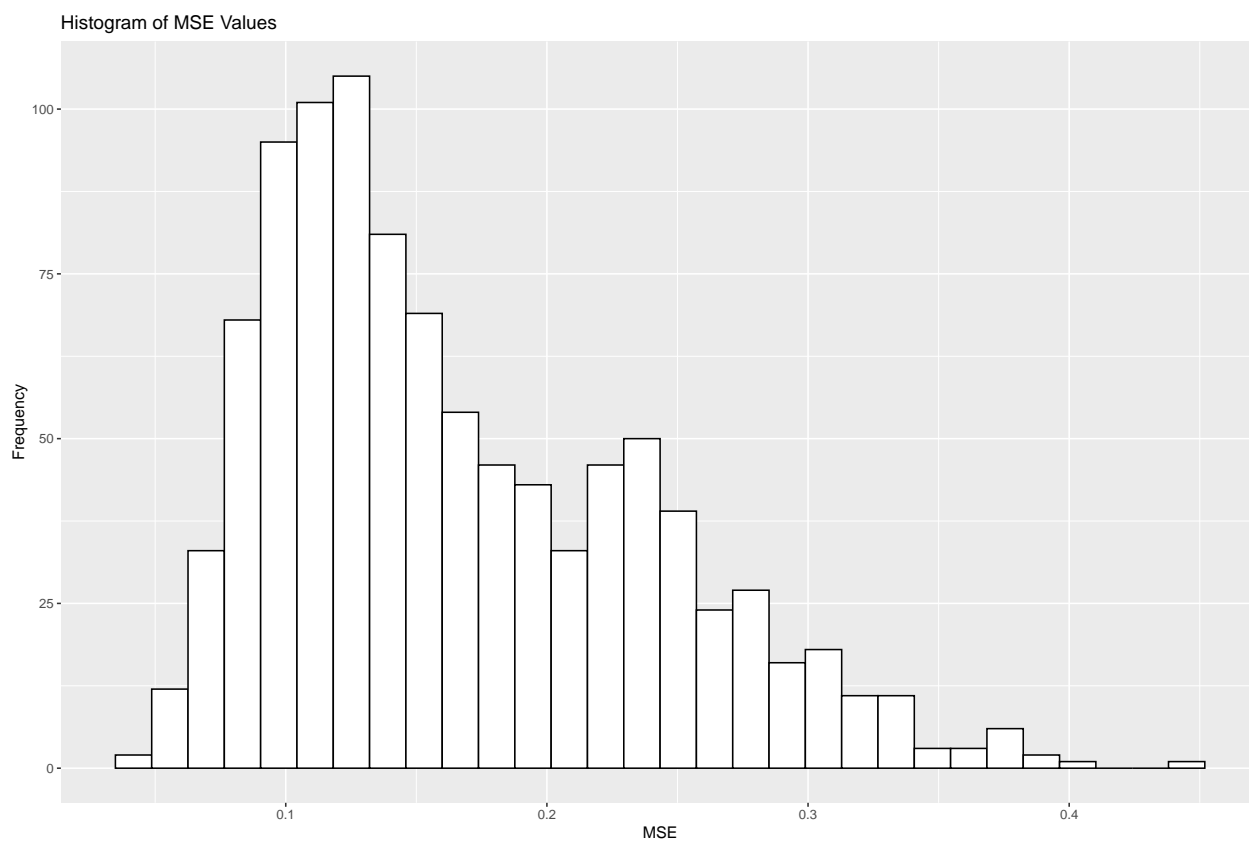
#### 6 genes -> proliferation score

```
## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0.373
##
## CORRELATIONS RESULTS
## Mean: 0.09196628
## Median: 0.1502755
## Variance: 0.09413904
## st.dev.: 0.3068209
```





```
## MSE RESULTS
## Mean: 0.1655931
## Median: 0.1468293
## Variance: 0.005160684
## st.dev.: 0.0718379
```

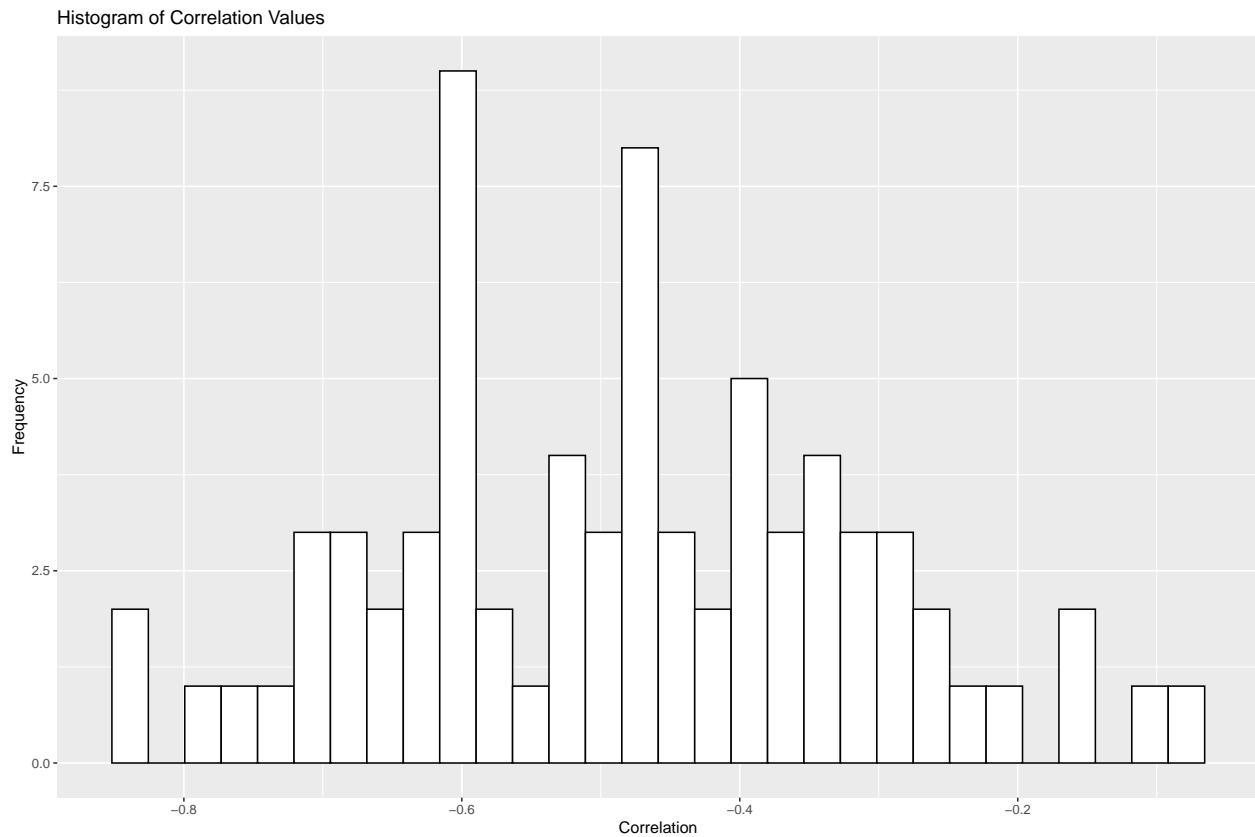


##

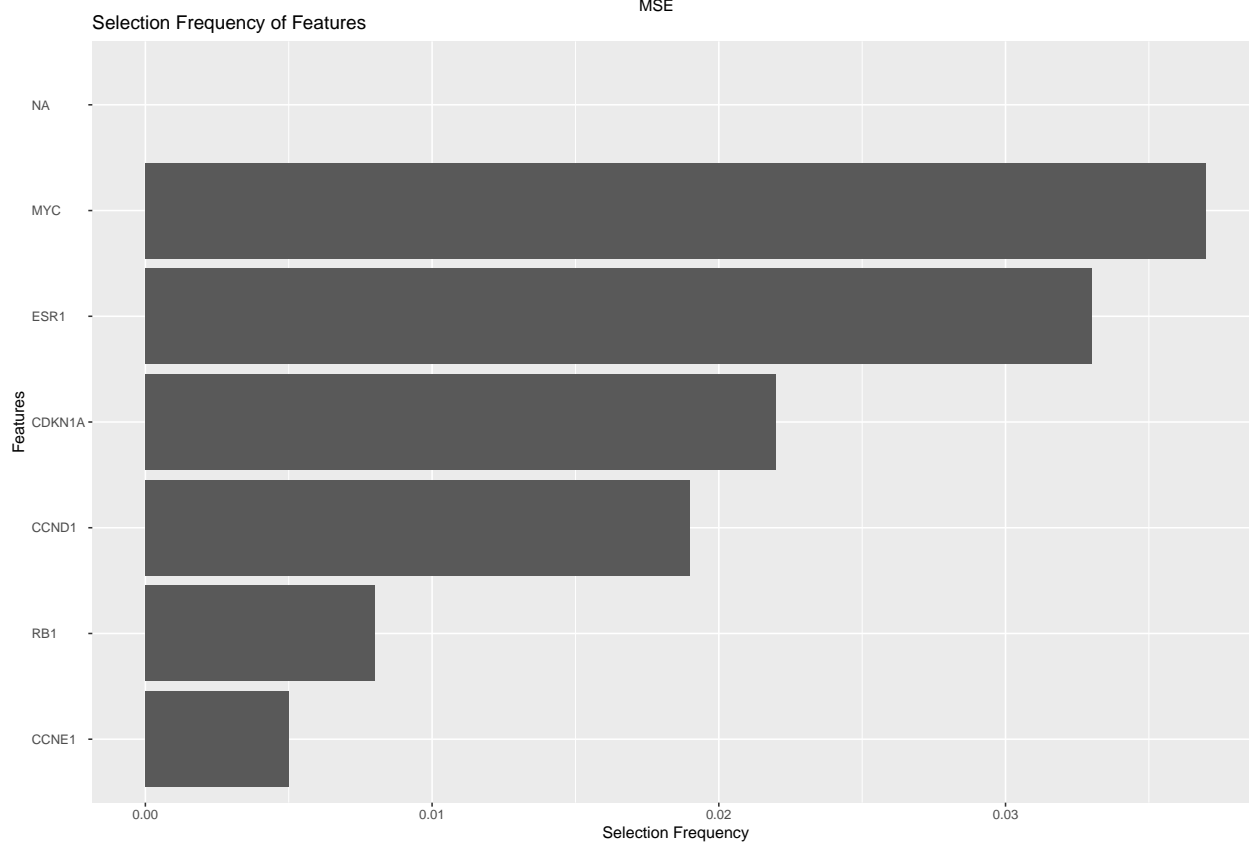
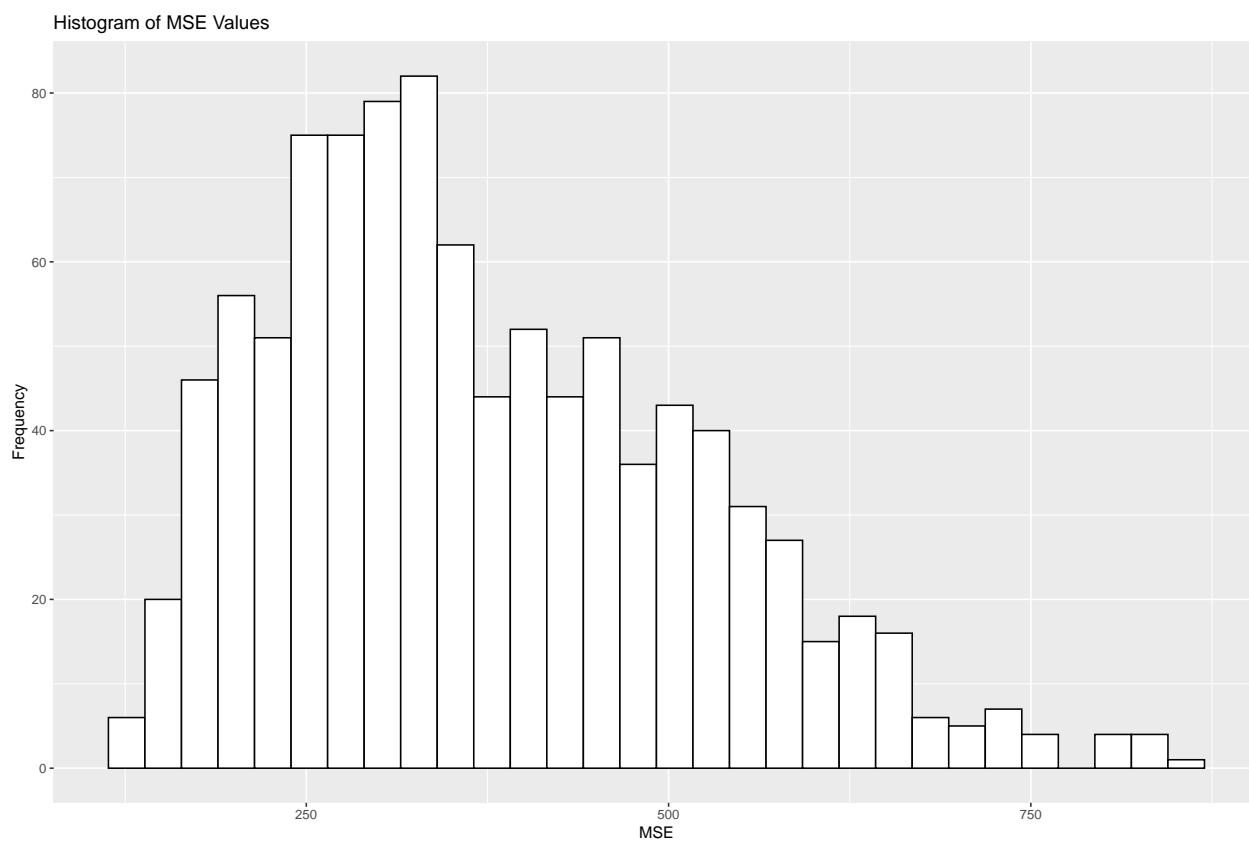
```
## Features selected 50% or more times:
## CCND1 ESR1
## Top 20 featruess:
## [1] "ESR1" "CCND1" "CCNE1" "RB1" "CDKN1A" "MYC" NA NA
## [9] NA NA NA NA NA NA NA NA
## [17] NA NA NA NA
```

**6 genes -> ROR\_proliferation score**

```
## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0.926
##
## CORRELATIONS RESULTS
## Mean: -0.4822298
## Median: -0.4810641
## Variance: 0.02975572
## st.dev.: 0.1724985
```



```
## MSE RESULTS
## Mean: 374.1519
## Median: 343.2105
## Variance: 20780.92
## st.dev.: 144.1559
```



##

```
## Features selected 50% or more times:
```

```
##
```

```
## Top 20 features:
```

```
## [1] "MYC"      "ESR1"      "CDKN1A"    "CCND1"     "RB1"       "CCNE1"     NA        NA
## [9] NA         NA          NA          NA          NA          NA          NA        NA
## [17] NA         NA          NA          NA
```

```
771 genes -> proliferation score
```

```
## number of models fitted: 1000
```

```
## Fraction of model fits with no selected genes: 0.011
```

```
##
```

```
## CORRELATIONS RESULTS
```

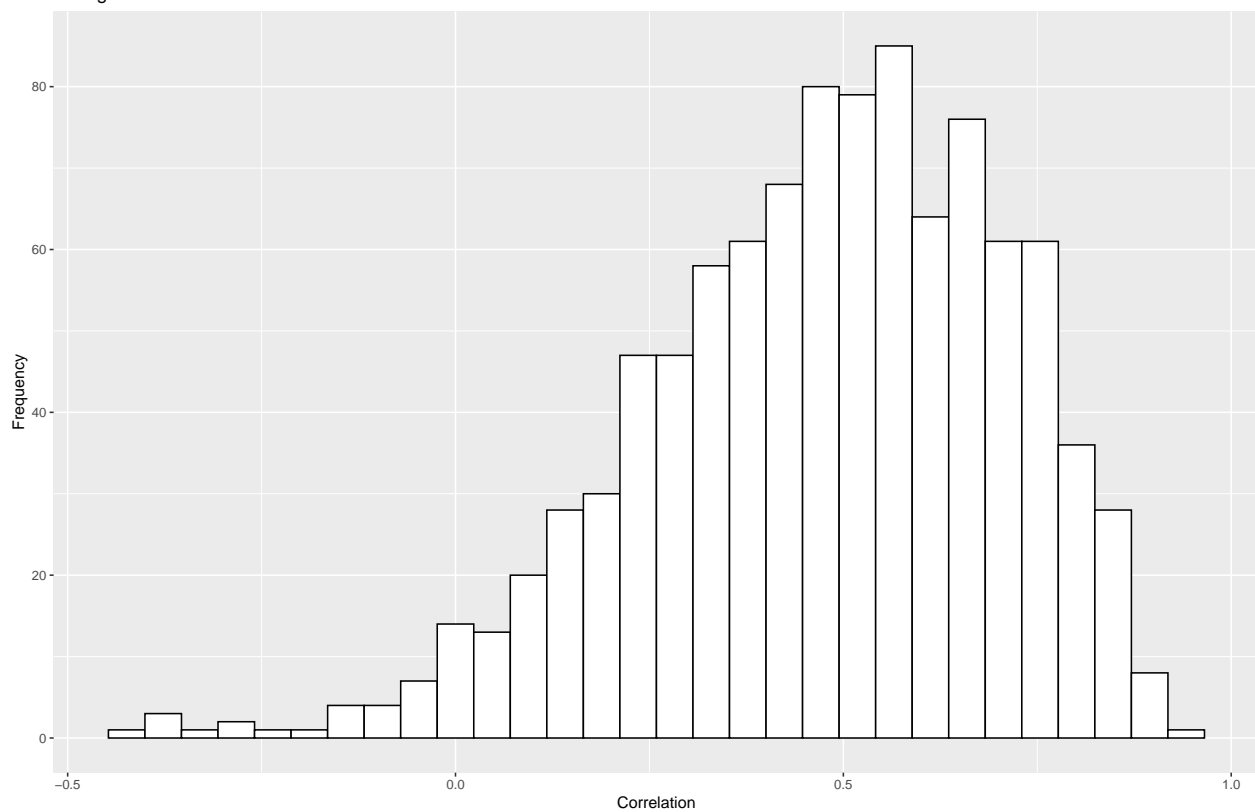
```
## Mean: 0.4737037
```

```
## Median: 0.4959203
```

```
## Variance: 0.05337068
```

```
## st.dev.: 0.2310209
```

```
Histogram of Correlation Values
```



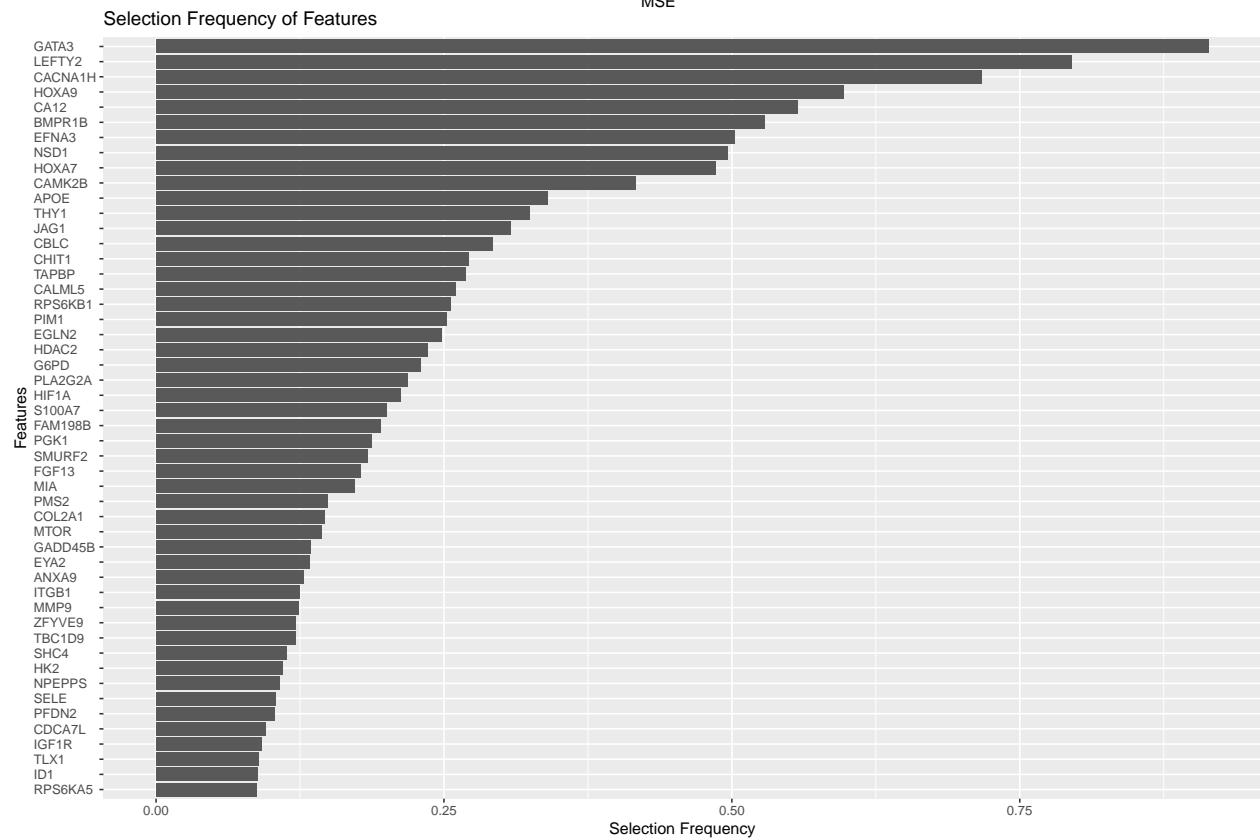
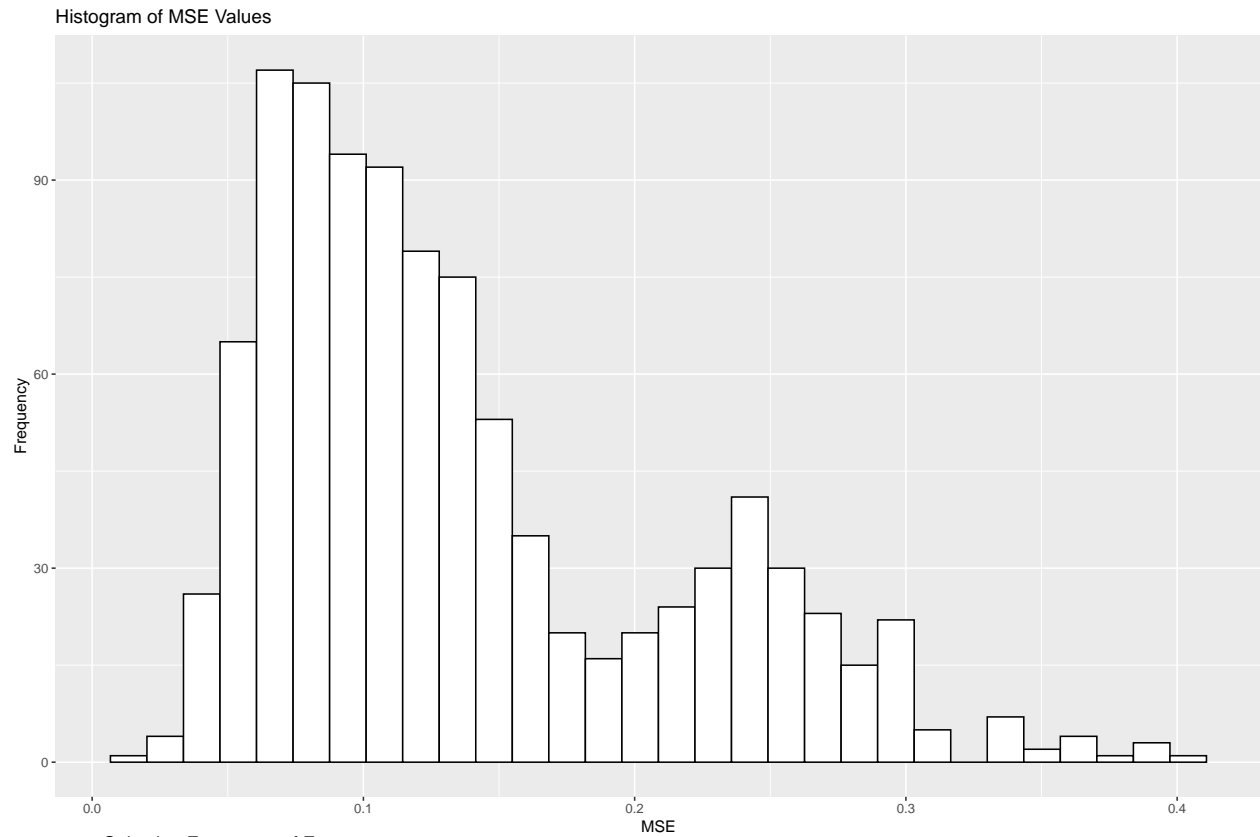
```
## MSE RESULTS
```

```
## Mean: 0.1376002
```

```
## Median: 0.1154157
```

```
## Variance: 0.005670929
```

```
## st.dev.: 0.07530557
```

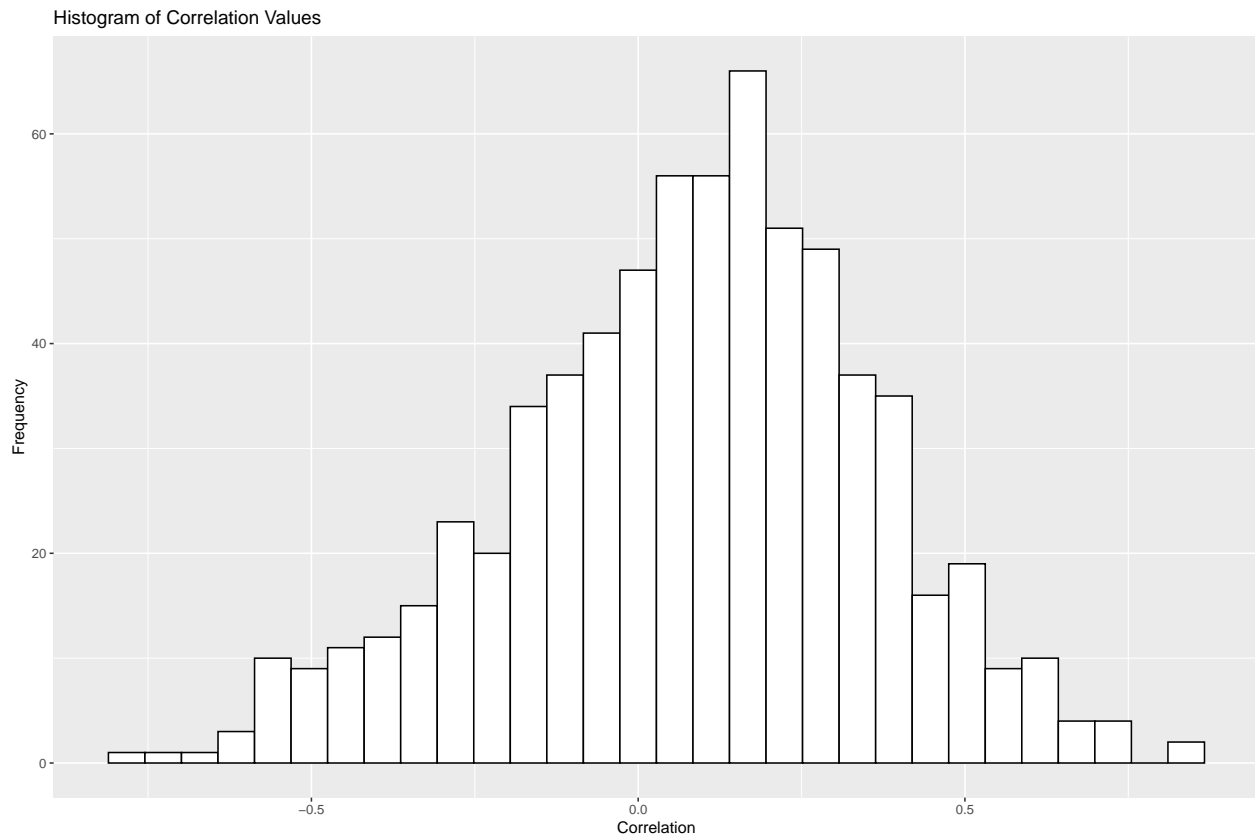


##

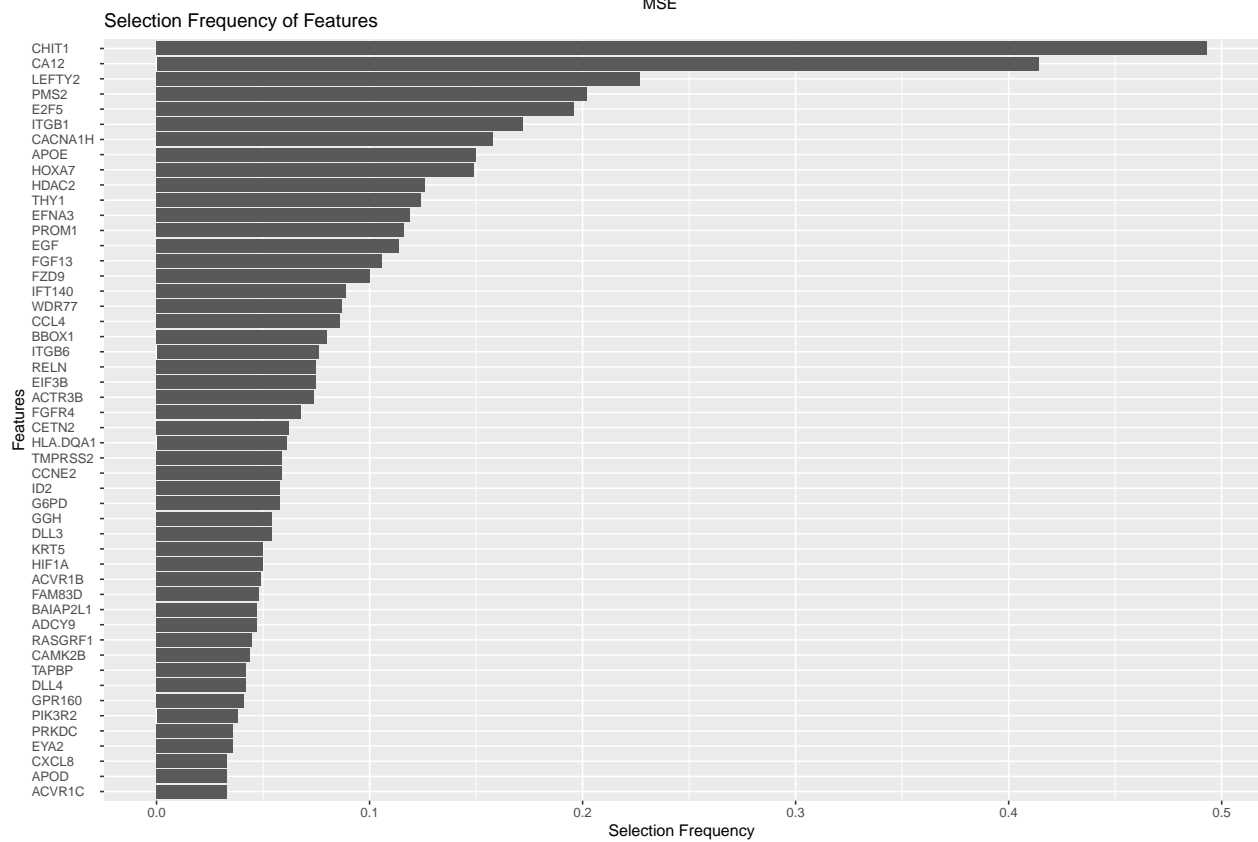
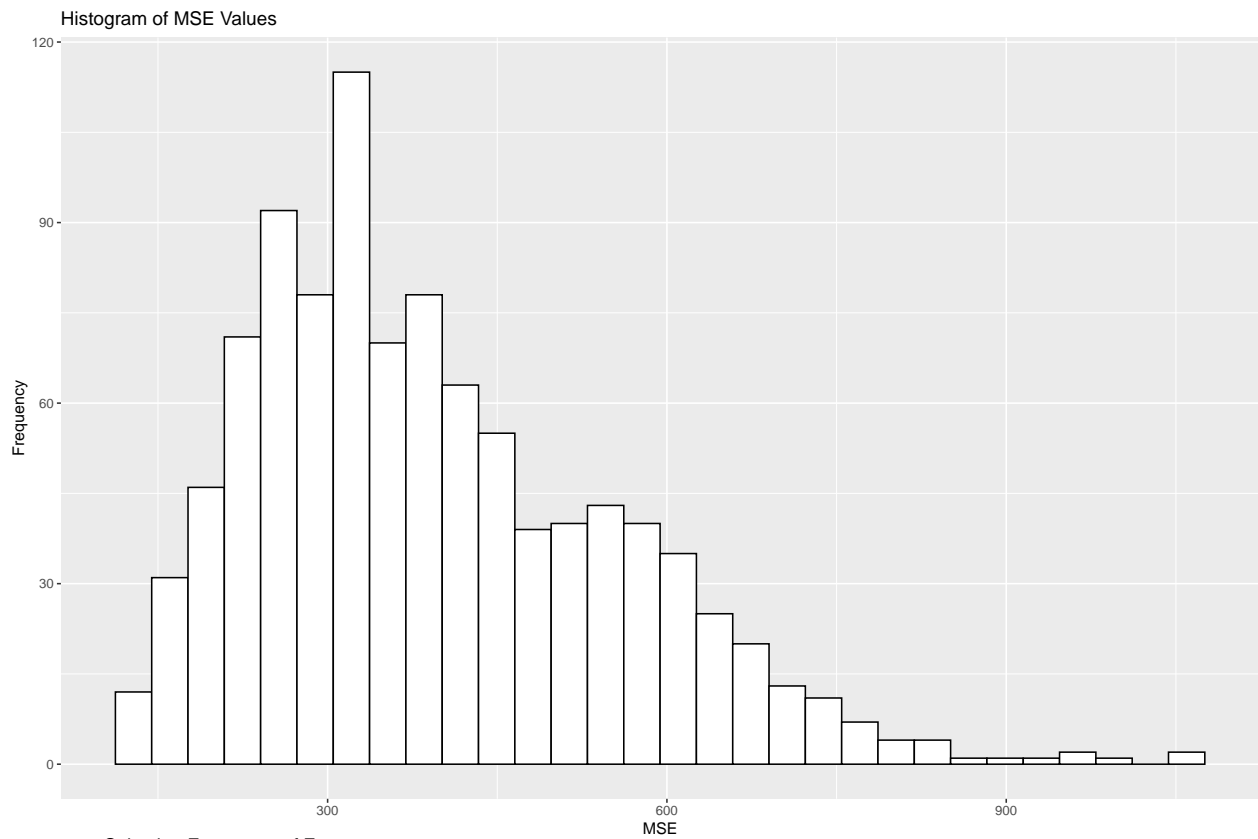
```
## Features selected 50% or more times:
## BMPR1B CA12 CACNA1H EFNA3 GATA3 HOXA9 LEFTY2
## Top 20 featrues:
## [1] "GATA3" "LEFTY2" "CACNA1H" "HOXA9" "CA12" "BMPR1B" "EFNA3"
## [8] "NSD1" "HOXA7" "CAMK2B" "APOE" "THY1" "JAG1" "CBLC"
## [15] "CHIT1" "TAPBP" "CALML5" "RPS6KB1" "PIM1" "EGLN2"
```

### 771 genes -> ROR-proliferation score

```
## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0.321
##
## CORRELATIONS RESULTS
## Mean: 0.08062366
## Median: 0.1014264
## Variance: 0.07657135
## st.dev.: 0.2767153
```



```
## MSE RESULTS
## Mean: 393.8069
## Median: 360.5105
## Variance: 25486.55
## st.dev.: 159.6451
```



##



```
## Features selected 50% or more times:
```

```
##
```

```
## Top 20 featrues:
```

```
## [1] "CHIT1" "CA12" "LEFTY2" "PMS2" "E2F5" "ITGB1" "CACNA1H"
```

```
## [8] "APOE" "HOXA7" "HDAC2" "THY1" "EFNA3" "PROM1" "EGF"
```

```
## [15] "FGF13" "FZD9" "IFT140" "WDR77" "CCL4" "BBOX1"
```

```
node values -> proliferation score
```

```
## number of models fitted: 1000
```

```
## Fraction of model fits with no selected genes: 0.063
```

```
##
```

```
## CORRELATIONS RESULTS
```

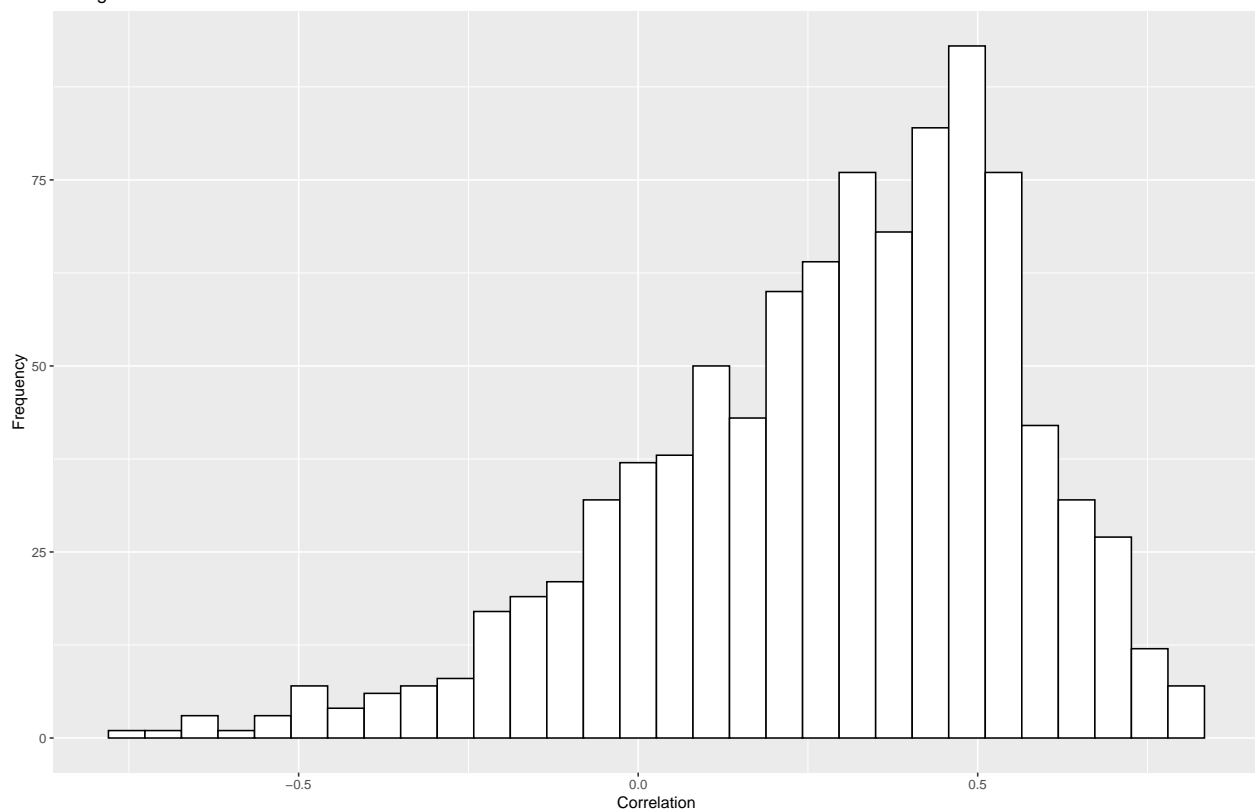
```
## Mean: 0.2842257
```

```
## Median: 0.3249779
```

```
## Variance: 0.07664357
```

```
## st.dev.: 0.2768458
```

```
Histogram of Correlation Values
```



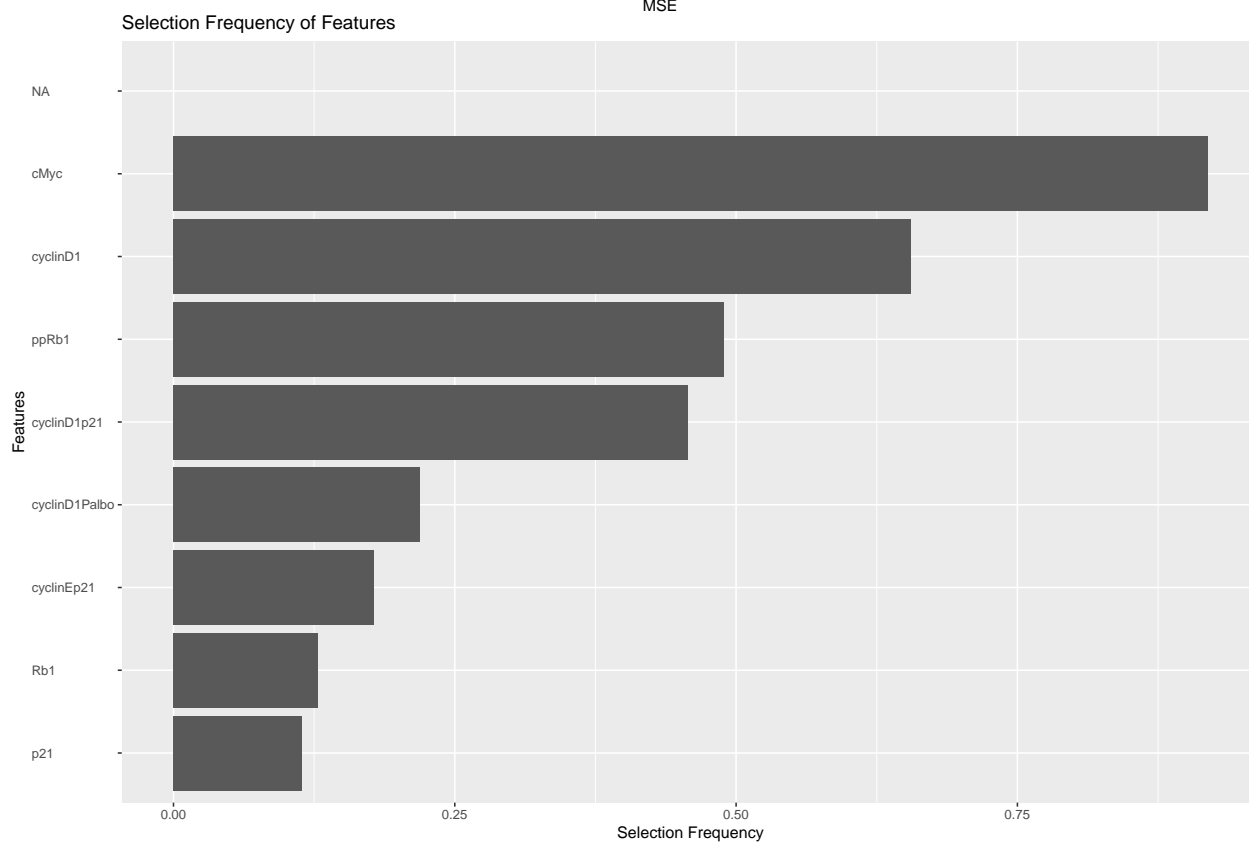
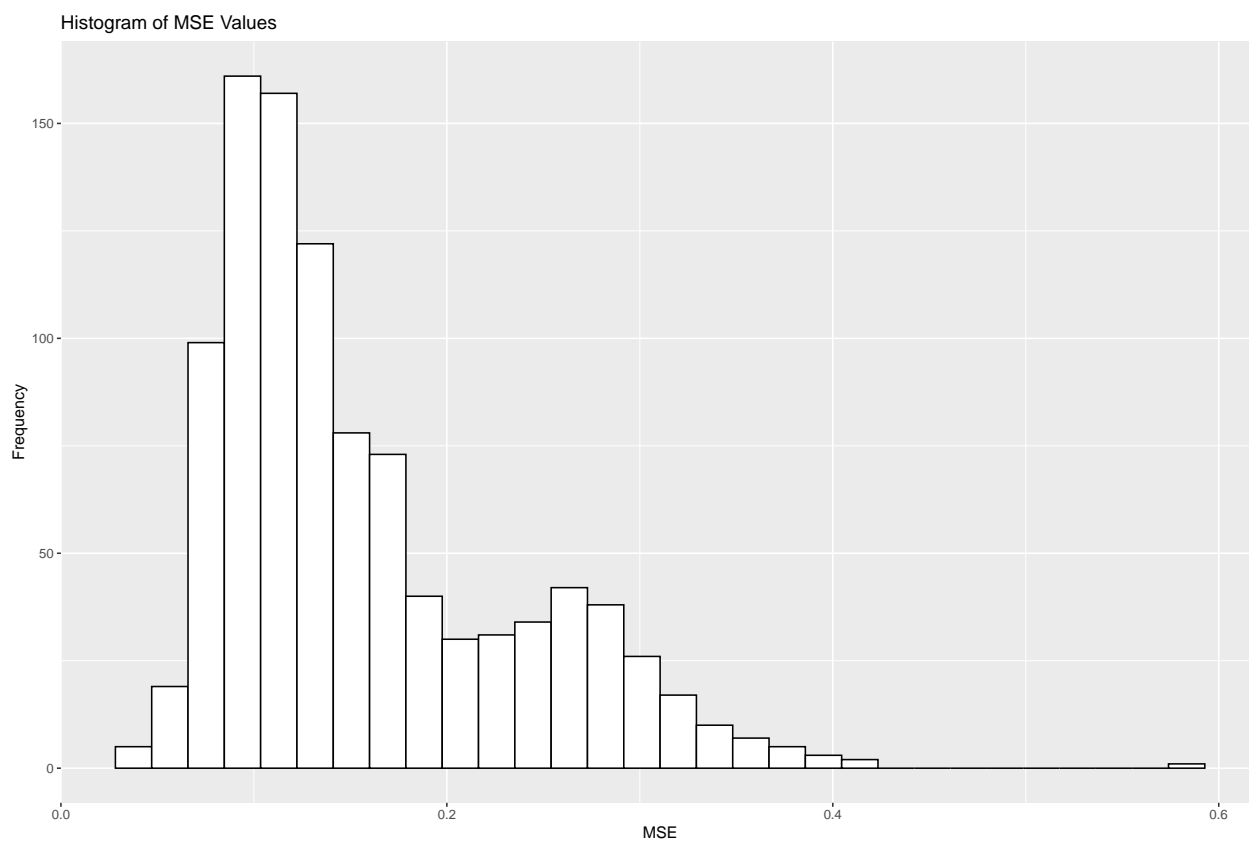
```
## MSE RESULTS
```

```
## Mean: 0.1560308
```

```
## Median: 0.1314678
```

```
## Variance: 0.005819908
```

```
## st.dev.: 0.07628832
```

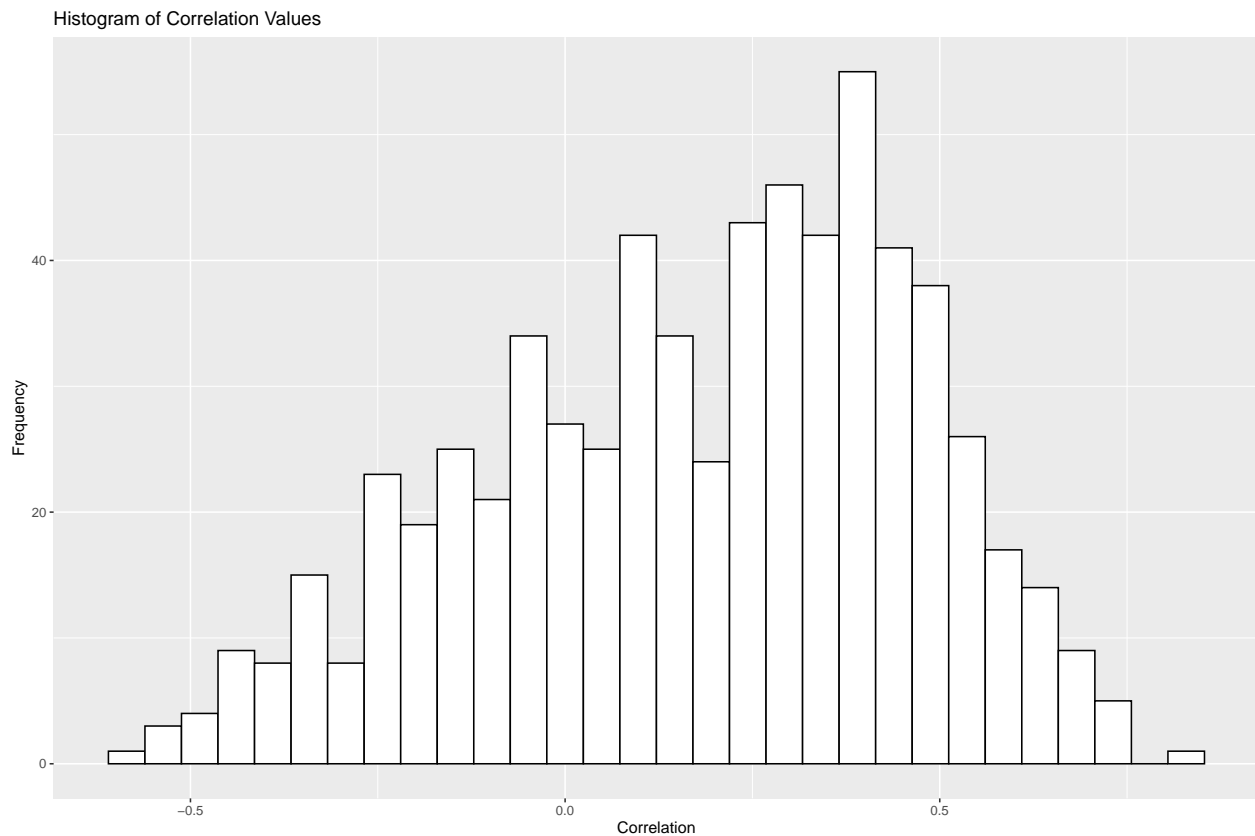


##

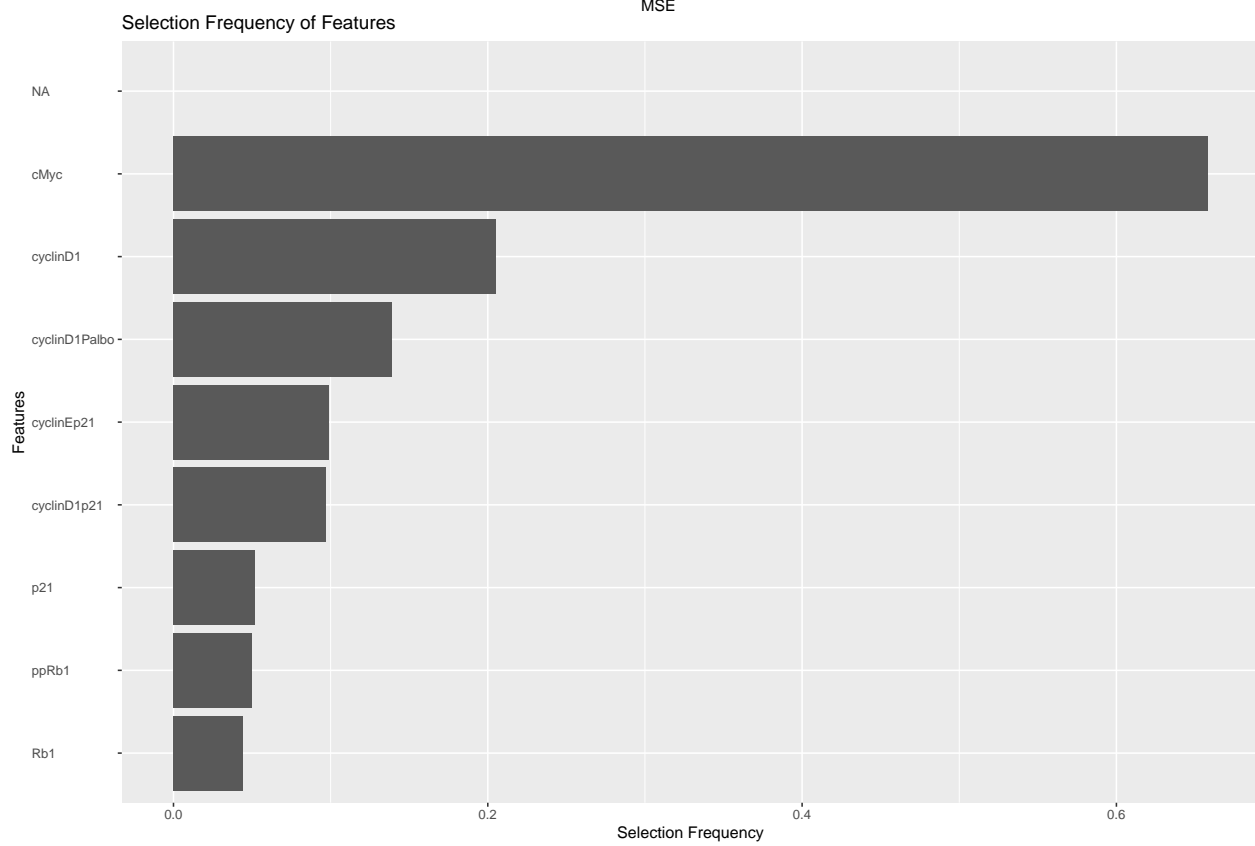
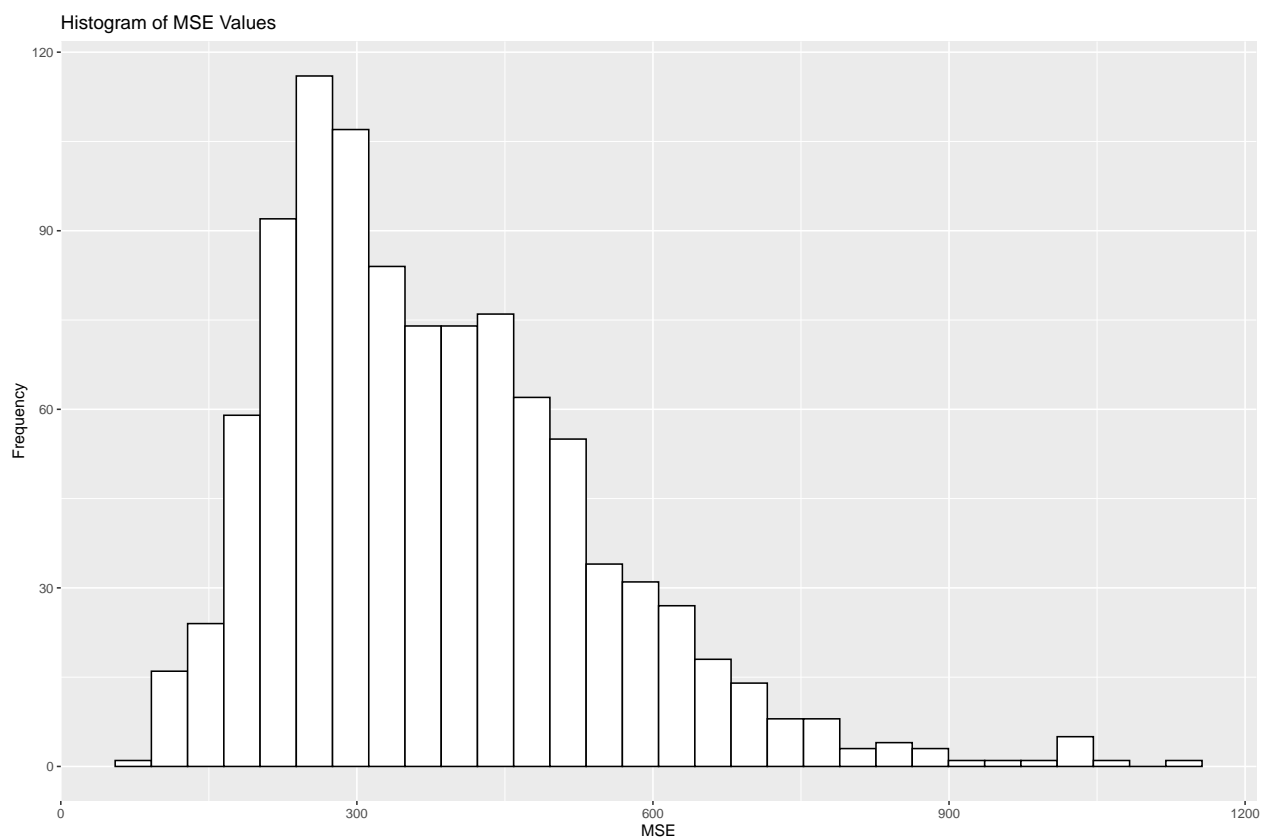
```
## Features selected 50% or more times:
## cyclinD1 cMyc
## Top 20 featrues:
## [1] "cMyc"          "cyclinD1"      "ppRb1"         "cyclinD1p21"
## [5] "cyclinD1Palbo" "cyclinEp21"    "Rb1"           "p21"
## [9] NA              NA              NA              NA
## [13] NA             NA              NA              NA
## [17] NA             NA              NA              NA
```

node values -> ROR-proliferation score

```
## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0.341
##
## CORRELATIONS RESULTS
## Mean: 0.1806504
## Median: 0.2237481
## Variance: 0.08150408
## st.dev.: 0.2854892
```



```
## MSE RESULTS
## Mean: 380.1157
## Median: 349.3312
## Variance: 27088.84
## st.dev.: 164.5869
```



##

```
## Features selected 50% or more times:
```

```
## cMyc
```

```
## Top 20 featrues:
```

```
## [1] "cMyc"          "cyclinD1"      "cyclinD1Palbo" "cyclinEp21"  
## [5] "cyclinD1p21"  "p21"          "ppRb1"         "Rb1"  
## [9] NA             NA             NA             NA  
## [13] NA            NA             NA             NA  
## [17] NA            NA             NA             NA
```

**Mechanistic + Residuals -> proliferation score (additive)**

```
## number of models fitted: 1000
```

```
## Fraction of model fits with no selected genes: 0
```

```
##
```

```
## CORRELATIONS RESULTS
```

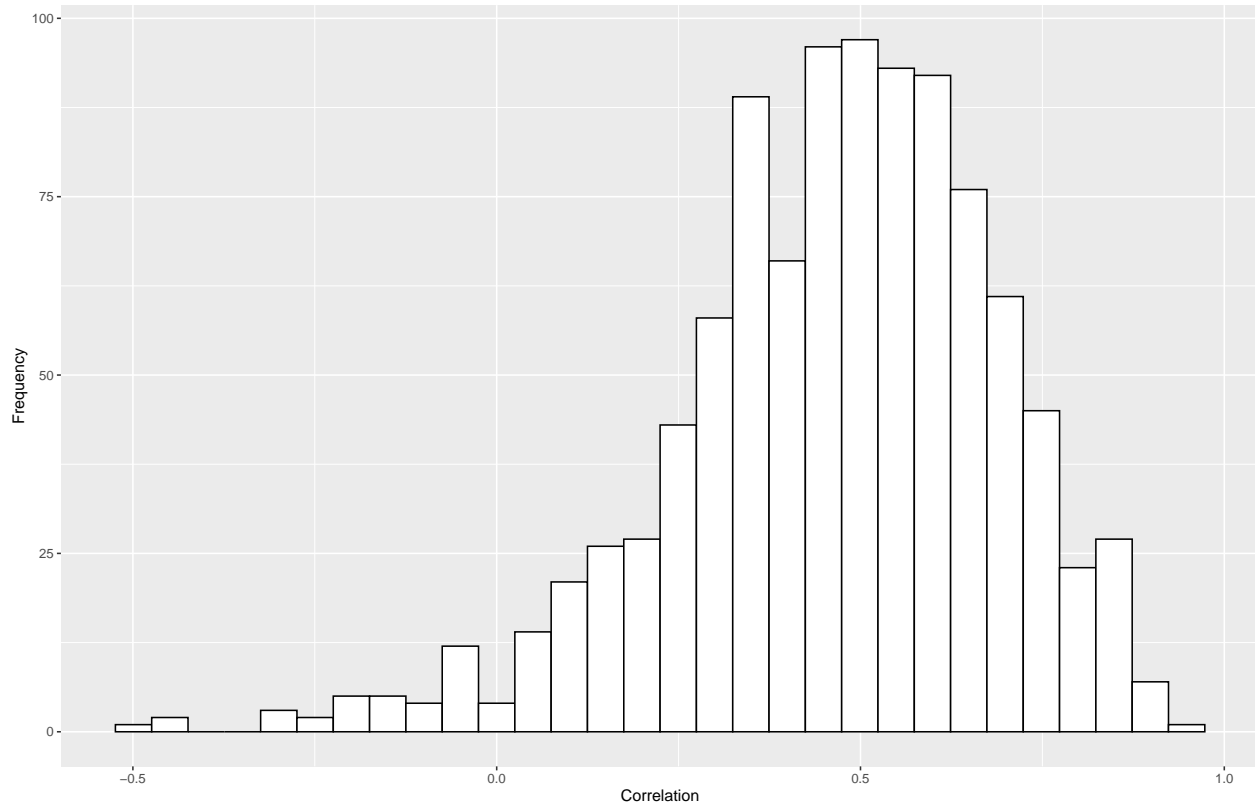
```
## Mean: 0.4633095
```

```
## Median: 0.4870052
```

```
## Variance: 0.04959996
```

```
## st.dev.: 0.2227105
```

Histogram of Correlation Values



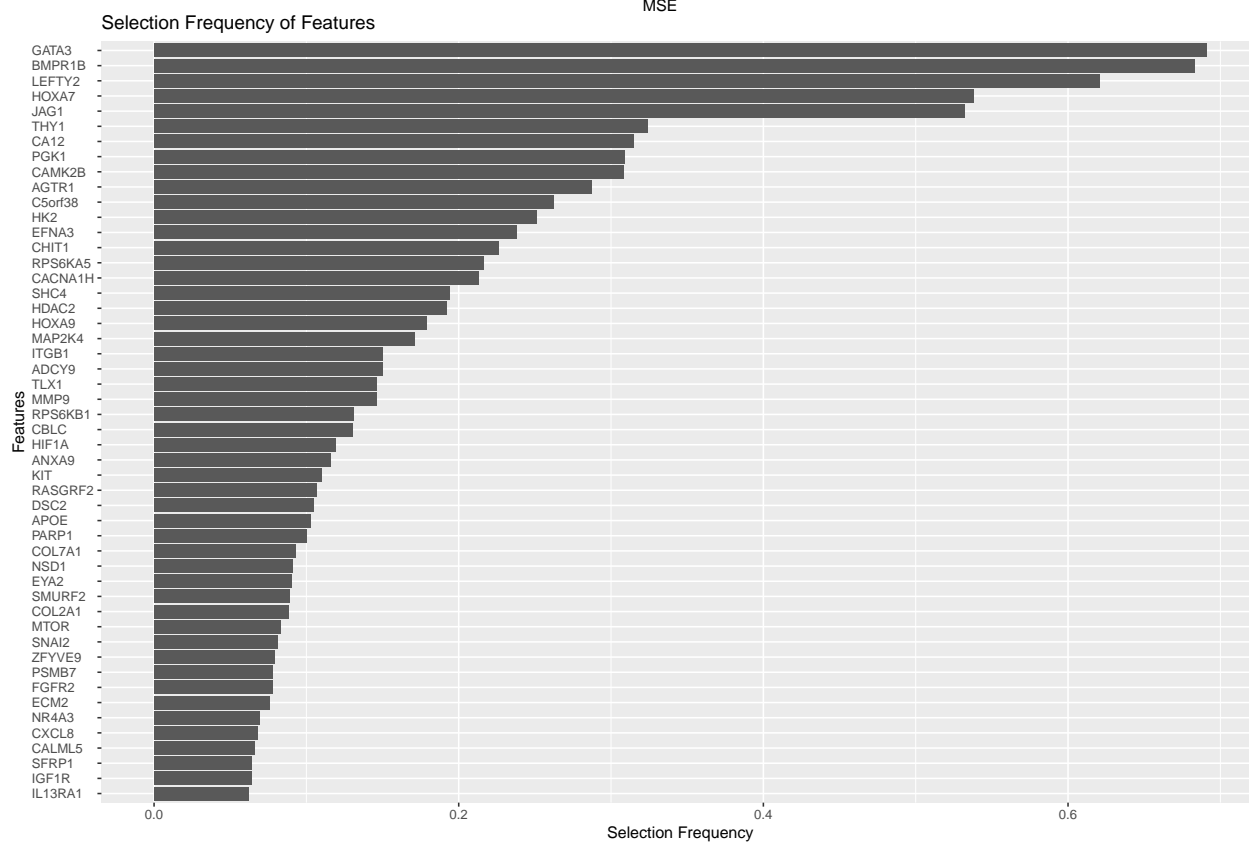
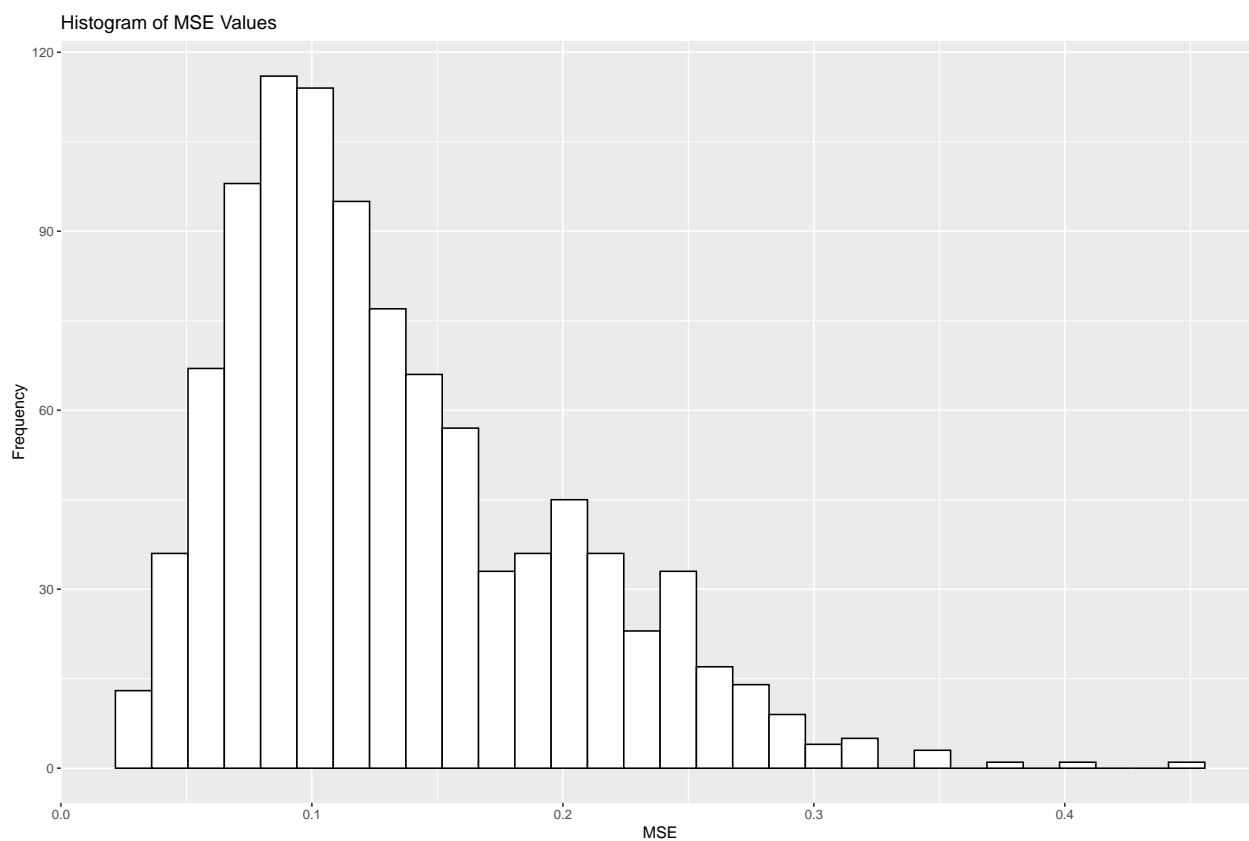
```
## MSE RESULTS
```

```
## Mean: 0.1331785
```

```
## Median: 0.1164927
```

```
## Variance: 0.004278014
```

```
## st.dev.: 0.06540653
```

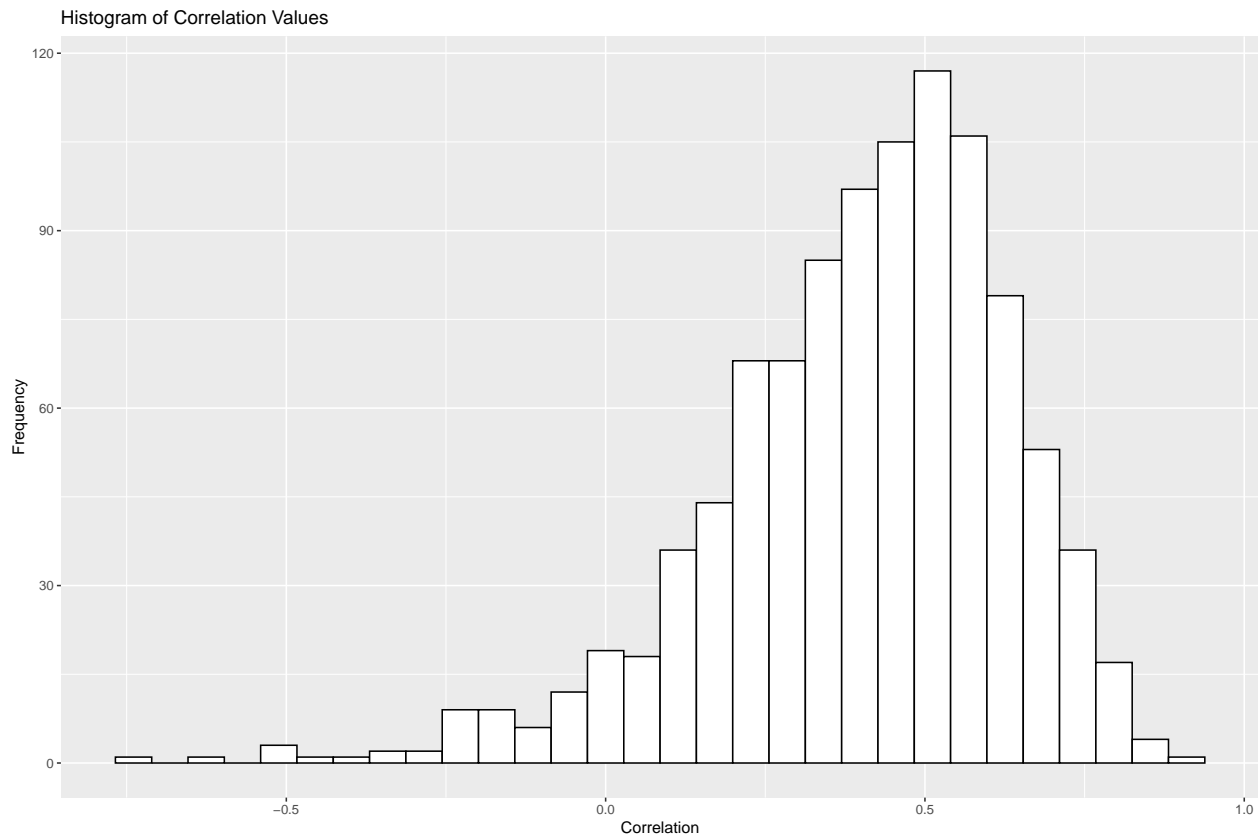


##

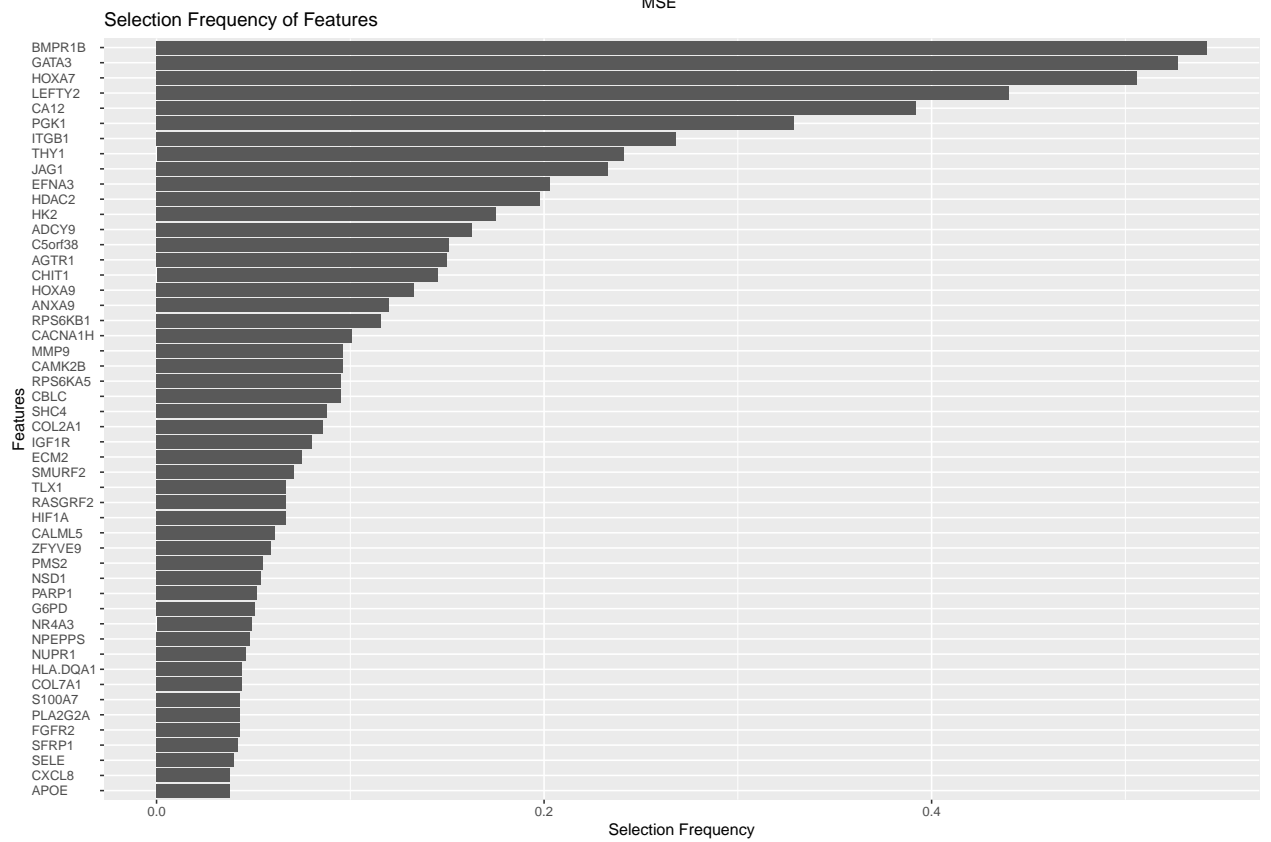
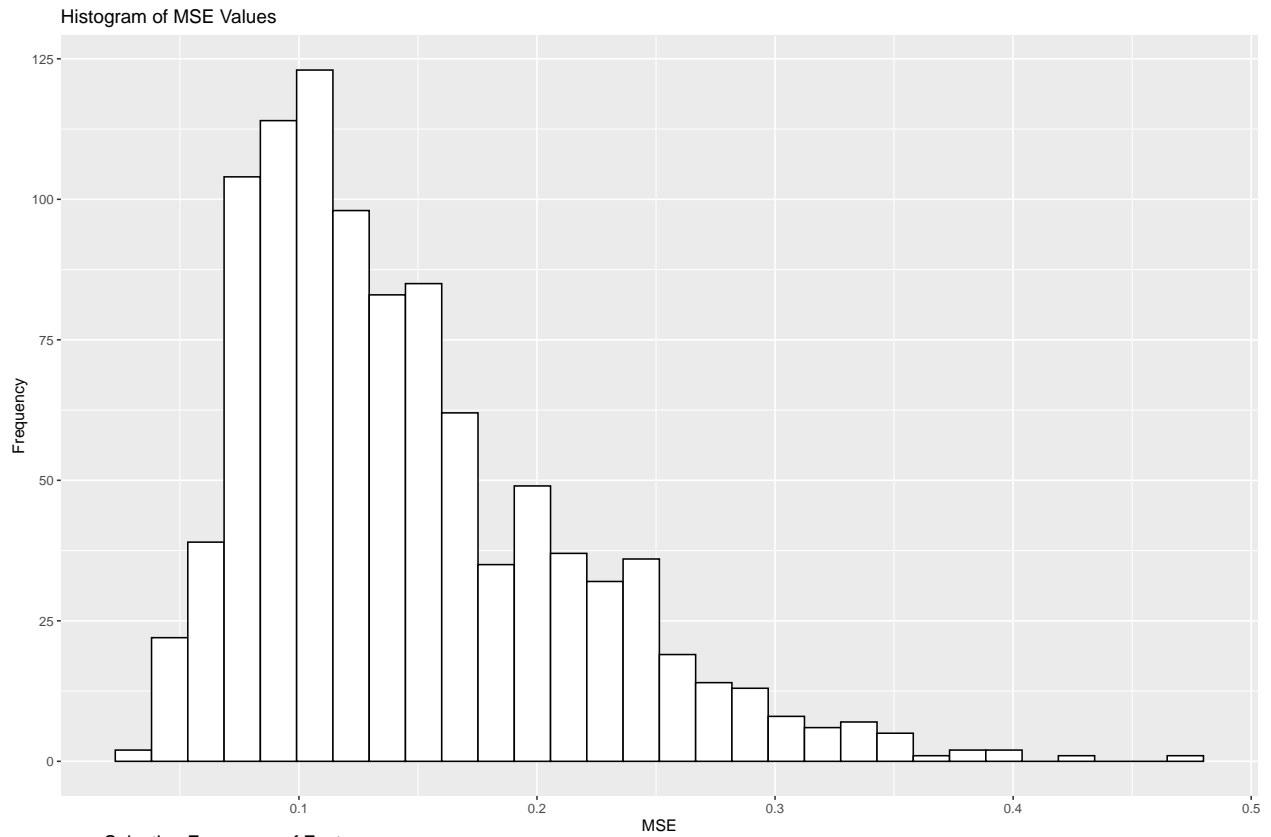
```
## Features selected 50% or more times:
## BMPR1B GATA3 HOXA7 JAG1 LEFTY2
## Top 20 featruess:
## [1] "GATA3" "BMPR1B" "LEFTY2" "HOXA7" "JAG1" "THY1" "CA12"
## [8] "PGK1" "CAMK2B" "AGTR1" "C5orf38" "HK2" "EFNA3" "CHIT1"
## [15] "RPS6KA5" "CACNA1H" "SHC4" "HDAC2" "HOXA9" "MAP2K4"
```

**Mechanistic + Residuals -> proliferation score (multiplicative)**

```
## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0
##
## CORRELATIONS RESULTS
## Mean: 0.4028471
## Median: 0.437445
## Variance: 0.05302116
## st.dev.: 0.2302632
```



```
## MSE RESULTS
## Mean: 0.1455819
## Median: 0.1286019
## Variance: 0.004632394
## st.dev.: 0.06806169
```



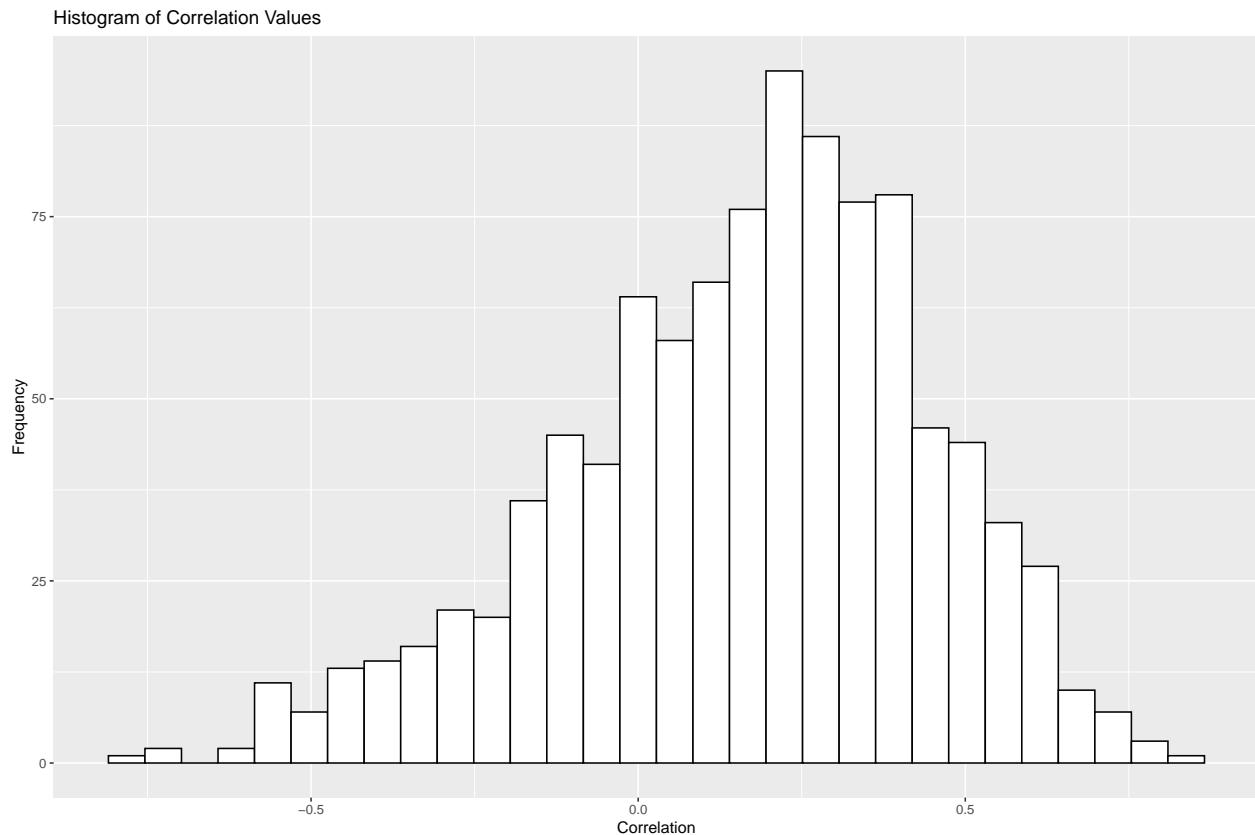
##



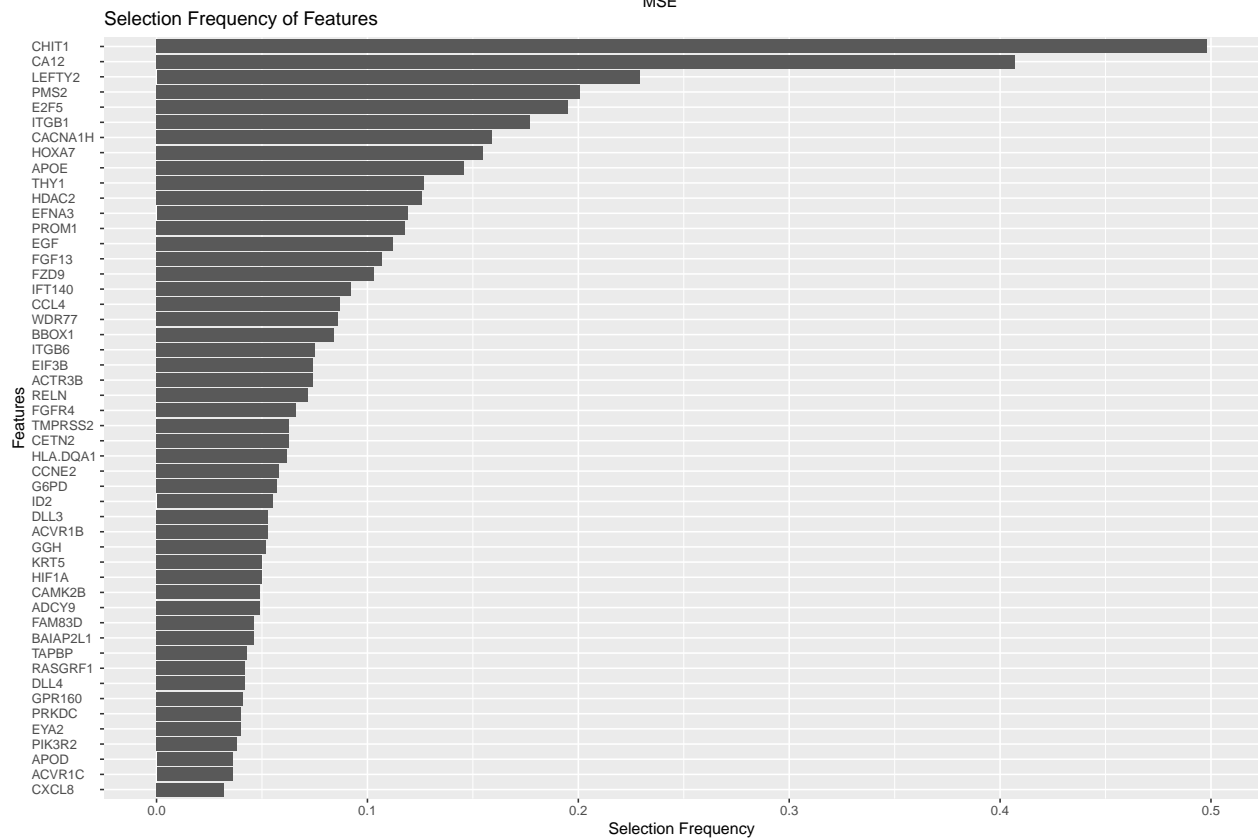
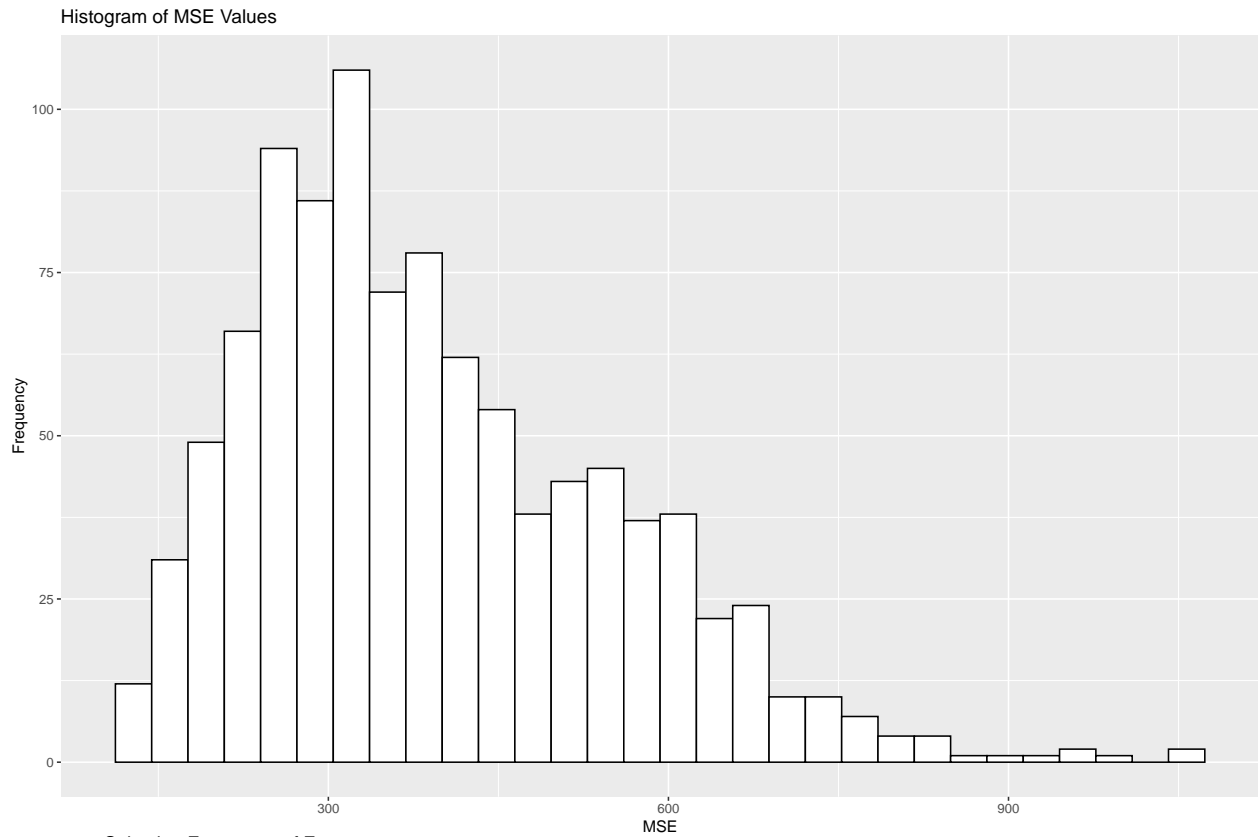
```
## Features selected 50% or more times:
## BMPR1B GATA3 HOXA7
## Top 20 featrues:
## [1] "BMPR1B" "GATA3" "HOXA7" "LEFTY2" "CA12" "PGK1" "ITGB1"
## [8] "THY1" "JAG1" "EFNA3" "HDAC2" "HK2" "ADCY9" "C5orf38"
## [15] "AGTR1" "CHIT1" "HOXA9" "ANXA9" "RPS6KB1" "CACNA1H"
```

**Mechnaistic + Residuals -> ROR-proliferation score (additive)**

```
## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0
##
## CORRELATIONS RESULTS
## Mean: 0.16425
## Median: 0.198308
## Variance: 0.07775369
## st.dev.: 0.2788435
```



```
## MSE RESULTS
## Mean: 392.5436
## Median: 360.3419
## Variance: 25240.73
## st.dev.: 158.8733
```



##

```
## Features selected 50% or more times:
```

```
##
```

```
## Top 20 featrues:
```

```
## [1] "CHIT1" "CA12" "LEFTY2" "PMS2" "E2F5" "ITGB1" "CACNA1H"
```

```
## [8] "HOXA7" "APOE" "THY1" "HDAC2" "EFNA3" "PROM1" "EGF"
```

```
## [15] "FGF13" "FZD9" "IFT140" "CCL4" "WDR77" "BBOX1"
```

**Mechnaistic + Residuals -> ROR-proliferation score (multiplicative)**

```
## number of models fitted: 1000
```

```
## Fraction of model fits with no selected genes: 0
```

```
##
```

```
## CORRELATIONS RESULTS
```

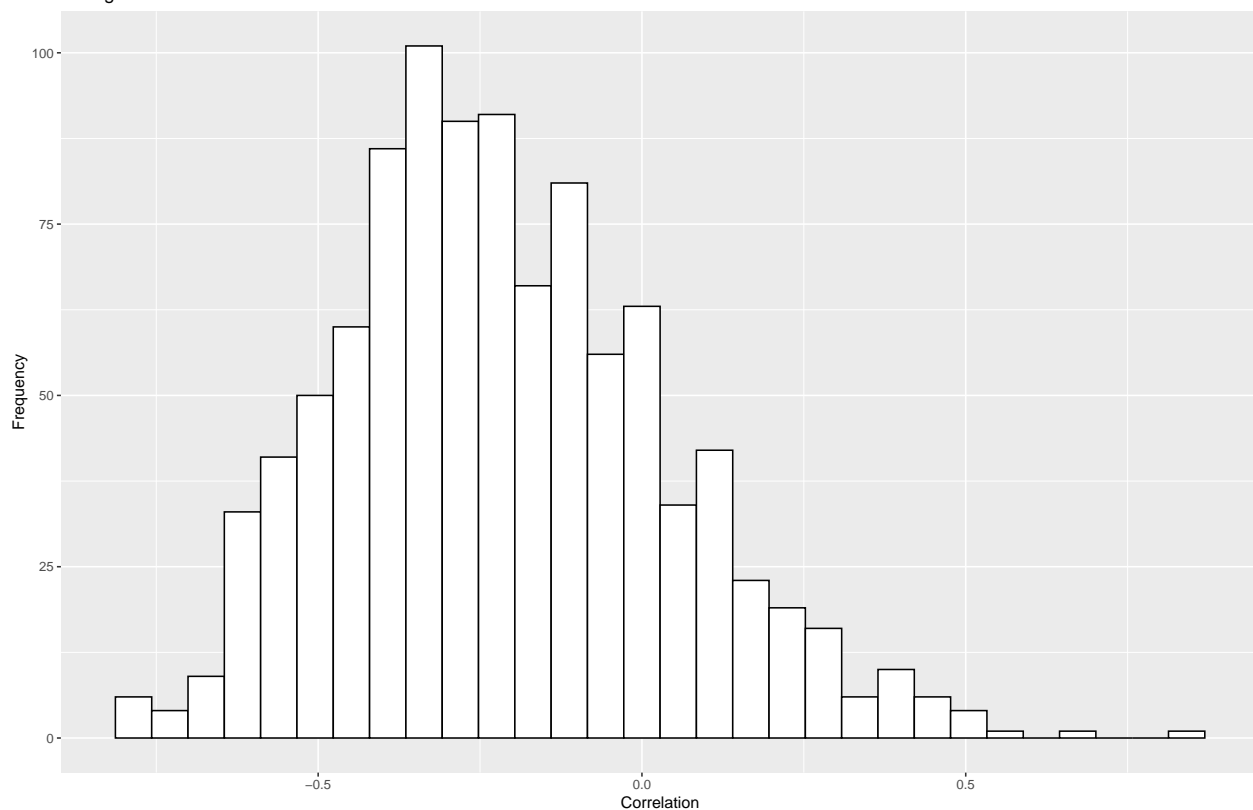
```
## Mean: -0.2145253
```

```
## Median: -0.2415987
```

```
## Variance: 0.06311304
```

```
## st.dev.: 0.2512231
```

Histogram of Correlation Values



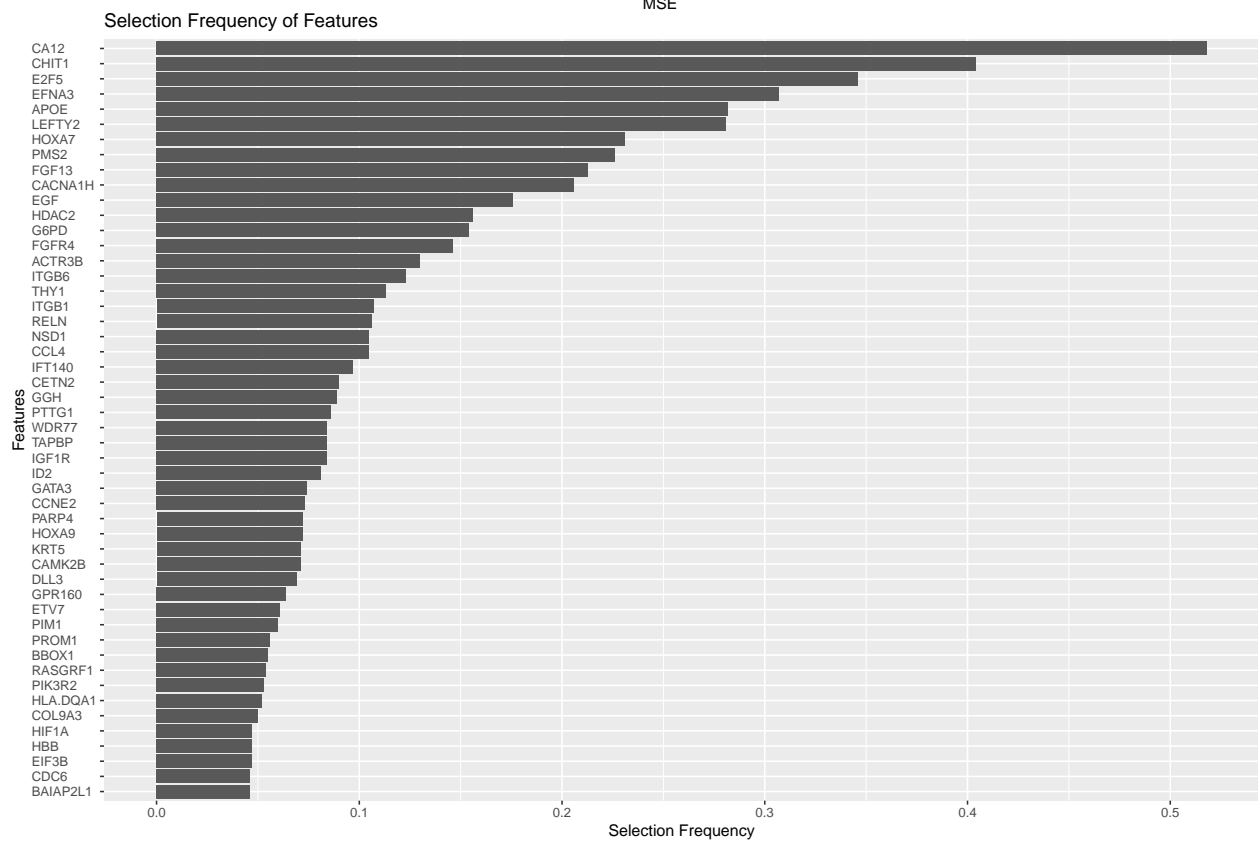
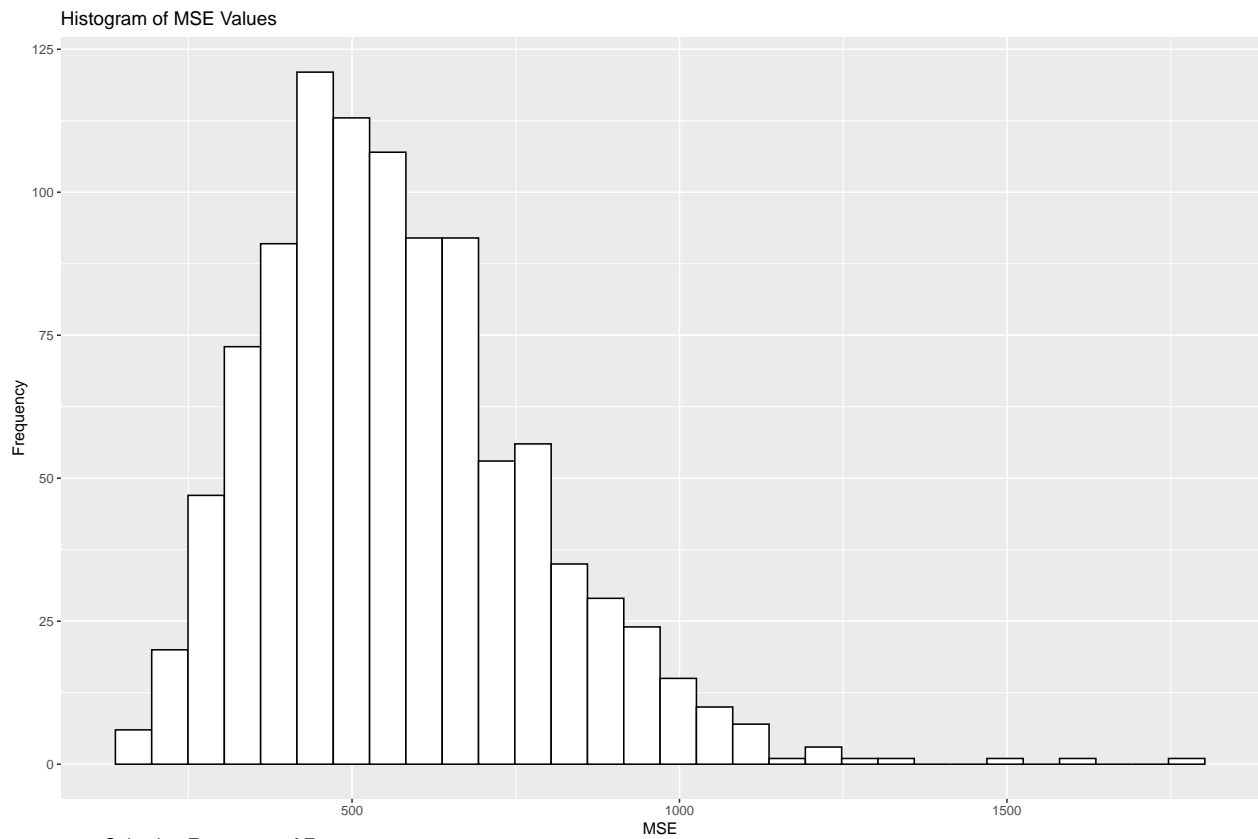
```
## MSE RESULTS
```

```
## Mean: 568.8063
```

```
## Median: 541.2023
```

```
## Variance: 43510.24
```

```
## st.dev.: 208.5911
```



##

```
## Features selected 50% or more times:
## CA12
## Top 20 featrues:
## [1] "CA12"      "CHIT1"     "E2F5"      "EFNA3"     "APOE"      "LEFTY2"    "HOXA7"
## [8] "PMS2"      "FGF13"     "CACNA1H"   "EGF"       "HDAC2"     "G6PD"      "FGFR4"
## [15] "ACTR3B"    "ITGB6"     "THY1"      "ITGB1"     "RELN"      "CCL4"
```

#### Summery results: lasso proliferation score (repeated cross-validation)

Model	cor_mean	sd_cor	MSE_mean	MSE_sd
lasso 6 genes	0.0919663	0.3068209	0.1655931	0.0718379
lasso 771 genes	0.4737037	0.2310209	0.0620913	0.0753056
Nodes	0.2842257	0.2768458	0.1560308	0.0762883
Residual additive	0.4633095	0.2227105	0.1331785	0.0654065
Residual multiplicative	0.4028471	0.2302632	0.1455819	0.0680617

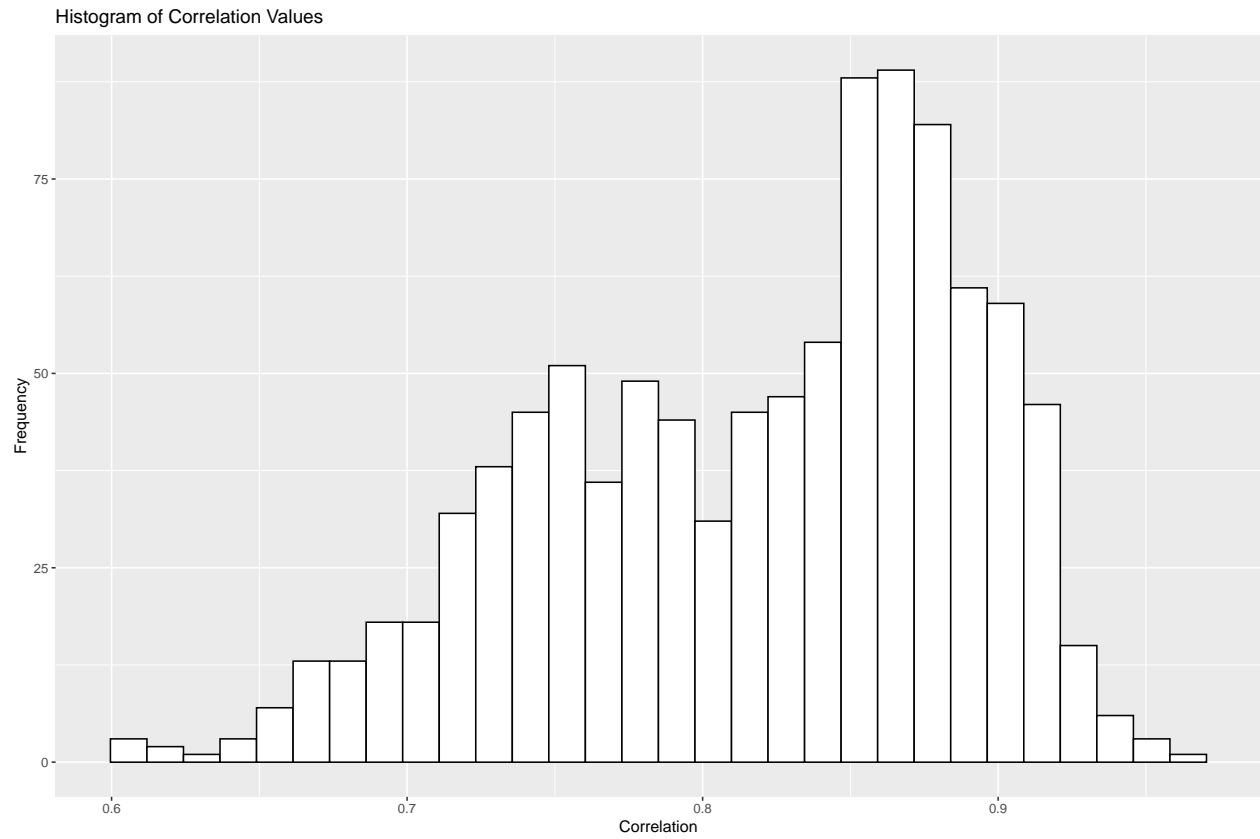
#### Summery results: lasso ROR+proliferation score (repeated cross-validation)

Model	cor_mean	sd_cor	MSE_mean	MSE_sd
lasso 6 genes	-0.4822298	0.1724985	374.1519	144.1559
lasso 771 genes	0.0806237	0.2767153	393.8069	159.6451
Nodes	0.1806504	0.2854892	380.1157	164.5869
Residual additive	0.1642500	0.2788435	392.5436	158.8733
Residual multiplicative	-0.2145253	0.2512231	568.8063	208.5911

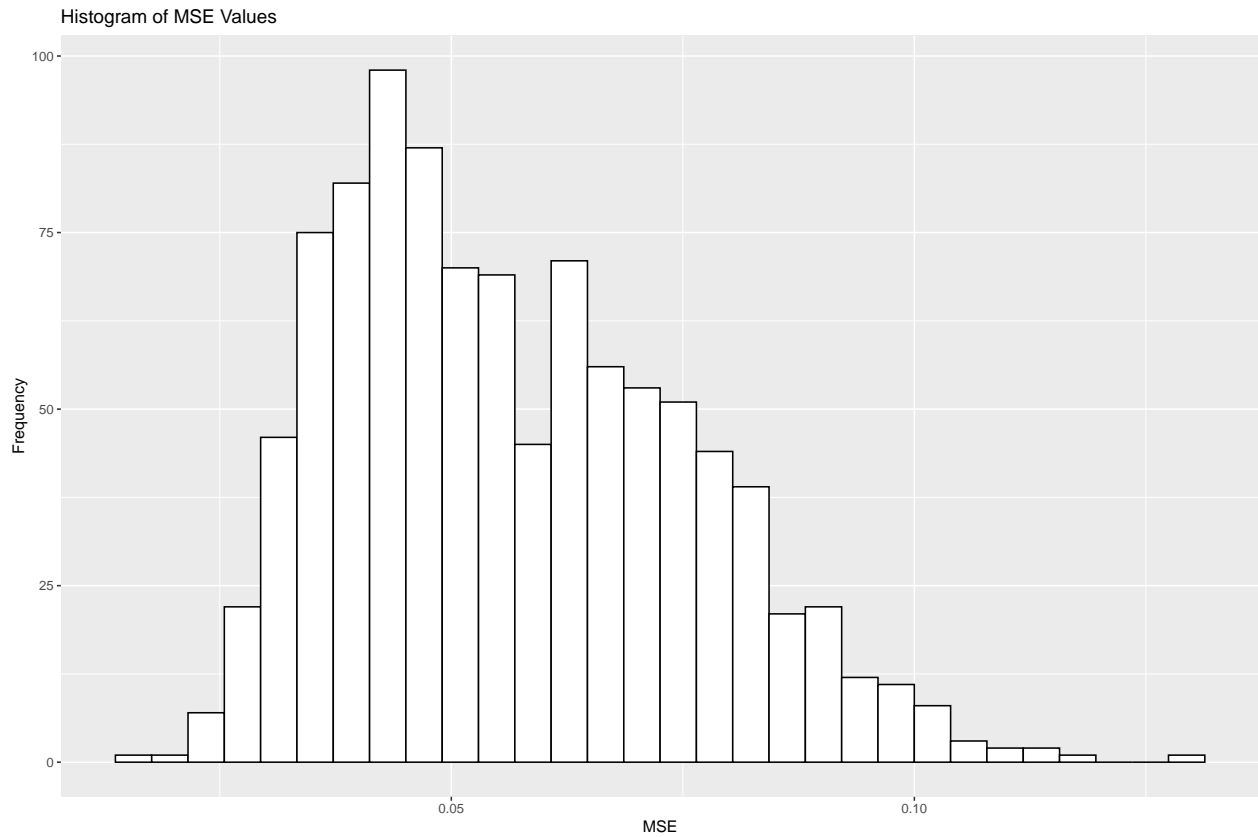
## Ridge bootstrap

### 771 genes -> proliferation score

```
## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0
##
## CORRELATIONS RESULTS
## Mean: 0.8189568
## Median: 0.8355063
## Variance: 0.005044925
## st.dev.: 0.07102764
```



```
## MSE RESULTS
## Mean: 0.05665241
## Median: 0.0532761
## Variance: 0.0003488416
## st.dev.: 0.0186773
```



### 771 genes -> ROR-proliferation score

## number of models fitted: 1000

## Fraction of model fits with no selected genes: 0

##

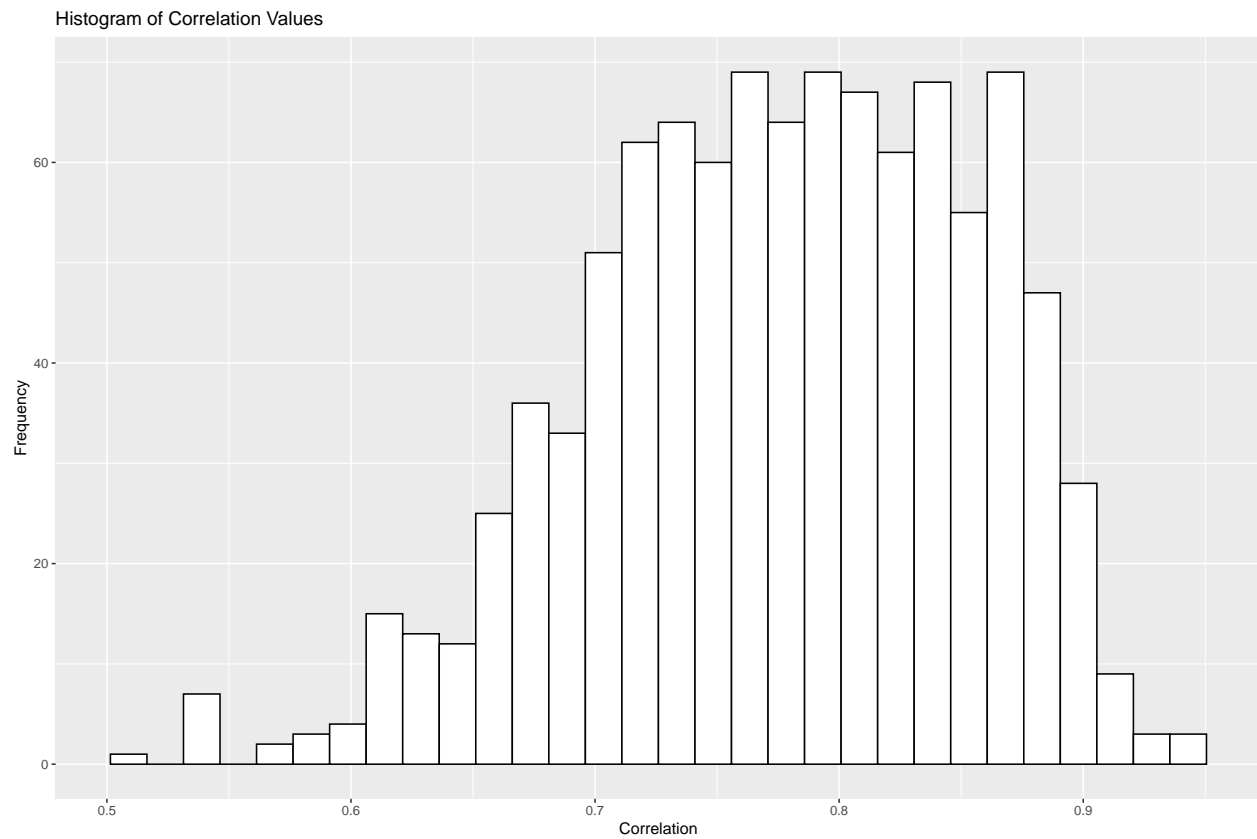
## CORRELATIONS RESULTS

## Mean: 0.7761924

## Median: 0.7811637

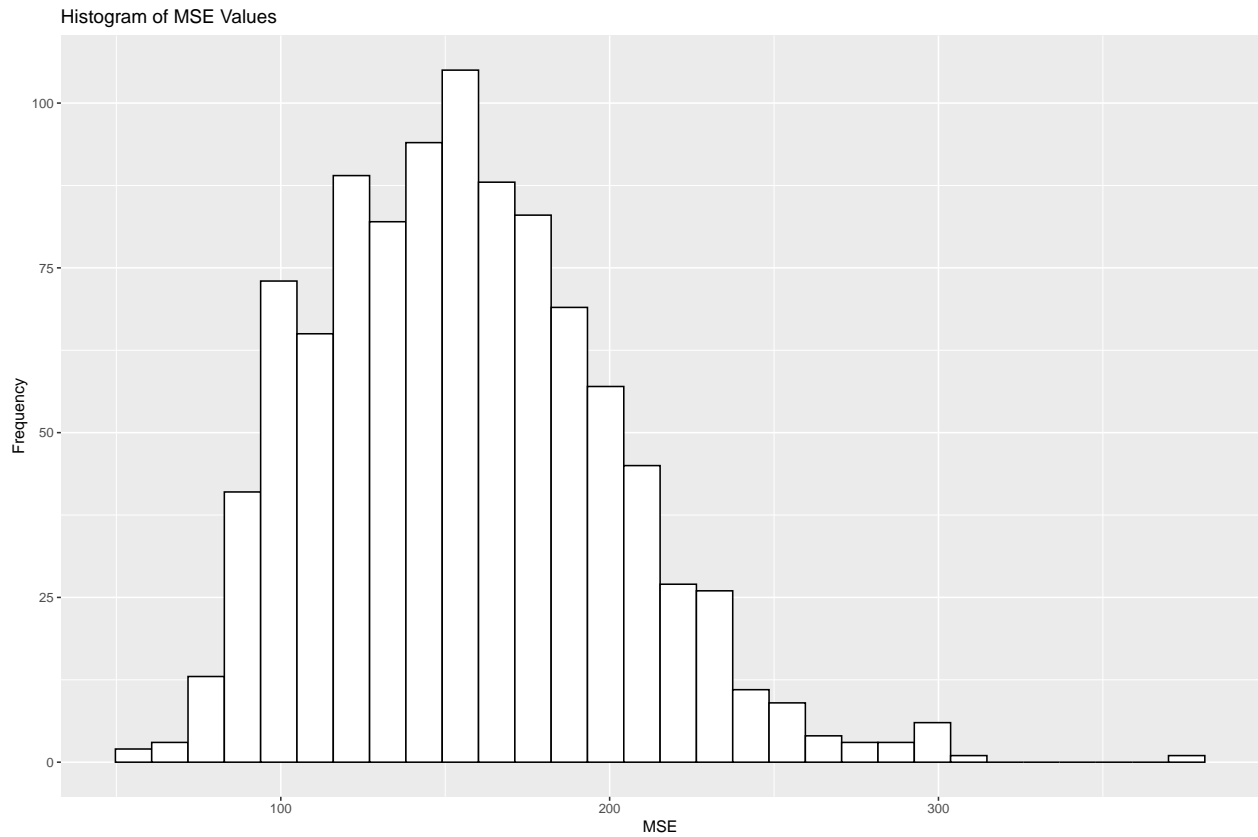
## Variance: 0.006001423

## st.dev.: 0.07746885



```
## MSE RESULTS
## Mean: 156.065
## Median: 154.0679
## Variance: 1952.025
## st.dev.: 44.18173
```

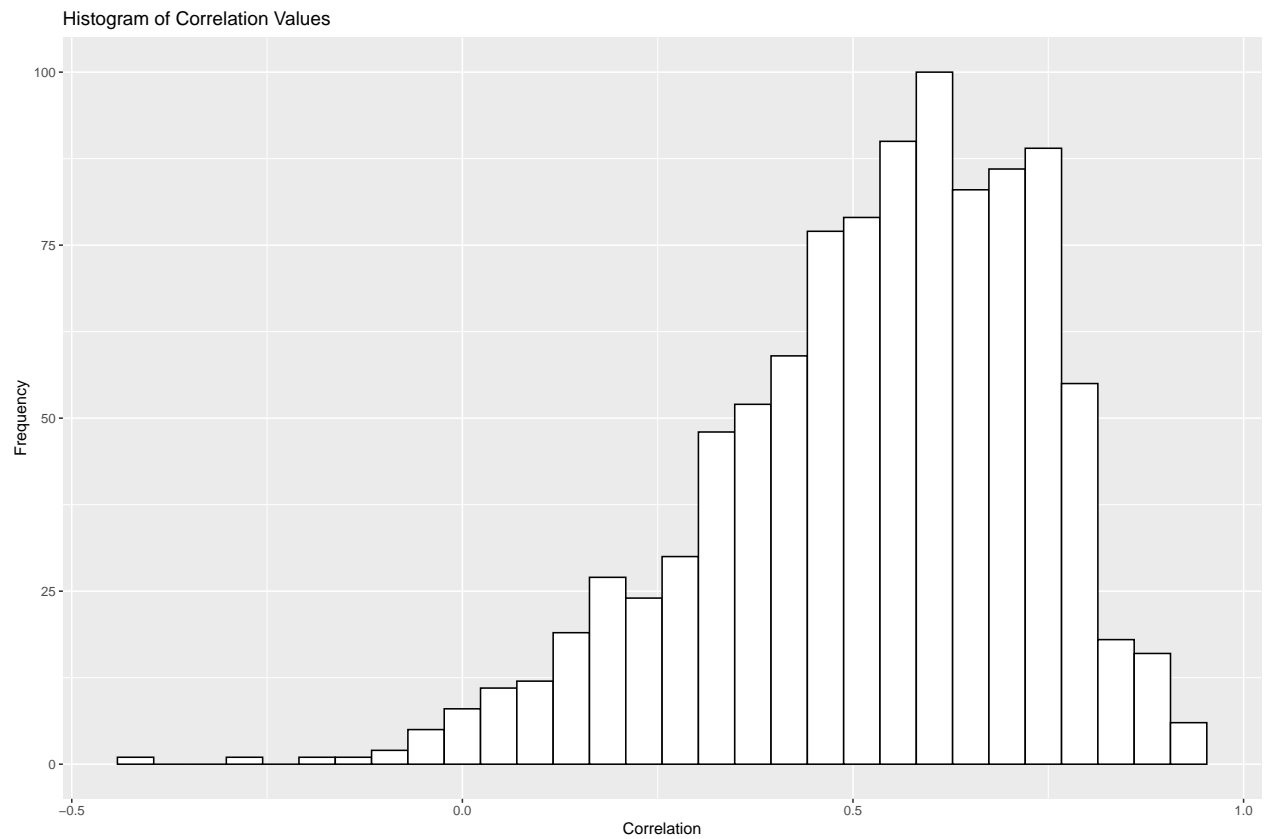




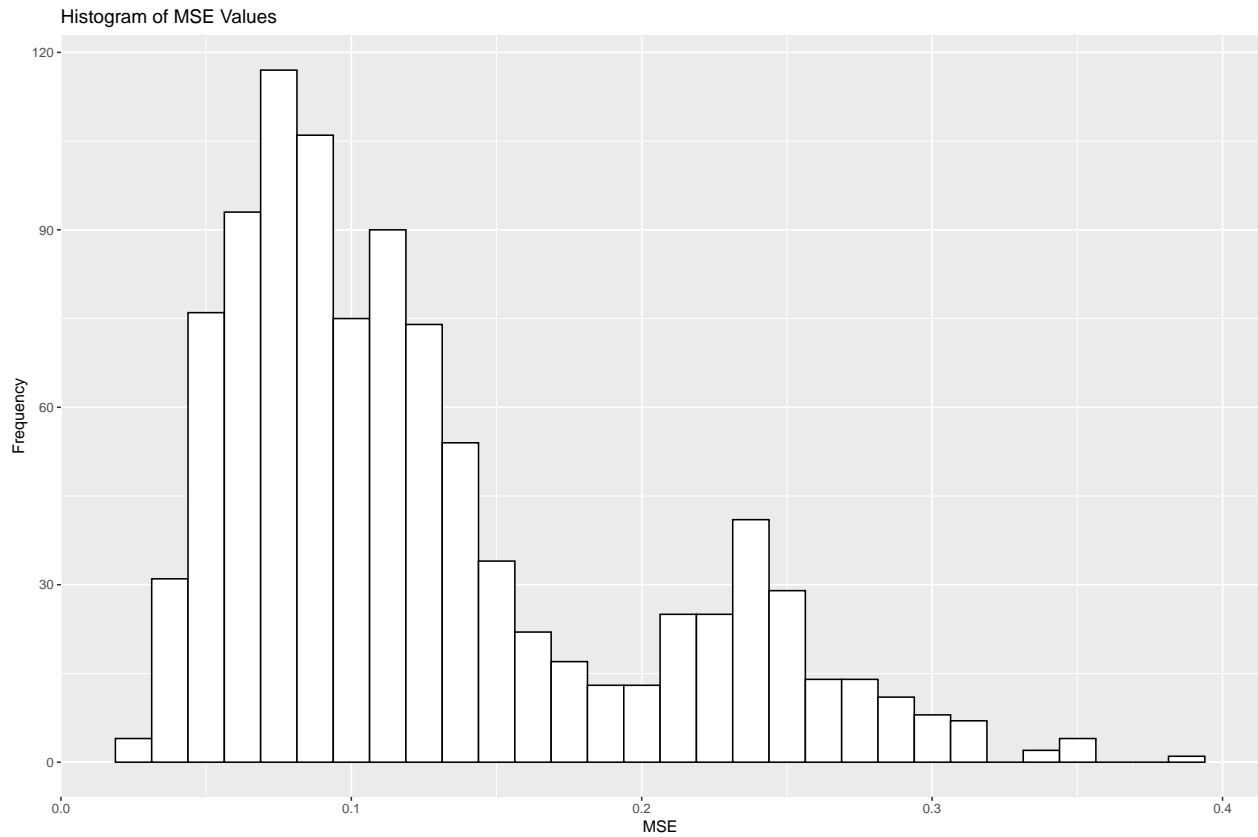
## Ridge repeated cross-validation

771 genes -> proliferation score

```
## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0
##
## CORRELATIONS RESULTS
## Mean: 0.5268342
## Median: 0.5562175
## Variance: 0.04291266
## st.dev.: 0.2071537
```



```
## MSE RESULTS
## Mean: 0.1256548
## Median: 0.1059589
## Variance: 0.004890454
## st.dev.: 0.06993178
```



### 771 genes -> ROR-proliferation score

## number of models fitted: 1000

## Fraction of model fits with no selected genes: 0.321

##

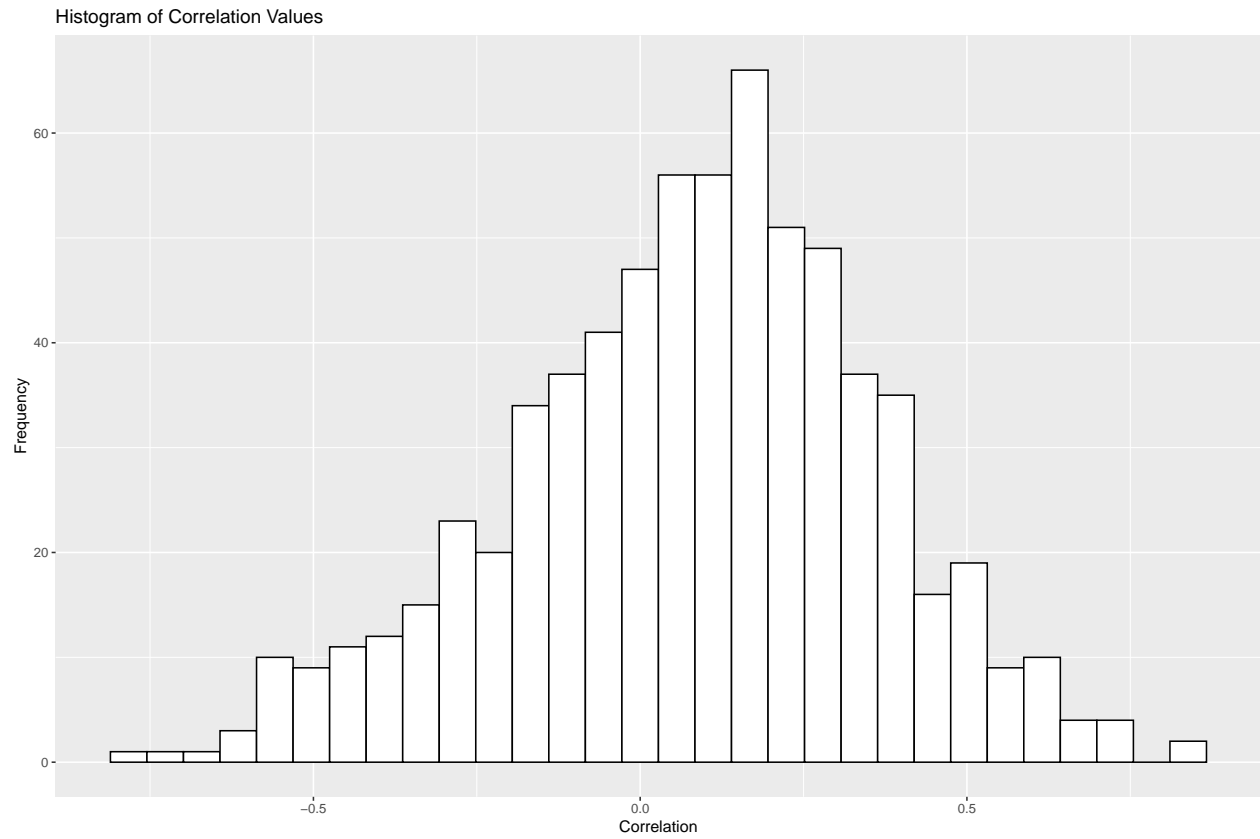
## CORRELATIONS RESULTS

## Mean: 0.08062366

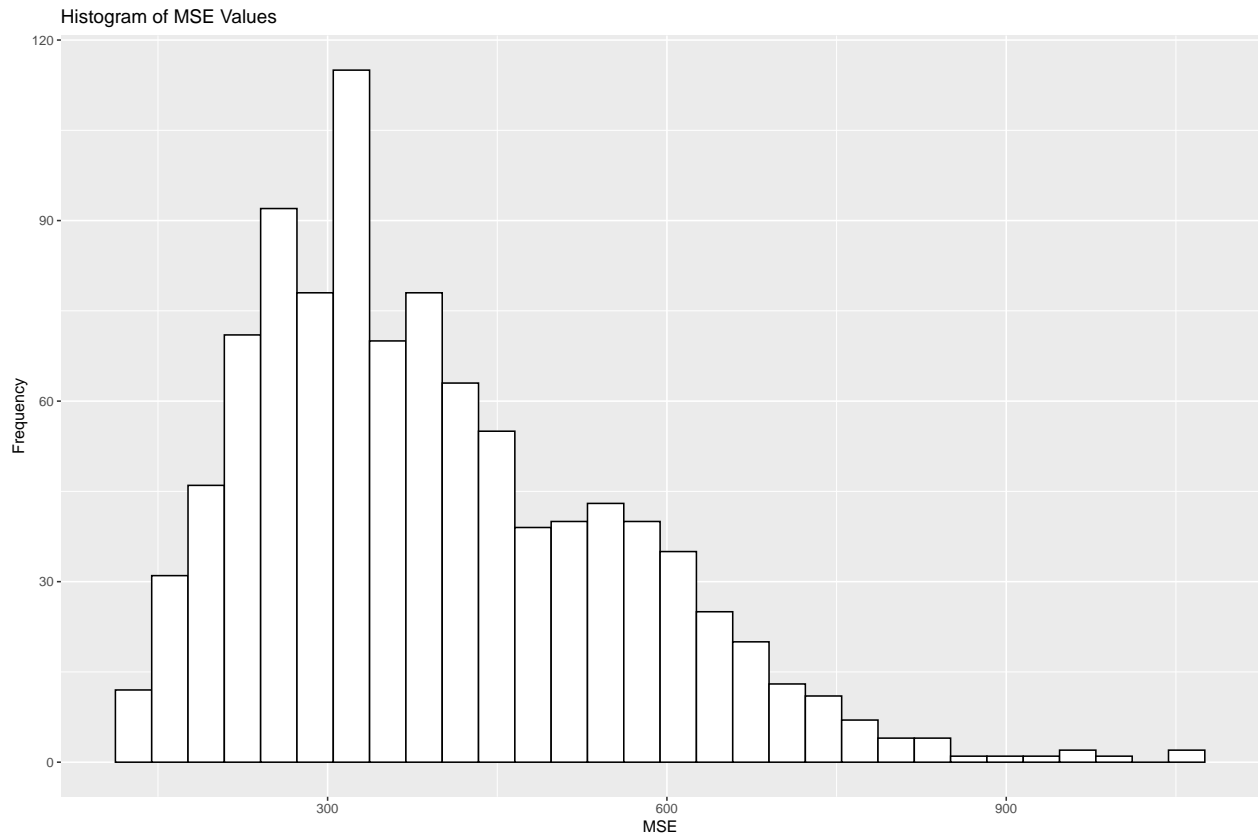
## Median: 0.1014264

## Variance: 0.07657135

## st.dev.: 0.2767153



```
## MSE RESULTS
## Mean: 393.8069
## Median: 360.5105
## Variance: 25486.55
## st.dev.: 159.6451
```



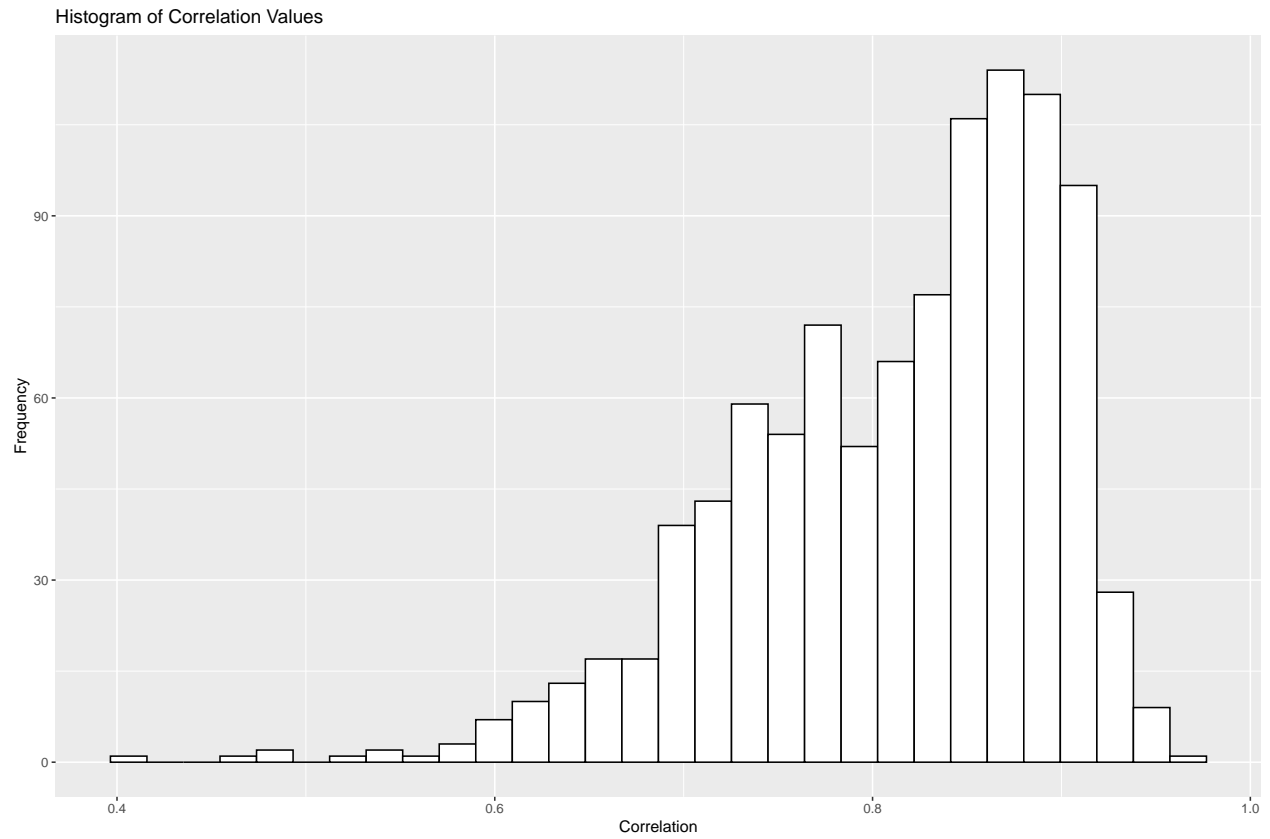
### Summery results: ridge 771 genes bootstrap and repeated cross-validation

Model	cor_mean	sd_cor	MSE_mean	MSE_sd
prolif boot	0.8189568	0.0710276	0.0566524	0.0186773
ROR-prolif boot	0.7761924	0.0774688	156.0649552	44.1817261
prolif rep cross-val	0.5268342	0.2071537	0.1256548	0.0699318
ROR-prolif rep cross-val	0.0806237	0.2767153	393.8068910	159.6450765

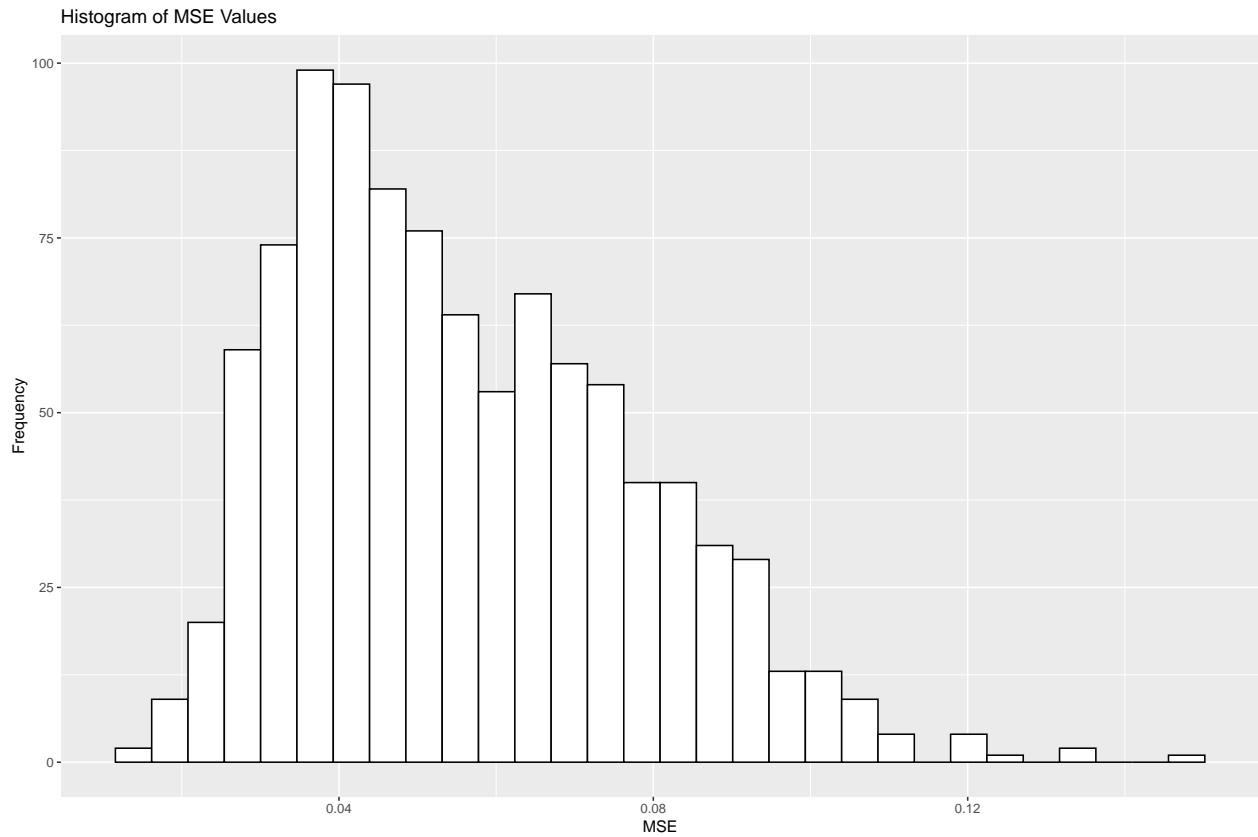
## Elastic Net - bootstrap

771 genes -> proliferation score

```
## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0
##
## CORRELATIONS RESULTS
## Mean: 0.8125591
## Median: 0.8324809
## Variance: 0.007038791
## st.dev.: 0.0838975
```



```
## MSE RESULTS
## Mean: 0.0558955
## Median: 0.05152763
## Variance: 0.0004710269
## st.dev.: 0.02170316
```



### 771 genes -> ROR-proliferation score

## number of models fitted: 1000

## Fraction of model fits with no selected genes: 0

##

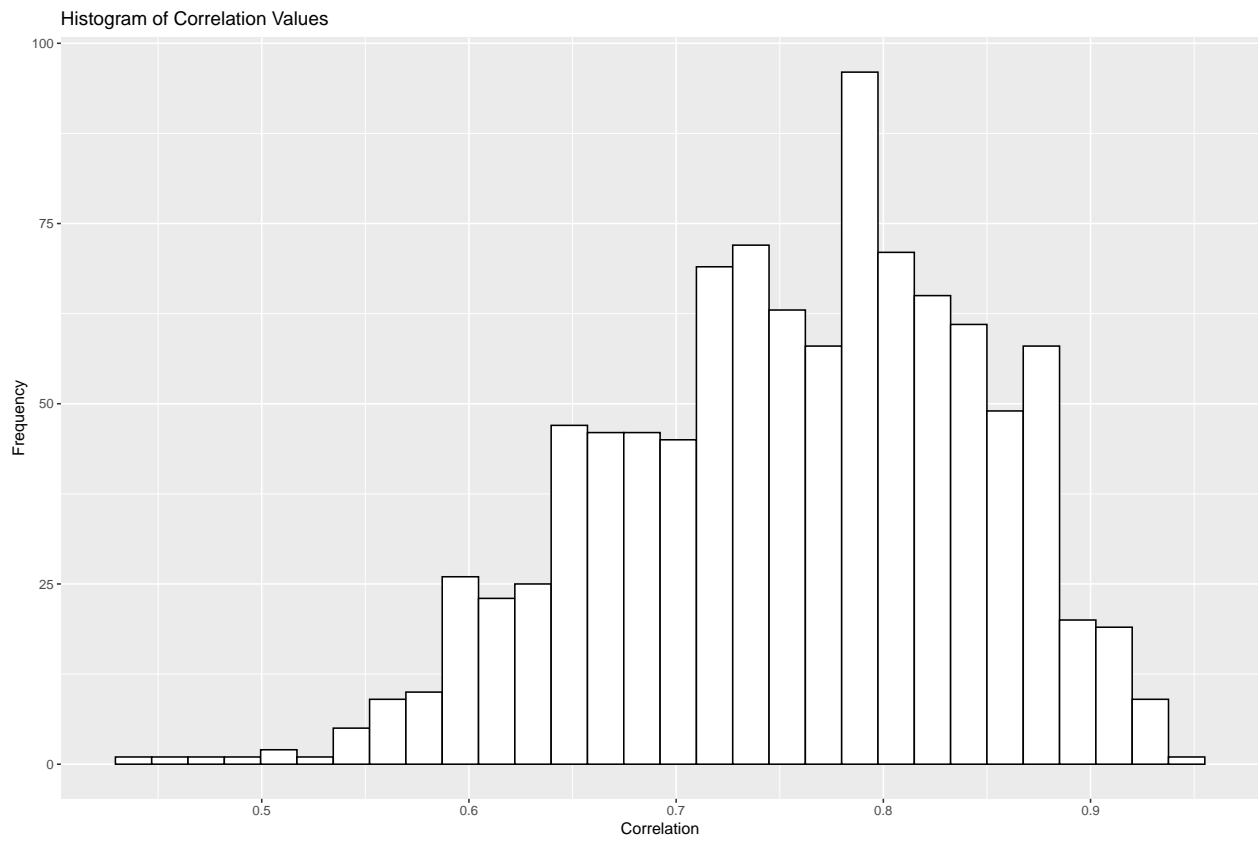
## CORRELATIONS RESULTS

## Mean: 0.7565123

## Median: 0.7644687

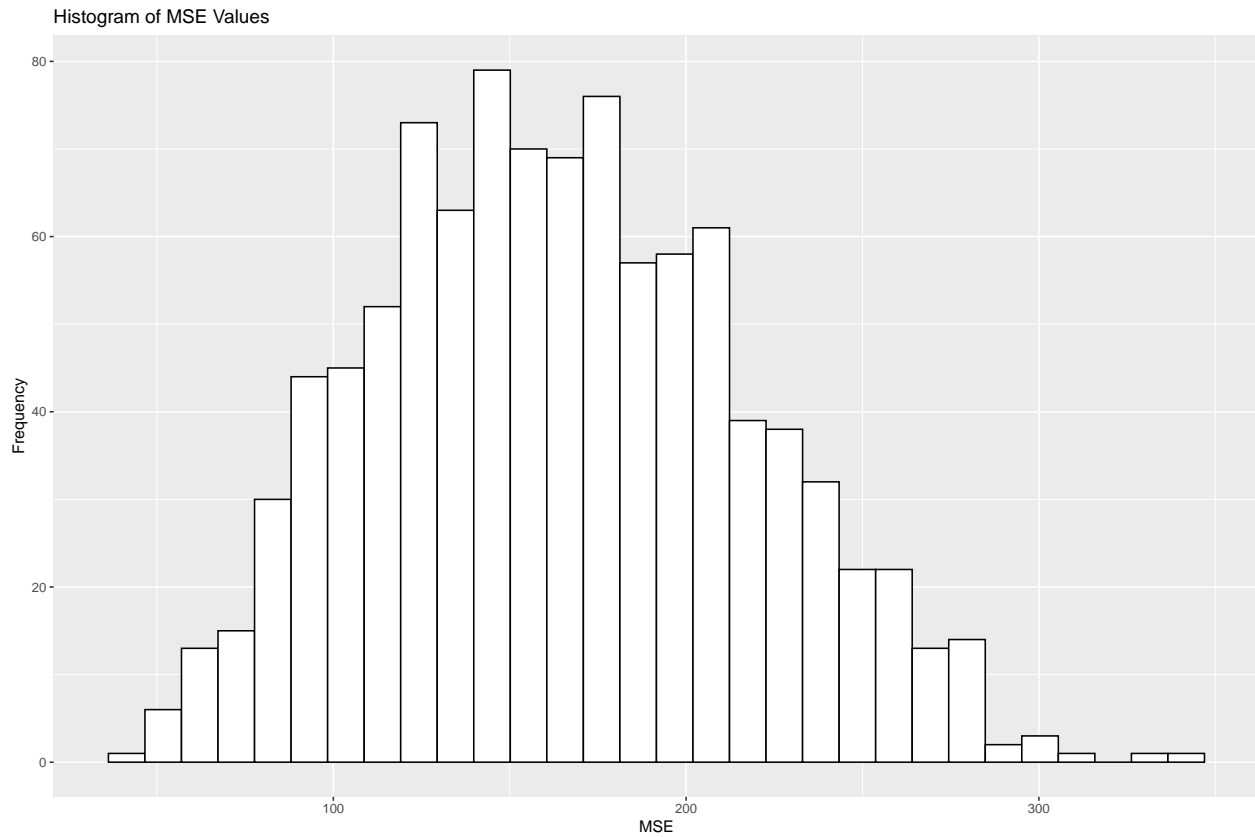
## Variance: 0.007887981

## st.dev.: 0.08881431



```
## MSE RESULTS
## Mean: 164.4116
## Median: 162.2643
## Variance: 2785.22
## st.dev.: 52.77518
```

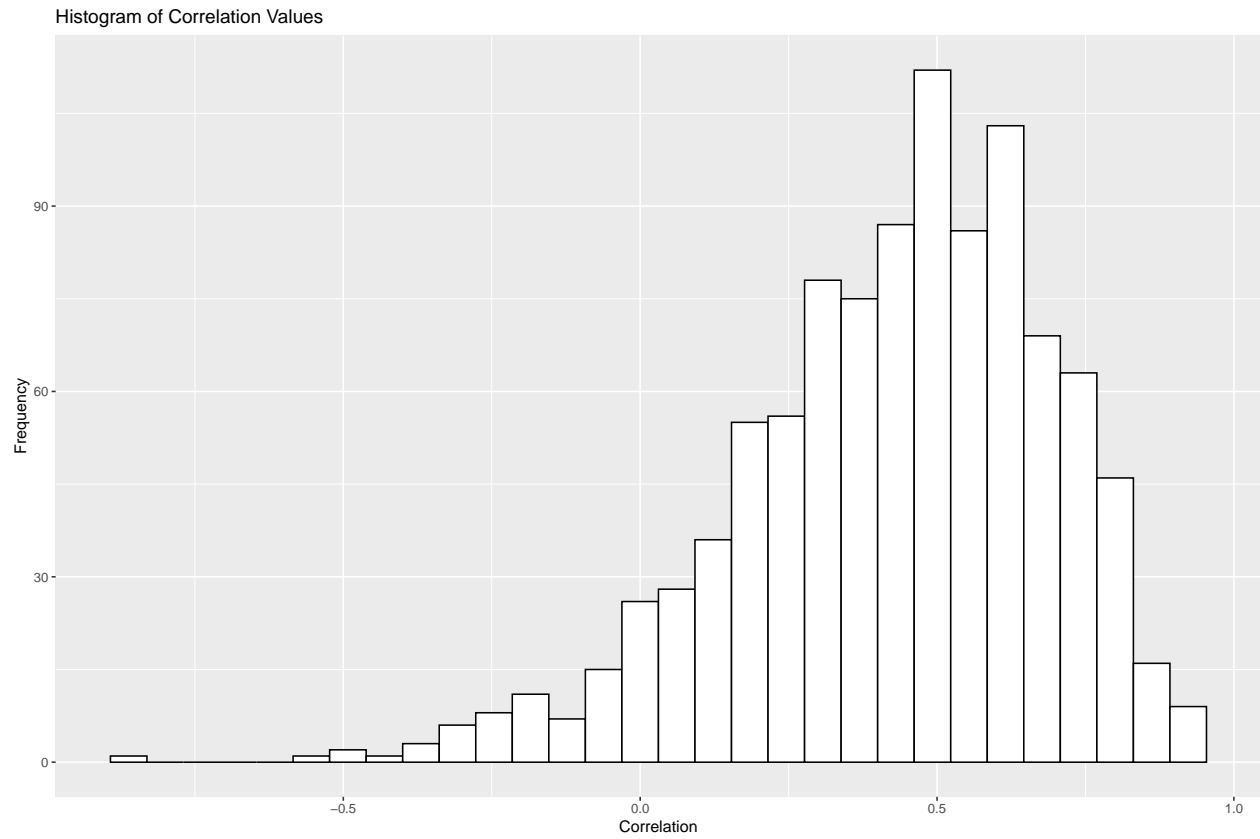




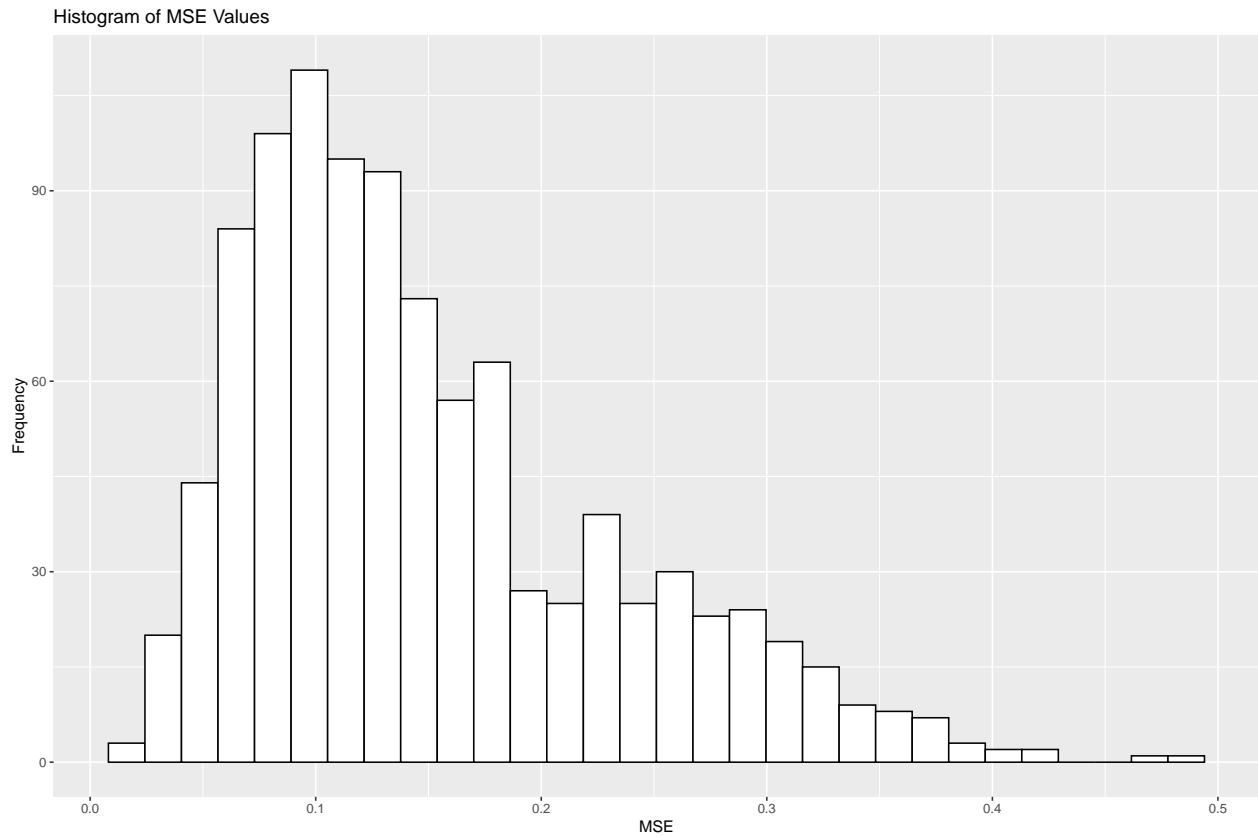
## Elastic Net: cross-validation

771 genes -> proliferation score

```
## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0
##
## CORRELATIONS RESULTS
## Mean: 0.427189
## Median: 0.4644365
## Variance: 0.06953924
## st.dev.: 0.2637029
```



```
## MSE RESULTS
## Mean: 0.1501025
## Median: 0.1284895
## Variance: 0.006763425
## st.dev.: 0.08224004
```



### 771 genes -> ROR-proliferation score

## number of models fitted: 1000

## Fraction of model fits with no selected genes: 0.002

##

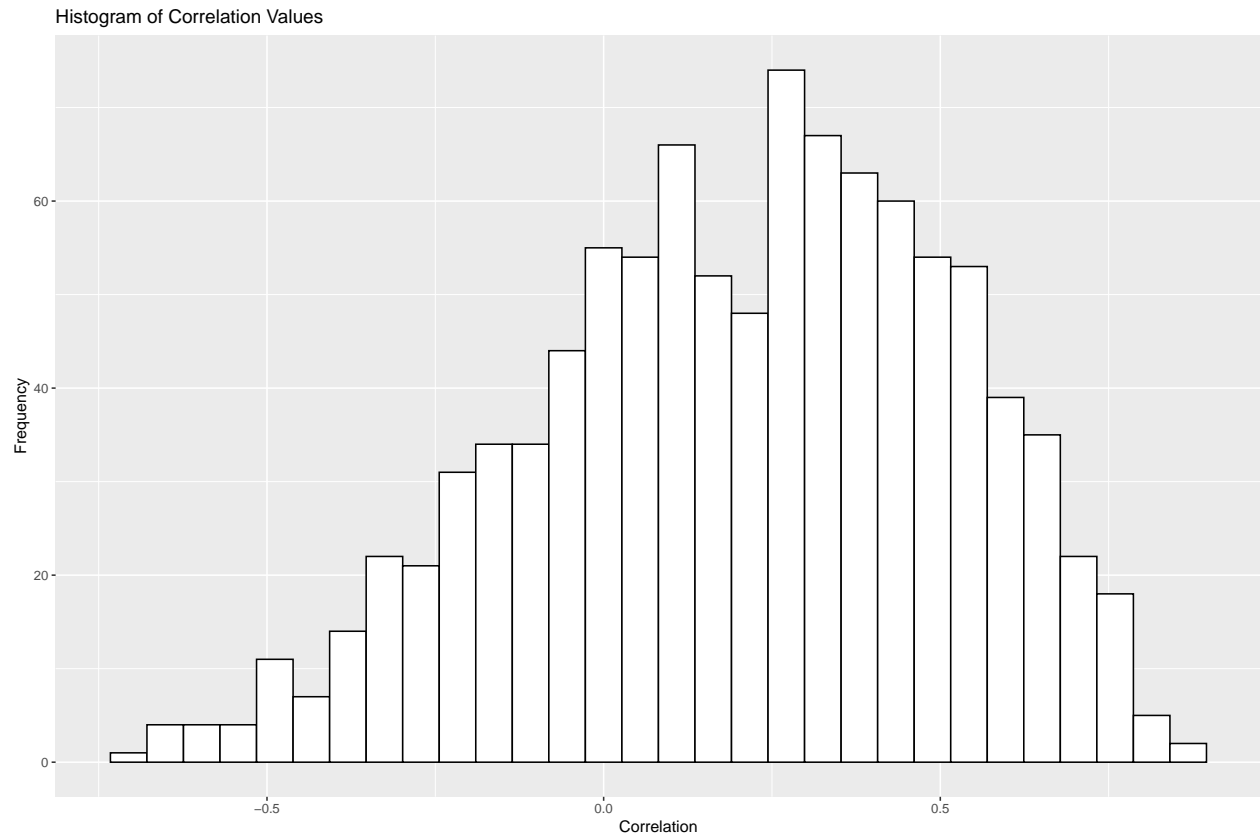
## CORRELATIONS RESULTS

## Mean: 0.2049341

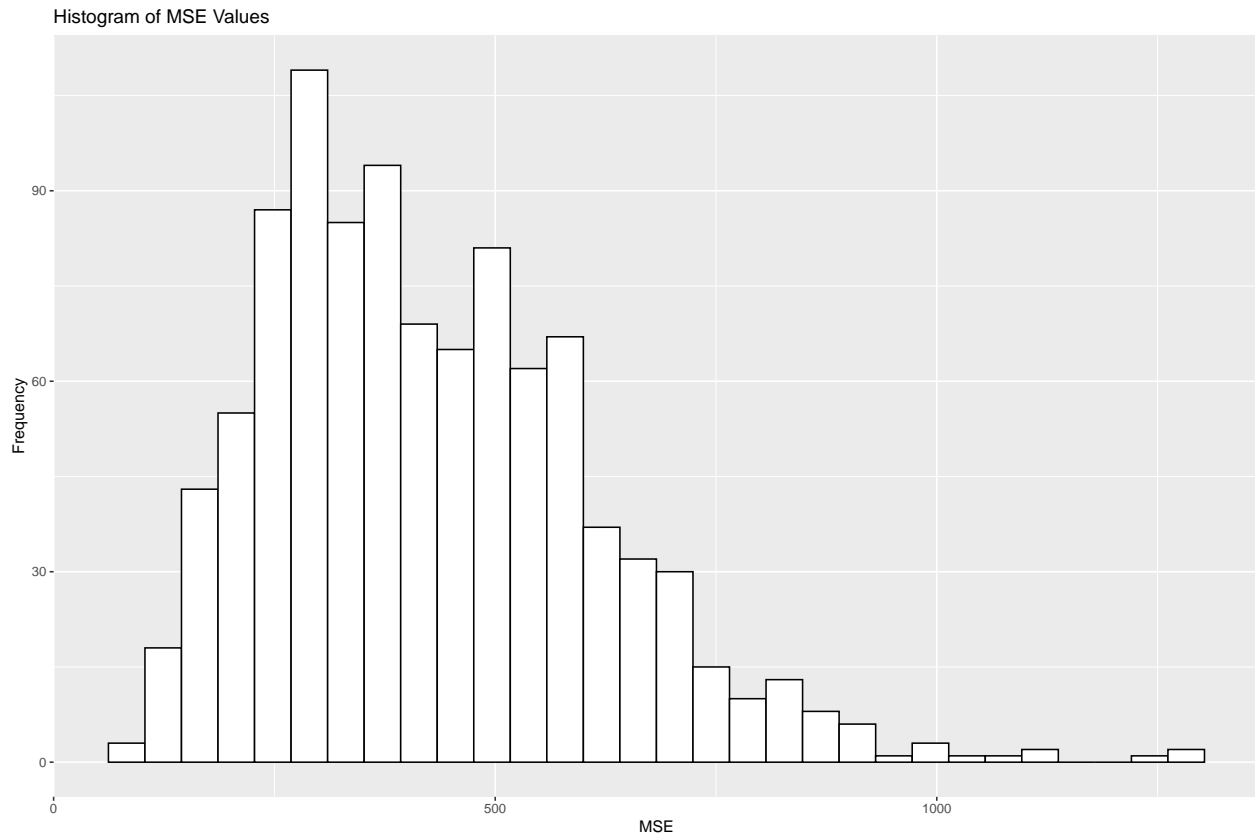
## Median: 0.226514

## Variance: 0.0968435

## st.dev.: 0.3111969



```
## MSE RESULTS
## Mean: 427.3517
## Median: 396.2622
## Variance: 34687.75
## st.dev.: 186.2465
```



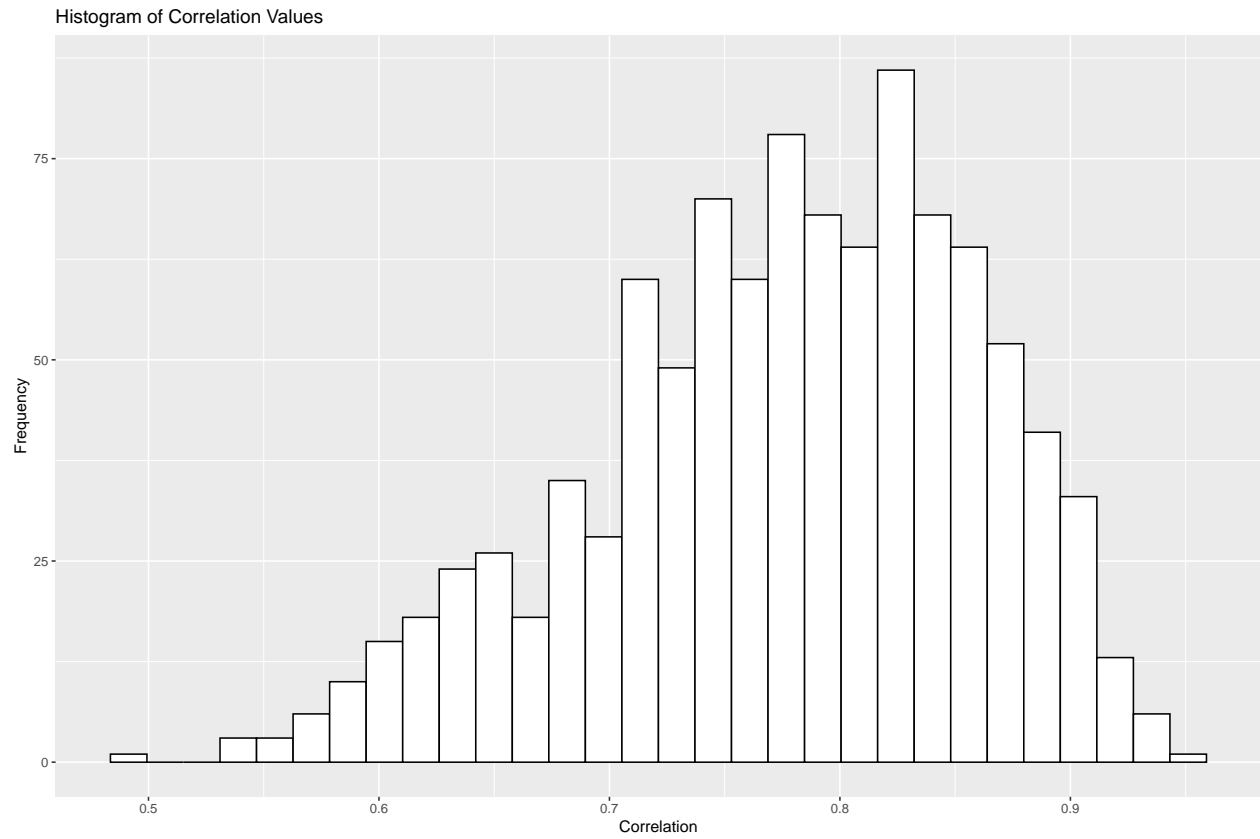
### Summery results: elastic net 771 genes bootstrap and repeated cross-validation

Model	cor_mean	sd_cor	MSE_mean	MSE_sd
prolif boot	0.8125591	0.0838975	0.0558955	0.0217032
ROR-prolif boot	0.7565123	0.0888143	164.4116160	52.7751849
prolif rep cross-val	0.4271890	0.2637029	0.1501025	0.0822400
ROR-prolif rep cross-val	0.2049341	0.3111969	427.3517412	186.2464725

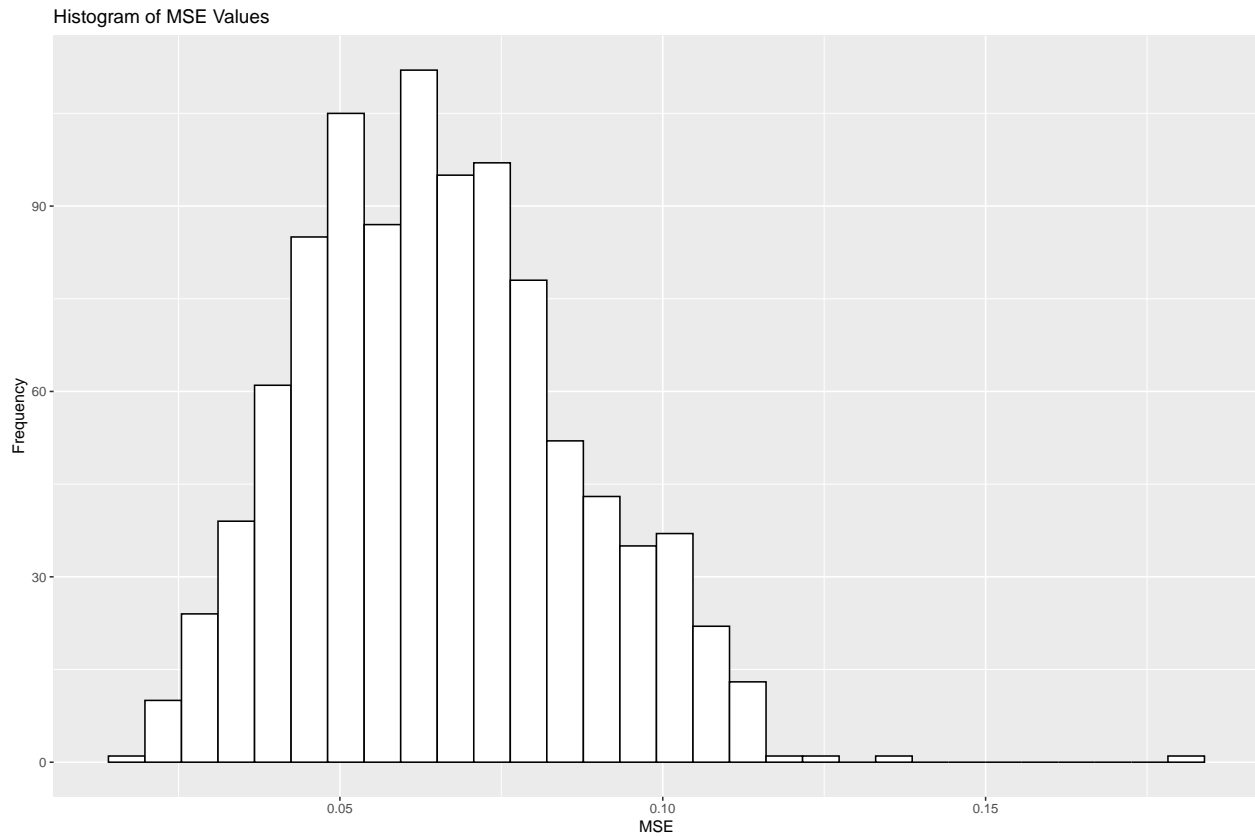
## Boosting with stumps as base learner - bootstrap

### 771 genes -> proliferation score

```
## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0
##
## CORRELATIONS RESULTS
## Mean: 0.7760479
## Median: 0.7841718
## Variance: 0.006853002
## st.dev.: 0.08278286
```

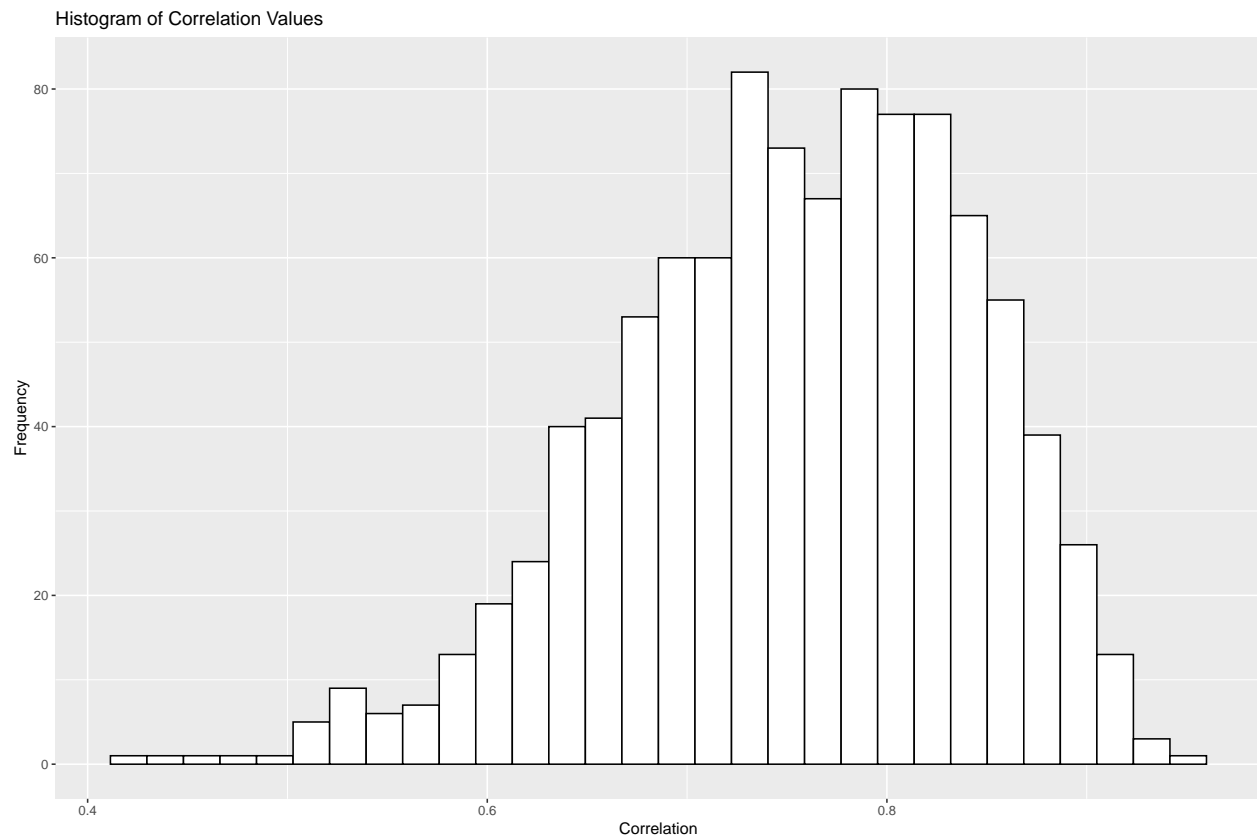


```
## MSE RESULTS
## Mean: 0.06537103
## Median: 0.06397191
## Variance: 0.0004410638
## st.dev.: 0.02100152
```



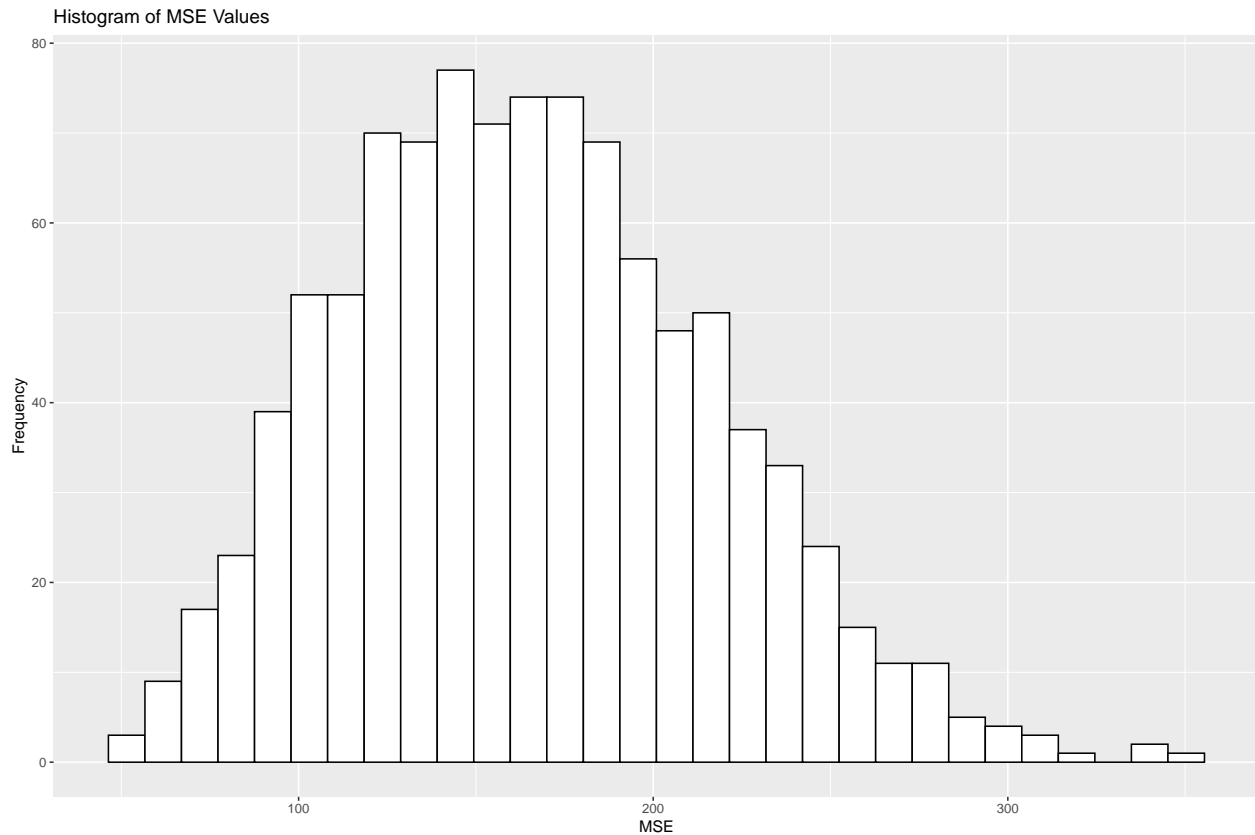
### 771 genes -> ROR-proliferation score

```
## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0
##
## CORRELATIONS RESULTS
## Mean: 0.7530515
## Median: 0.7593775
## Variance: 0.007786865
## st.dev.: 0.08824321
```



```
## MSE RESULTS
## Mean: 165.145
## Median: 162.2361
## Variance: 2690.091
## st.dev.: 51.86608
```

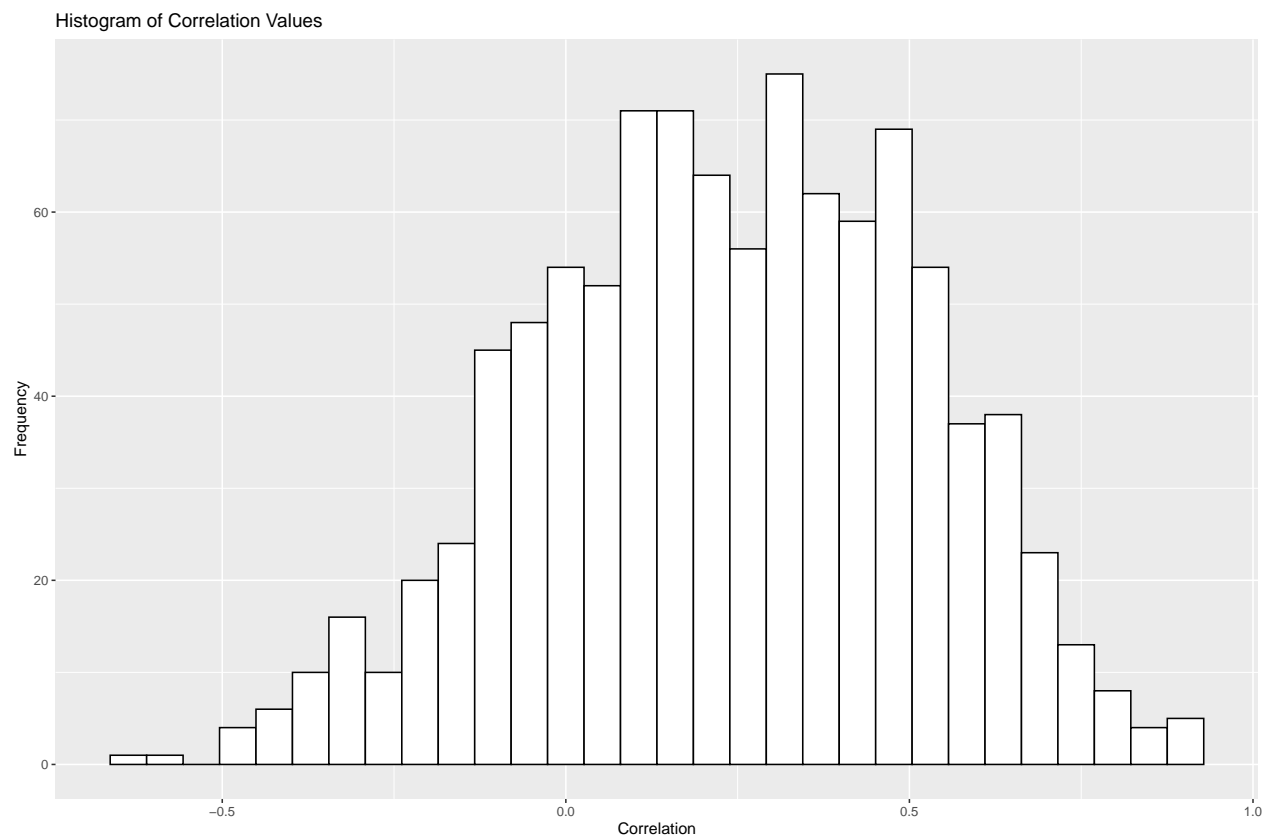




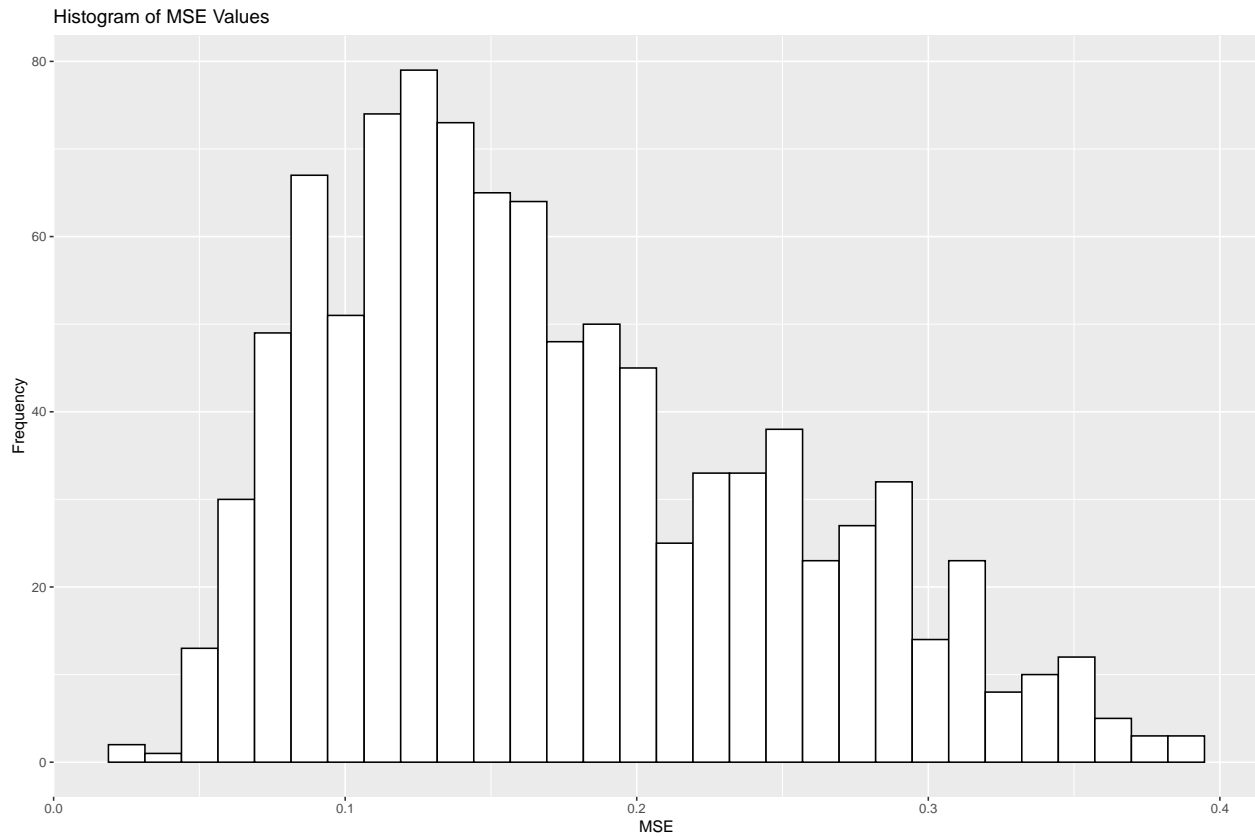
## Boosting with stumps as base learner cross-validation

771 genes -> proliferation score

```
## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0
##
## CORRELATIONS RESULTS
## Mean: 0.2364594
## Median: 0.2426694
## Variance: 0.07812256
## st.dev.: 0.2795041
```



```
## MSE RESULTS
## Mean: 0.1712618
## Median: 0.1554505
## Variance: 0.005837176
## st.dev.: 0.07640141
```



### 771 genes -> ROR-proliferation score

## number of models fitted: 1000

## Fraction of model fits with no selected genes: 0

##

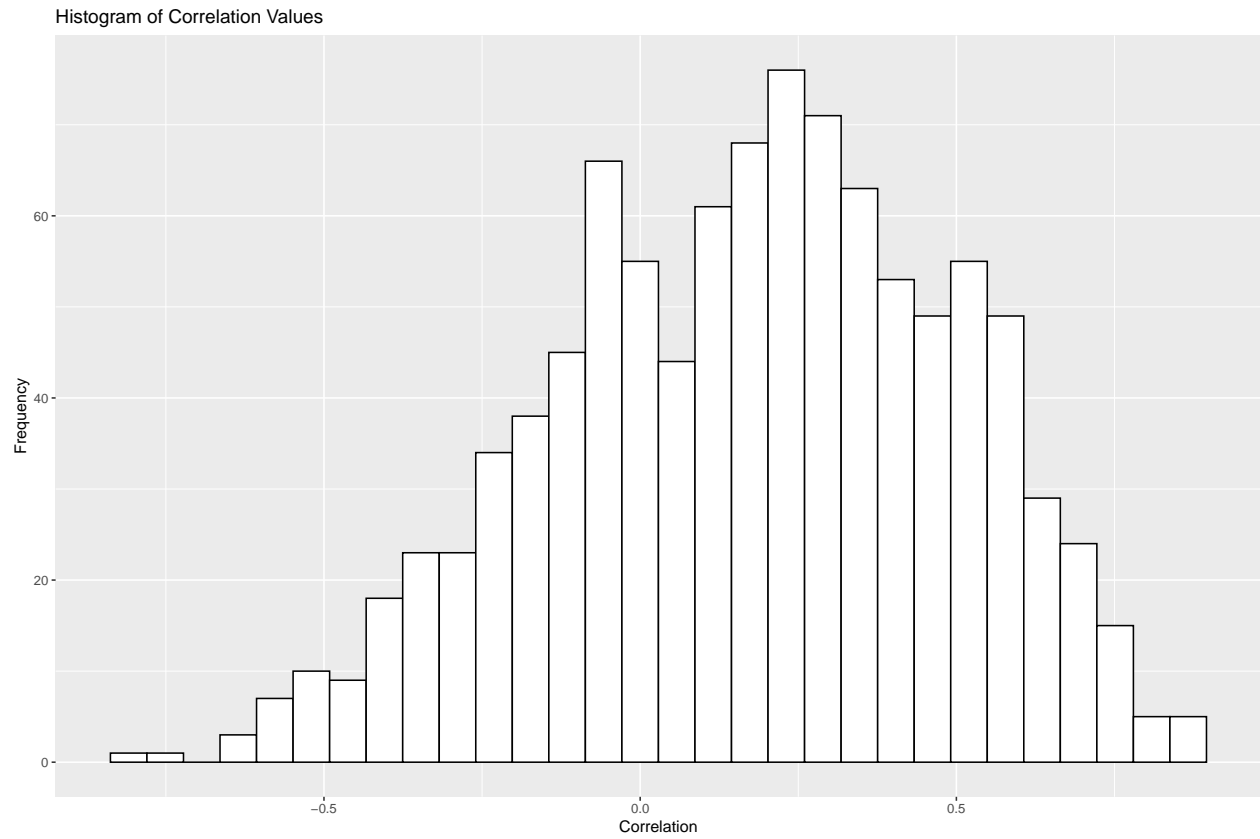
## CORRELATIONS RESULTS

## Mean: 0.1744792

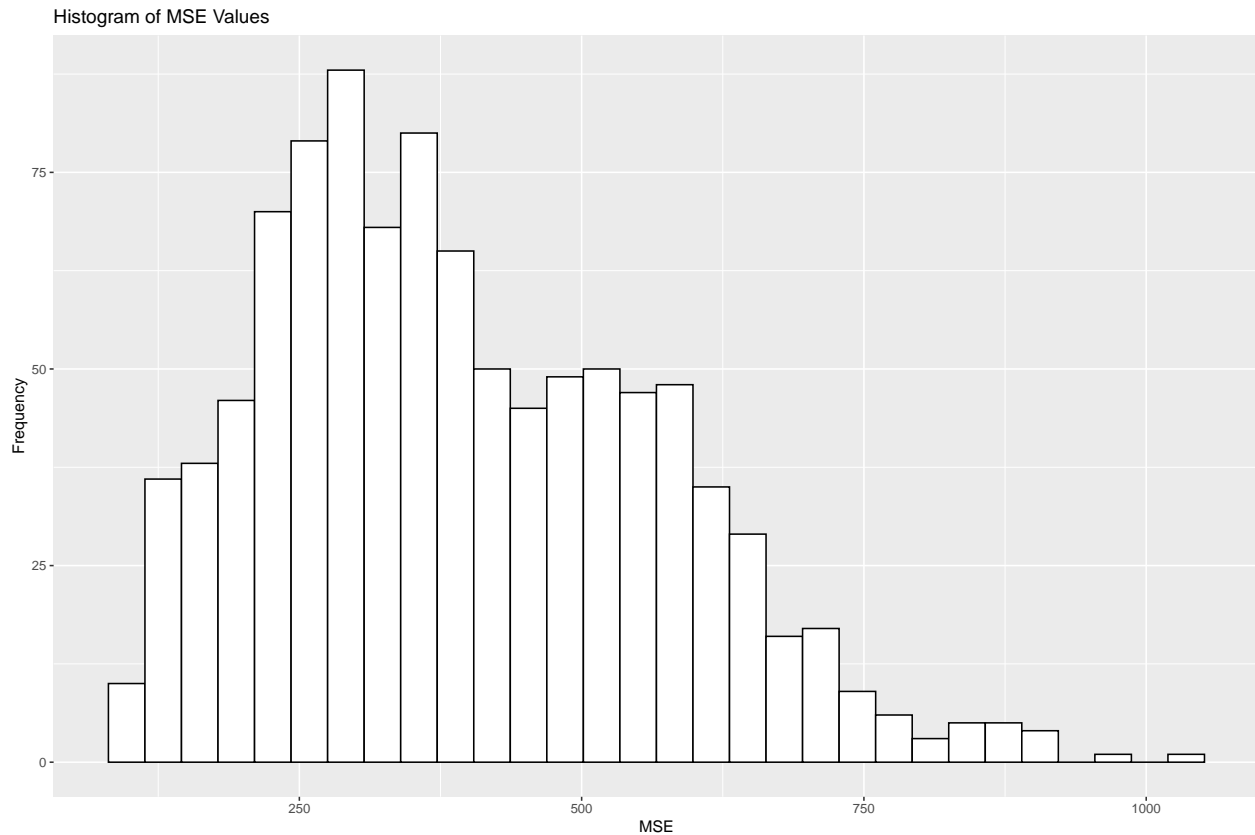
## Median: 0.1948469

## Variance: 0.09932263

## st.dev.: 0.3151549



```
## MSE RESULTS
## Mean: 394.2634
## Median: 366.3266
## Variance: 29461.83
## st.dev.: 171.6445
```



**Summery results: Boosting with stumps 771 genes bootstrap and repeated cross-validation**

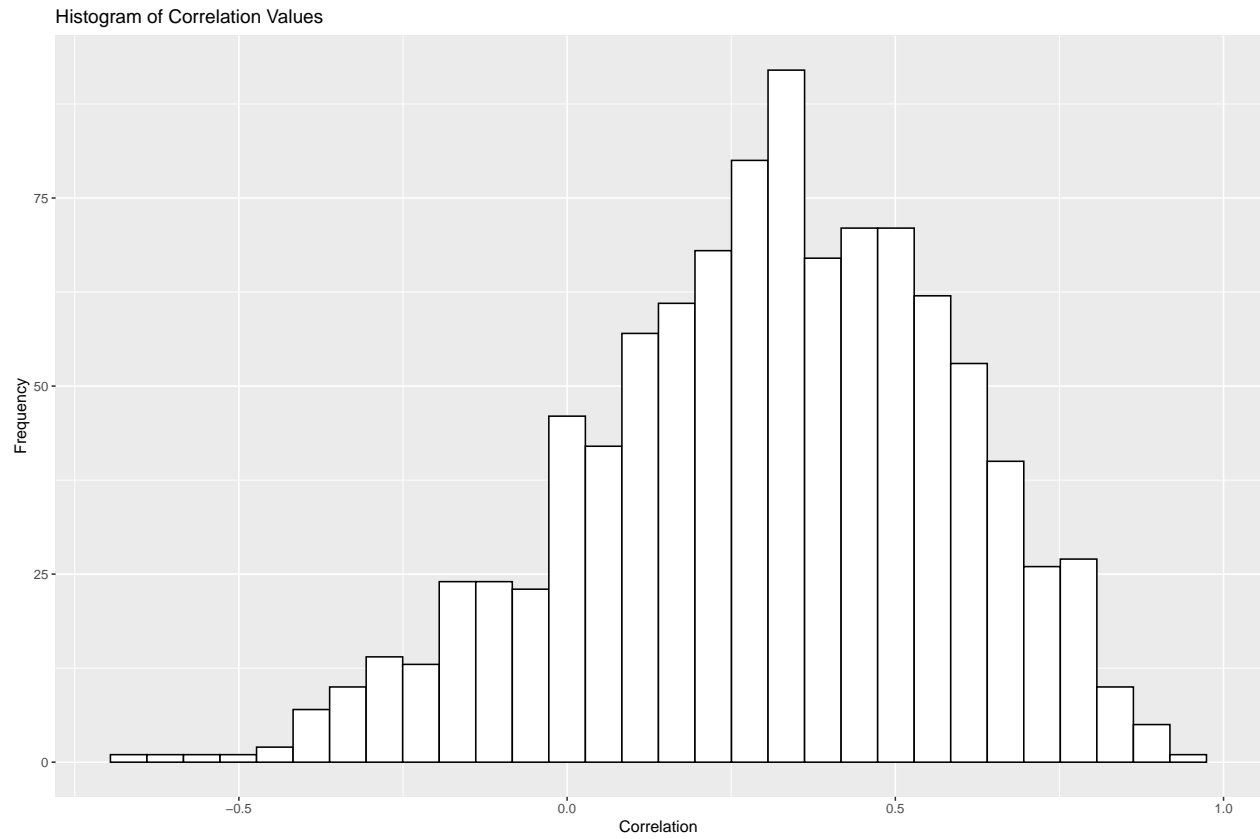
Model	cor_mean	sd_cor	MSE_mean	MSE_sd
prolif boot	0.7760479	0.0827829	0.0653710	0.0210015
ROR-prolif boot	0.7530515	0.0882432	165.1450271	51.8660843
prolif rep cross-val	0.2364594	0.2795041	0.1712618	0.0764014
ROR-prolif rep cross-val	0.1744792	0.3151549	394.2634498	171.6444924

## START USING DOMAIN KNOWLEDGE

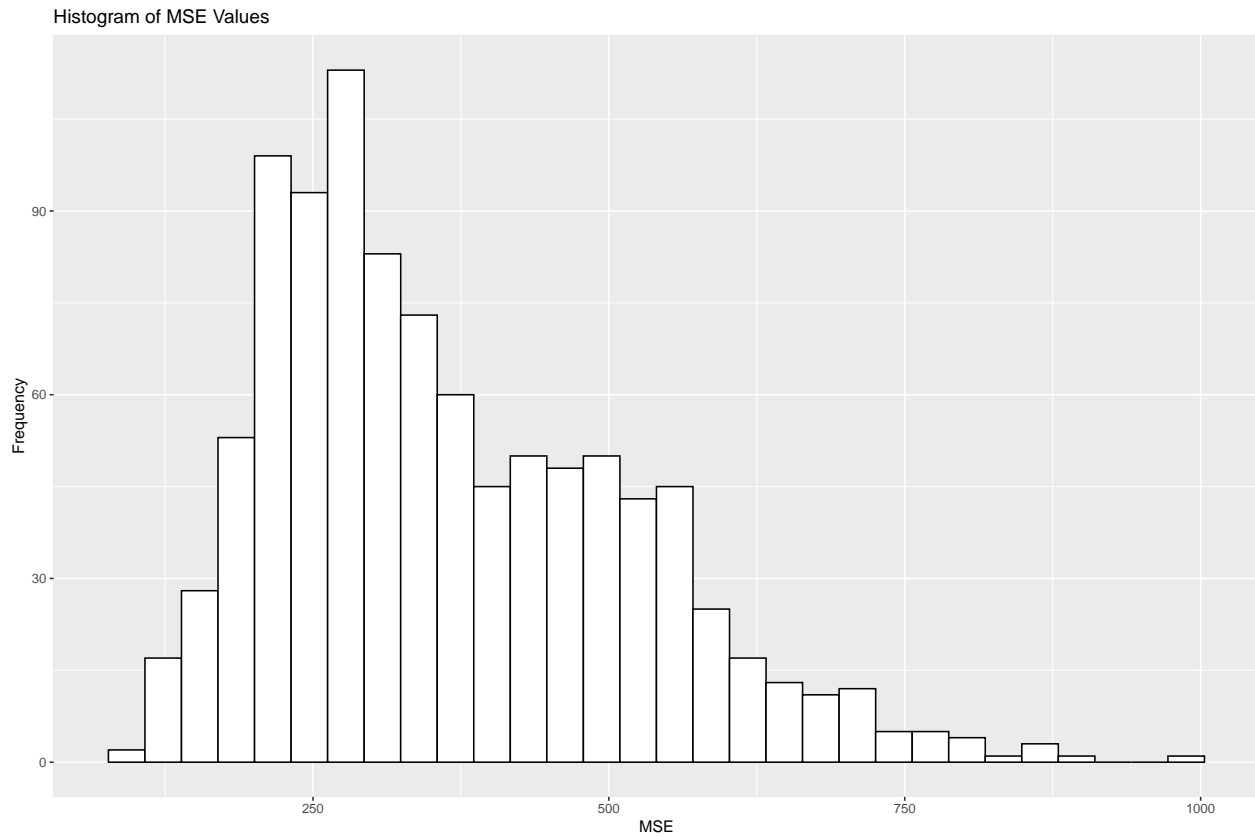
### PCA on signature gene sets using repeated cross-validation

**Ridge: 771 genes -> ROR-proliferation score**

```
## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0
##
## CORRELATIONS RESULTS
## Mean: 0.3028091
## Median: 0.319312
## Variance: 0.07725244
## st.dev.: 0.2779432
```

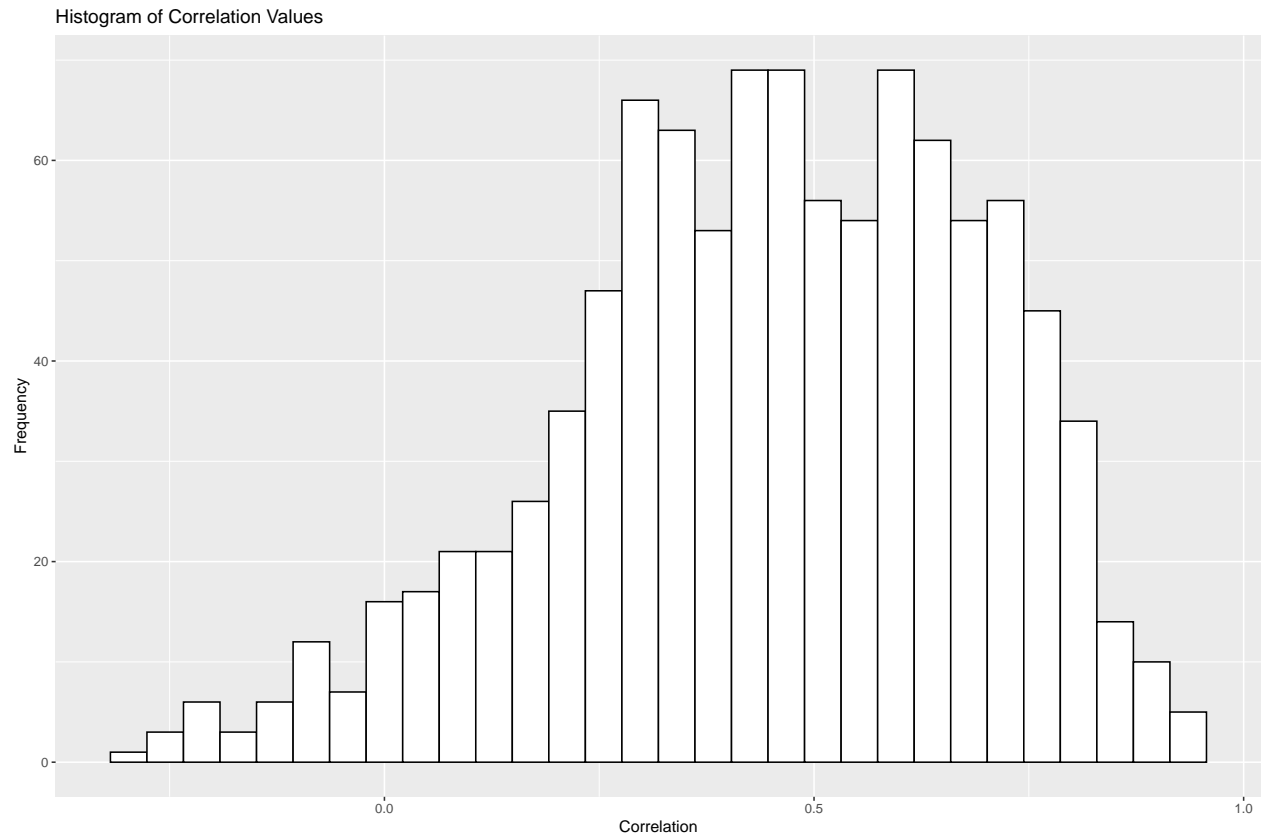


```
## MSE RESULTS
## Mean: 364.5733
## Median: 327.0747
## Variance: 22807.28
## st.dev.: 151.0208
```



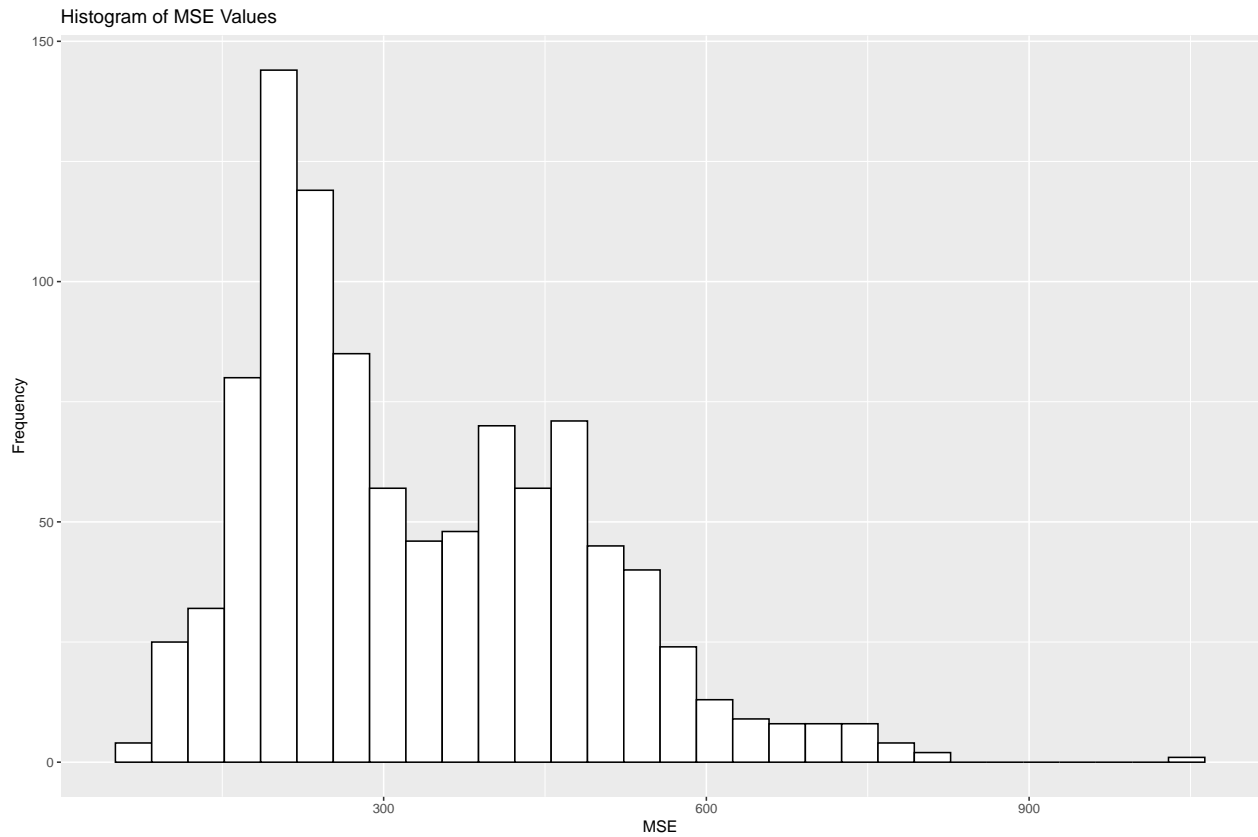
**Ridge: 771 genes -> ROR-proliferation score + interactions between PCs**

```
## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0
##
## CORRELATIONS RESULTS
## Mean: 0.4505837
## Median: 0.463892
## Variance: 0.05781415
## st.dev.: 0.2404457
```



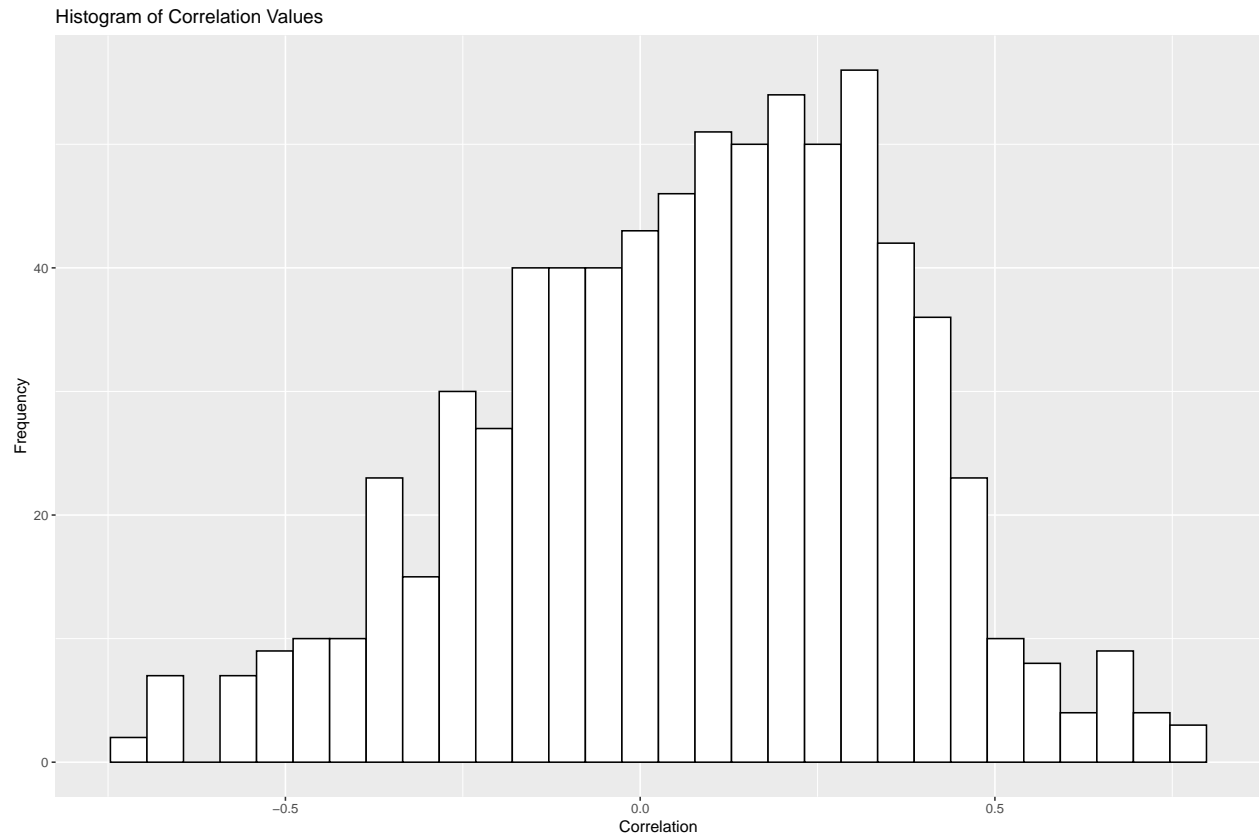
```
## MSE RESULTS
## Mean: 333.3975
## Median: 291.1335
## Variance: 23000.06
## st.dev.: 151.6577
```



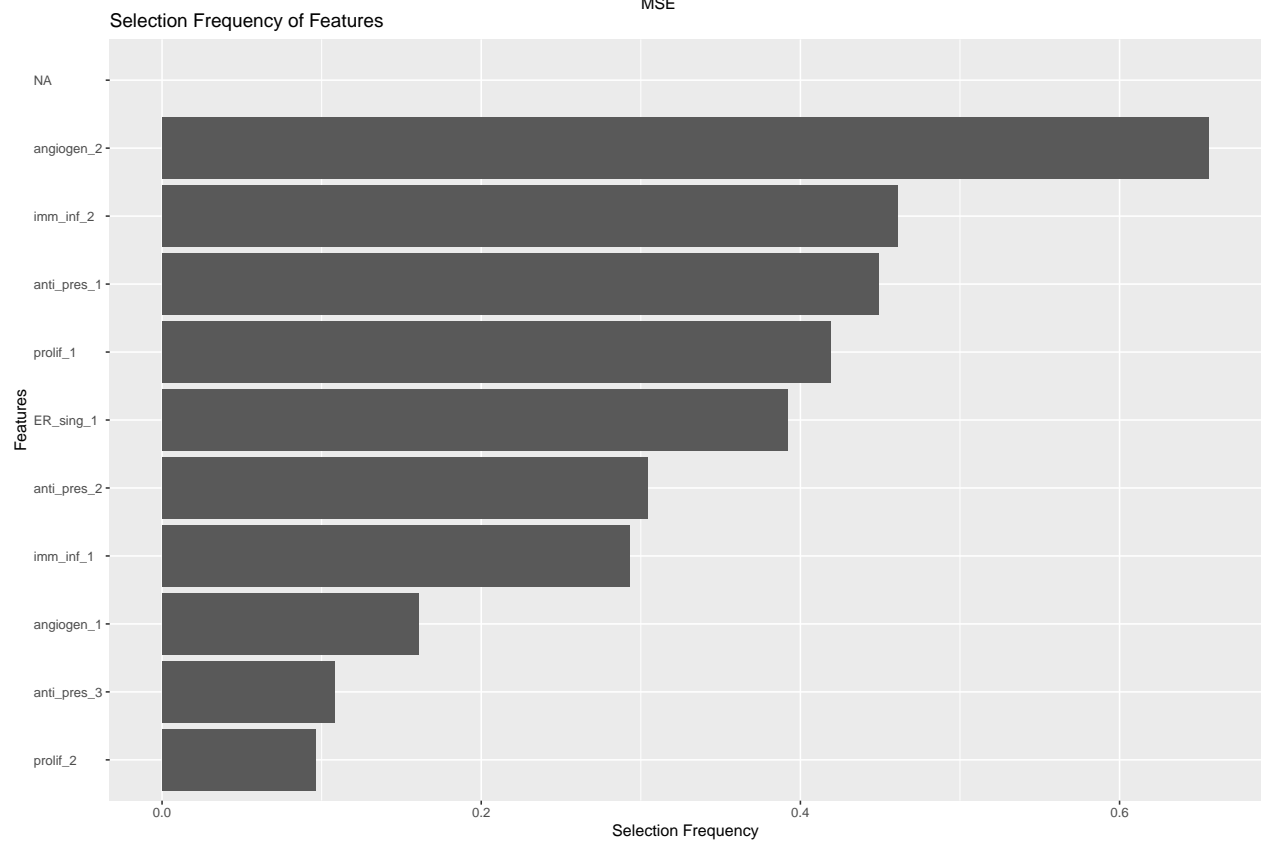
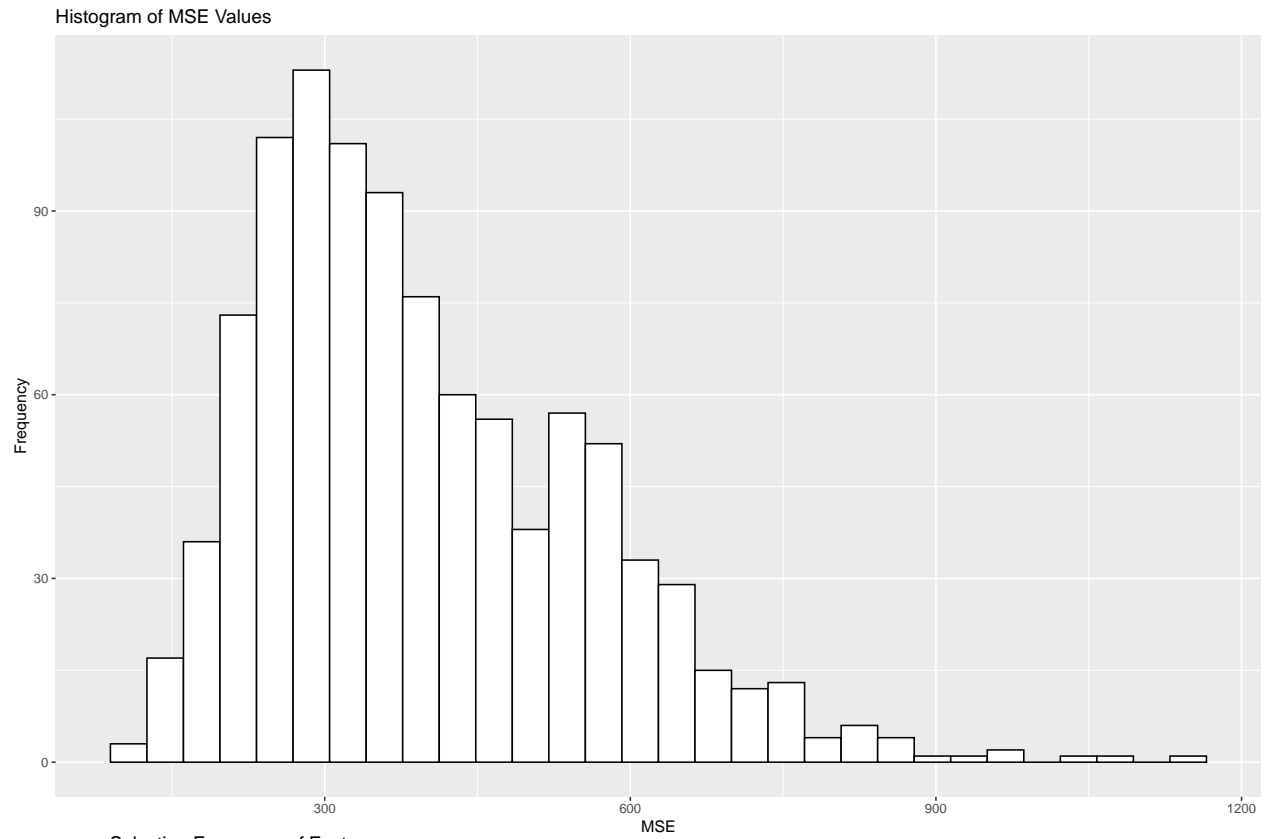


**Lasso: 771 genes -> ROR-proliferation score**

```
## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0.251
##
## CORRELATIONS RESULTS
## Mean: 0.07849613
## Median: 0.1028317
## Variance: 0.08158919
## st.dev.: 0.2856382
```



```
## MSE RESULTS
## Mean: 396.4902
## Median: 361.1201
## Variance: 25641.71
## st.dev.: 160.1303
```



##

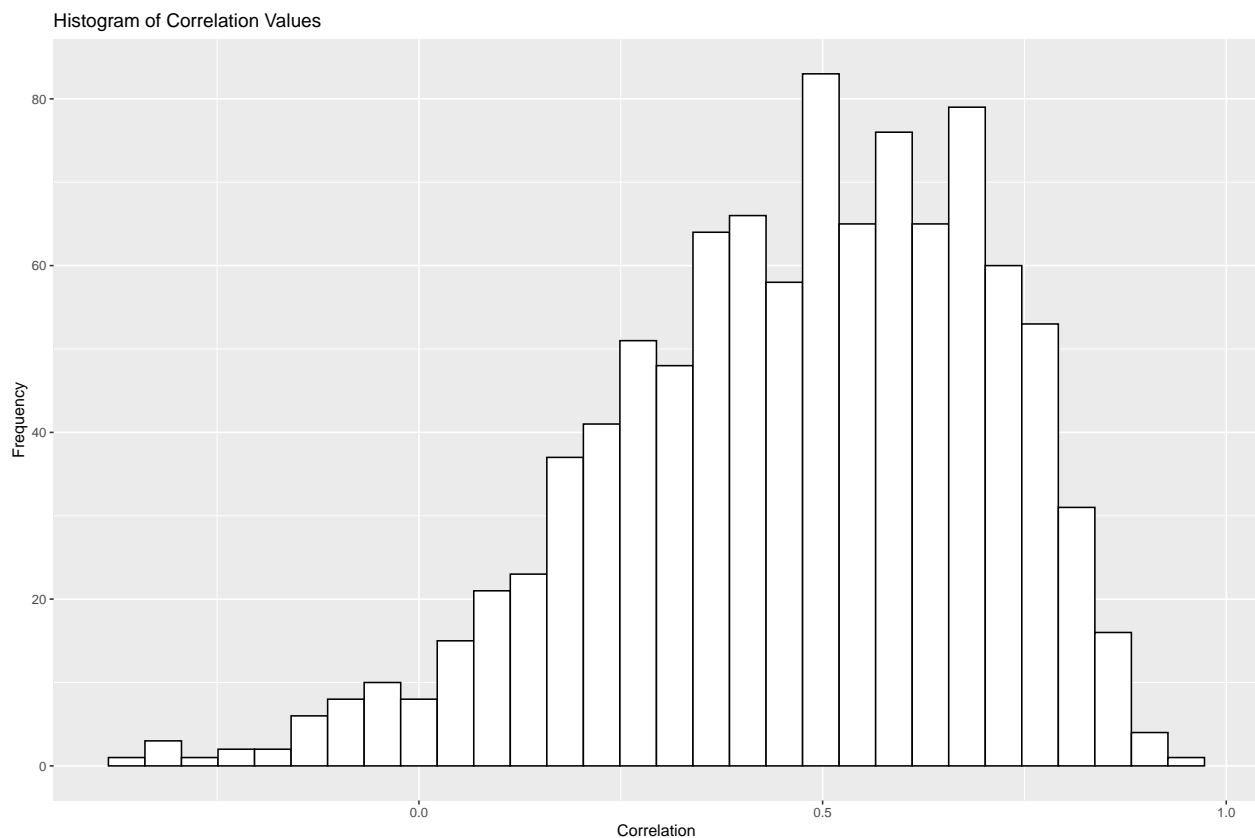
```
## Features selected 50% or more times:
## angiogen_2
## Top 20 featrues:
## [1] "angiogen_2" "imm_inf_2" "anti_pres_1" "prolif_1" "ER_sing_1"
## [6] "anti_pres_2" "imm_inf_1" "angiogen_1" "anti_pres_3" "prolif_2"
## [11] NA NA NA NA NA
## [16] NA NA NA NA NA
```

**Lasso: 771 genes -> ROR-proliferation score + interactions between PCs**

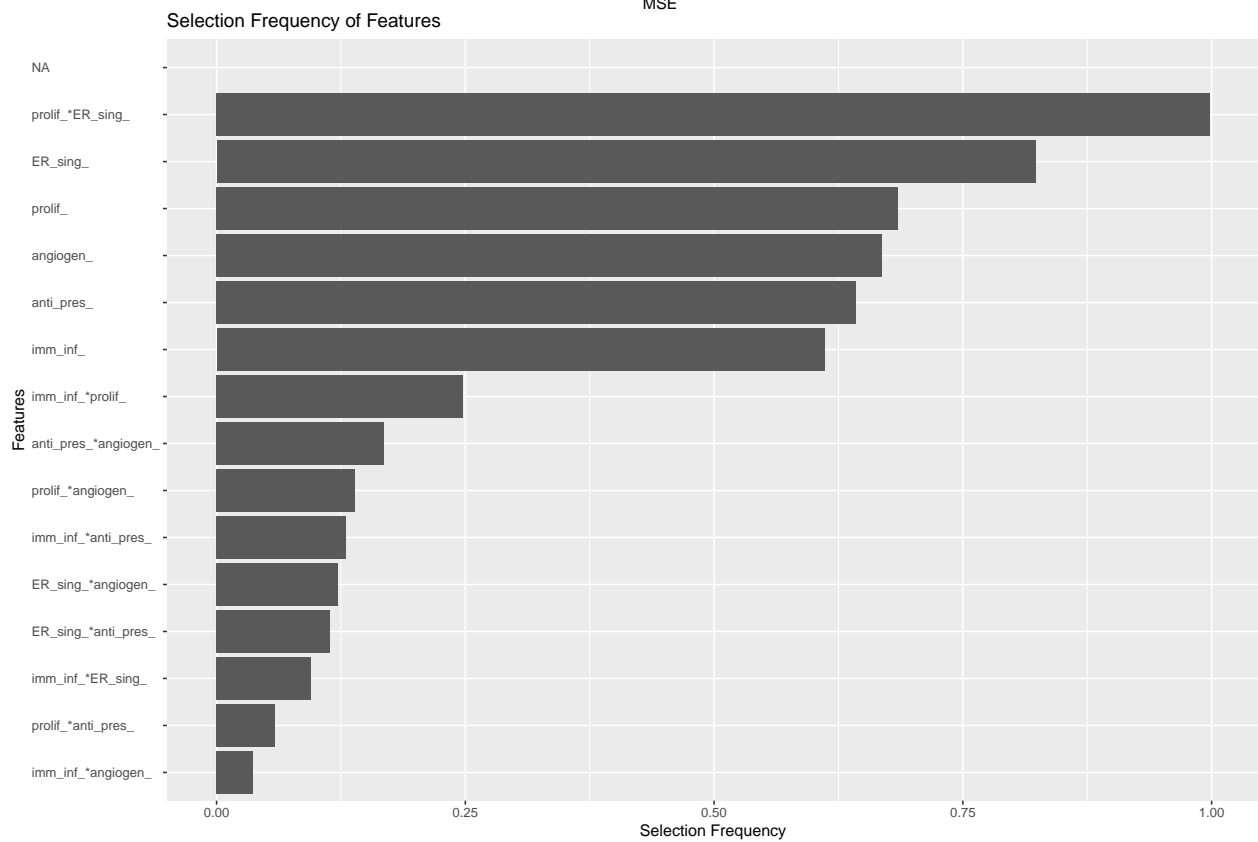
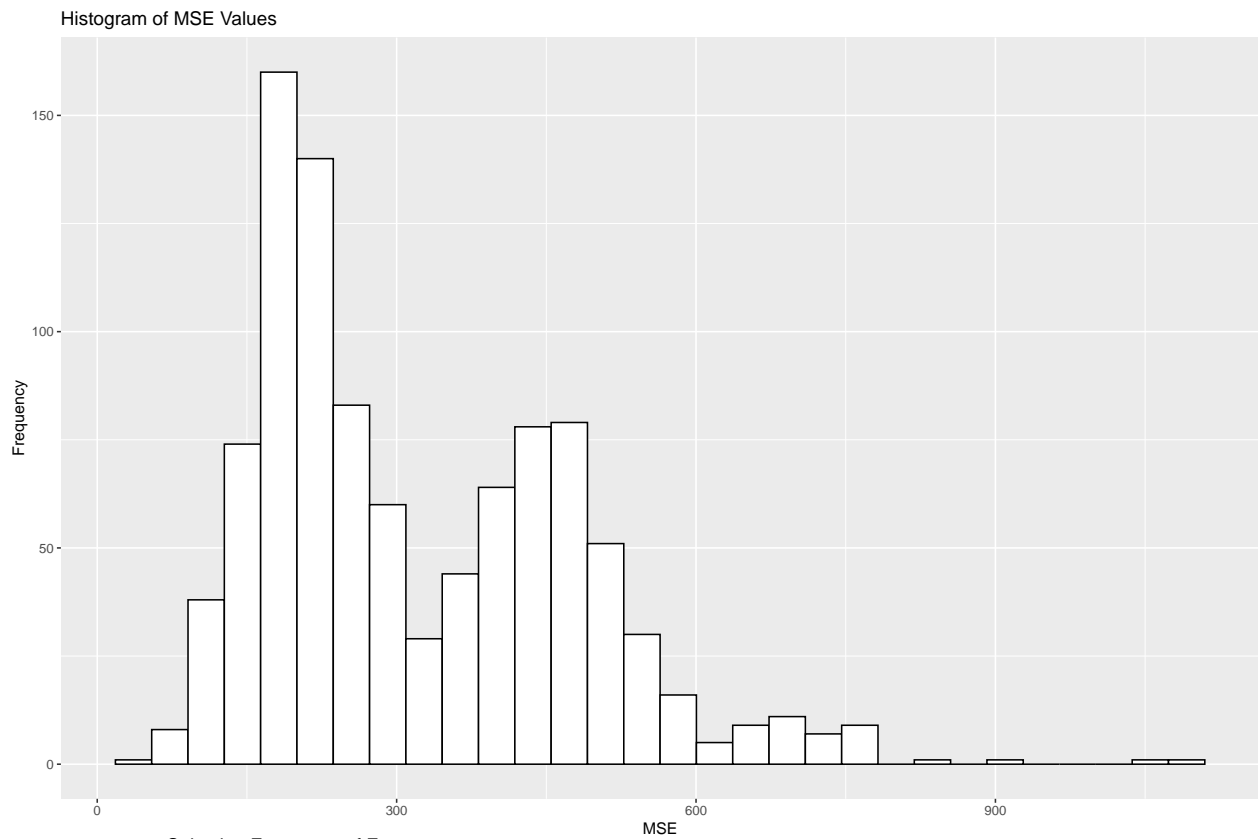
```
## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0.002
##
```

#### ## CORRELATIONS RESULTS

```
## Mean: 0.4687056
## Median: 0.4972697
## Variance: 0.05426225
## st.dev.: 0.2329426
```



```
## MSE RESULTS
## Mean: 321.0086
## Median: 265.9525
## Variance: 24834.46
## st.dev.: 157.5895
```



##

```

## Features selected 50% or more times:
## imm_inf_prolif_ER_sing_anti_pres_angiogen_prolif_*ER_sing_
## Top 20 featrues:
## [1] "prolif_*ER_sing_"      "ER_sing_"           "prolif_"
## [4] "angiogen_"            "anti_pres_"         "imm_inf_"
## [7] "imm_inf_*prolif_"      "anti_pres_*angiogen_" "prolif_*angiogen_"
## [10] "imm_inf_*anti_pres_"   "ER_sing_*angiogen_"  "ER_sing_*anti_pres_"
## [13] "imm_inf_*ER_sing_"     "prolif_*anti_pres_"   "imm_inf_*angiogen_"
## [16] NA                      NA                    NA
## [19] NA                      NA                    NA

```

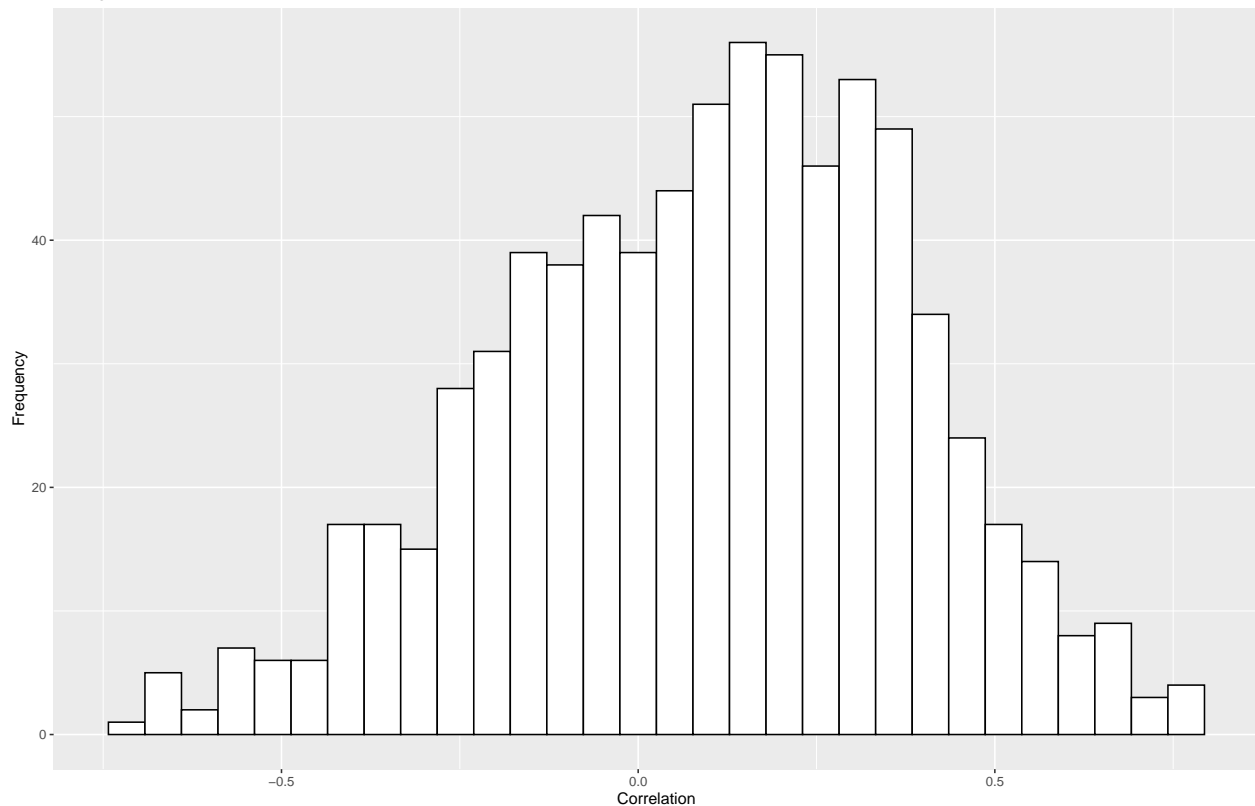
### ElasticNet: 771 genes -> ROR-proliferation score

```

## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0.24
##
## CORRELATIONS RESULTS
## Mean: 0.09606929
## Median: 0.1167623
## Variance: 0.08091802
## st.dev.: 0.2844609

```

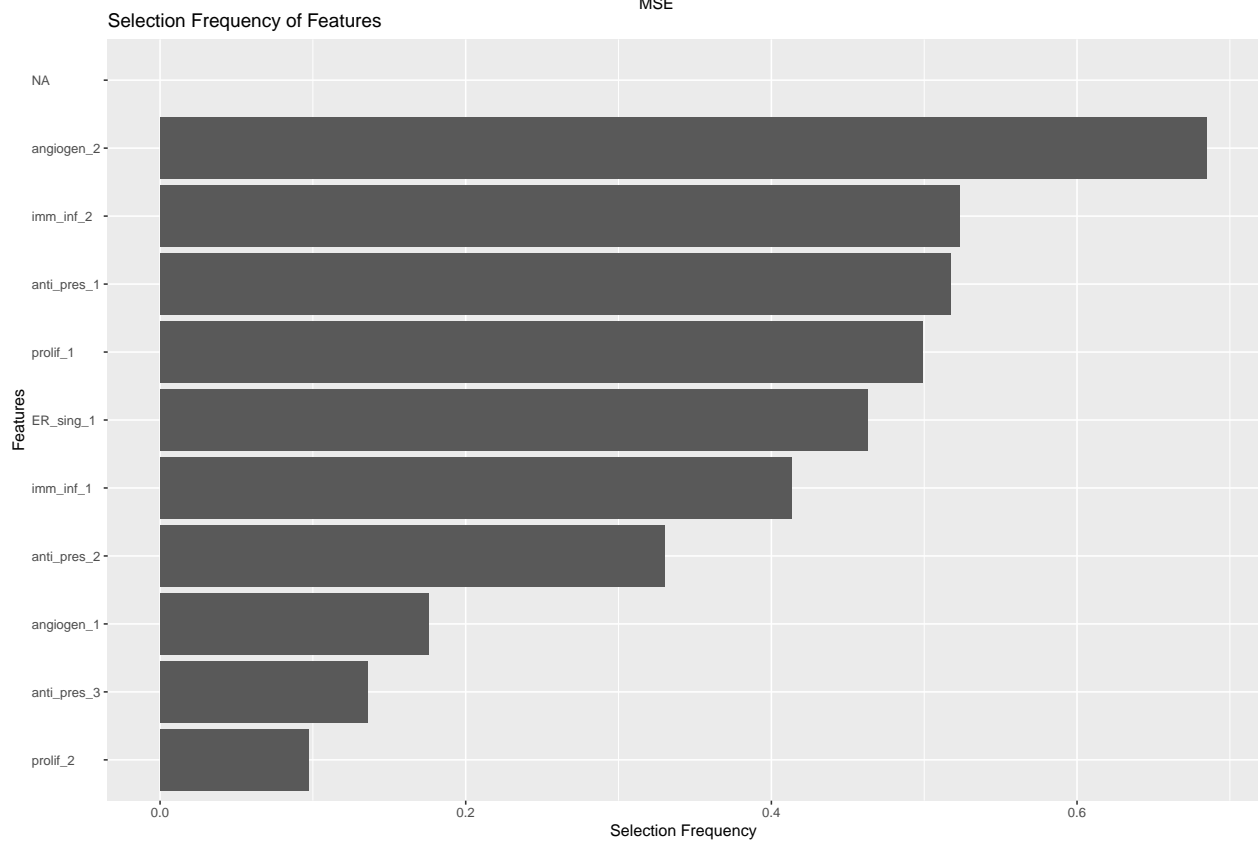
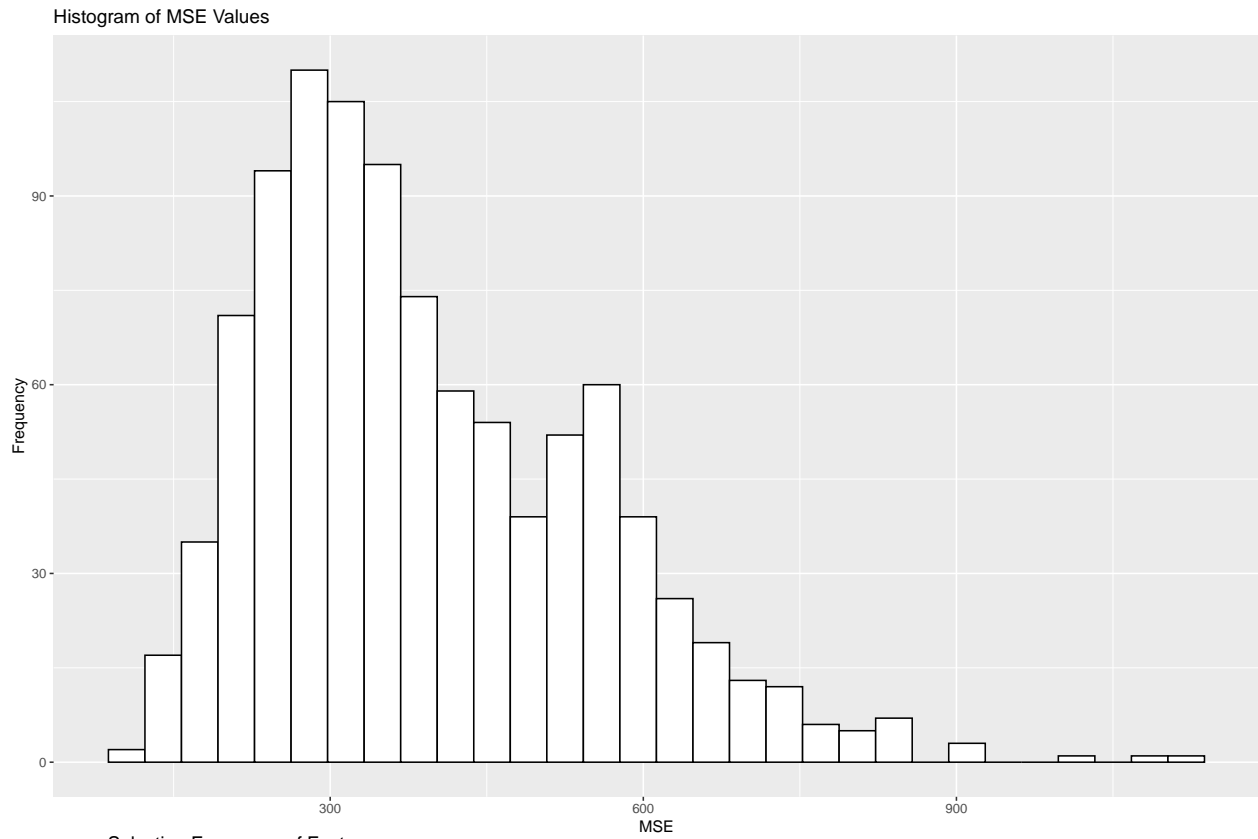
Histogram of Correlation Values



```

## MSE RESULTS
## Mean: 392.3862
## Median: 358.5637
## Variance: 24990.96
## st.dev.: 158.0853

```

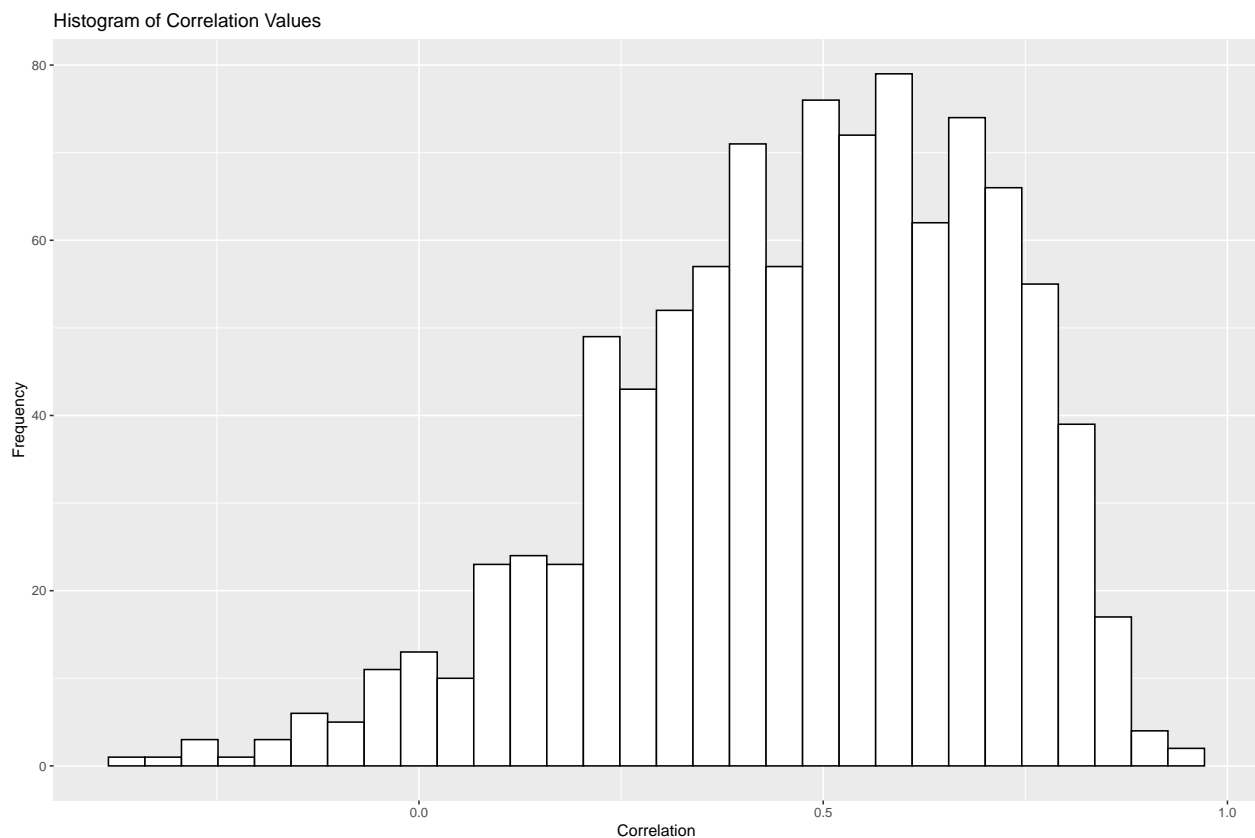


##

```
## Features selected 50% or more times:
## imm_inf_2 anti_pres_1 angiogen_2
## Top 20 featrues:
## [1] "angiogen_2" "imm_inf_2" "anti_pres_1" "prolif_1" "ER_sing_1"
## [6] "imm_inf_1" "anti_pres_2" "angiogen_1" "anti_pres_3" "prolif_2"
## [11] NA NA NA NA NA
## [16] NA NA NA NA NA
```

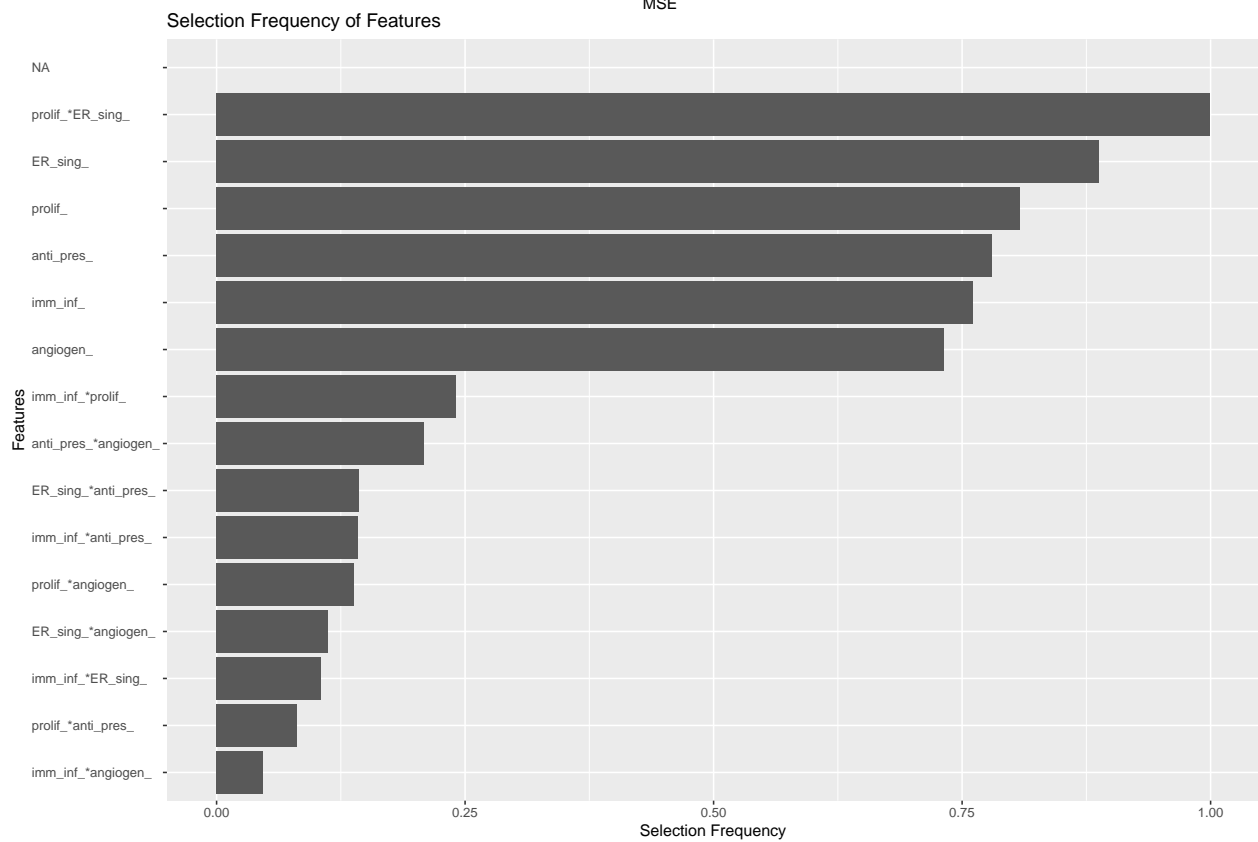
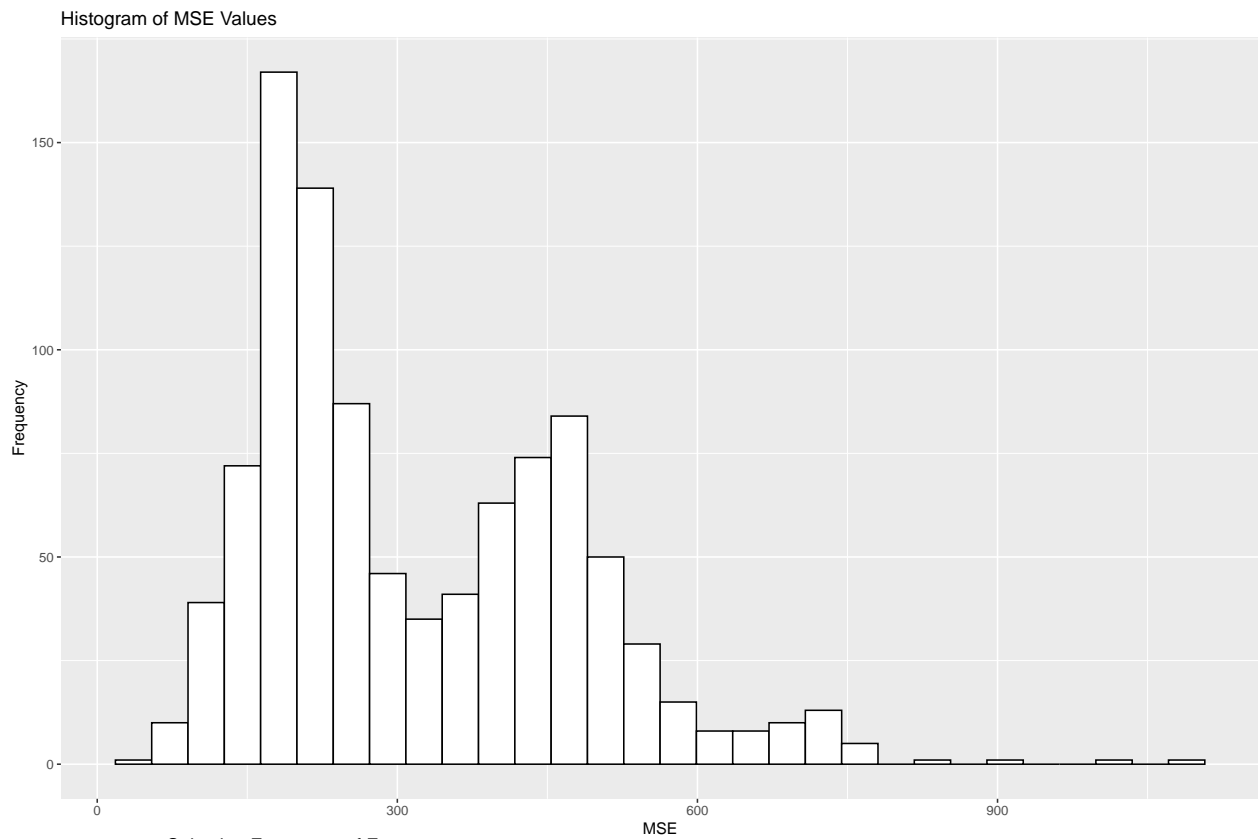
**ElasticNet: 771 genes -> ROR-proliferation score + interactions between PCs**

```
## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0.001
##
## CORRELATIONS RESULTS
## Mean: 0.4749342
## Median: 0.5041917
## Variance: 0.05452847
## st.dev.: 0.2335133
```



```
## MSE RESULTS
## Mean: 319.7269
## Median: 263.5692
## Variance: 24916.52
## st.dev.: 157.8497
```





##

```

## Features selected 50% or more times:
## imm_inf_ prolif_ ER_sing_ anti_pres_ angiogen_ prolif_*ER_sing_
## Top 20 featrues:
## [1] "prolif_*ER_sing_"      "ER_sing_"              "prolif_"
## [4] "anti_pres_"           "imm_inf_"              "angiogen_"
## [7] "imm_inf_*prolif_"      "anti_pres_*angiogen_"  "ER_sing_*anti_pres_"
## [10] "imm_inf_*anti_pres_"   "prolif_*angiogen_"     "ER_sing_*angiogen_"
## [13] "imm_inf_*ER_sing_"     "prolif_*anti_pres_"     "imm_inf_*angiogen_"
## [16] NA                      NA                      NA
## [19] NA                      NA                      NA

```

Summery results: PCA ROR+proliferation score (repeated cross-validation)

Model	cor_mean	sd_cor	MSE_mean	MSE_sd
ridge	0.3028091	0.2779432	364.5733	151.0208
ridge_interac	0.4505837	0.2404457	333.3975	151.6577
lasso	0.0784961	0.2856382	396.4902	160.1303
lasso_interact	0.4687056	0.2329426	321.0086	157.5895
elastic	0.0960693	0.2844609	392.3862	158.0853
elastic_interact	0.4749342	0.2335133	319.7269	157.8497

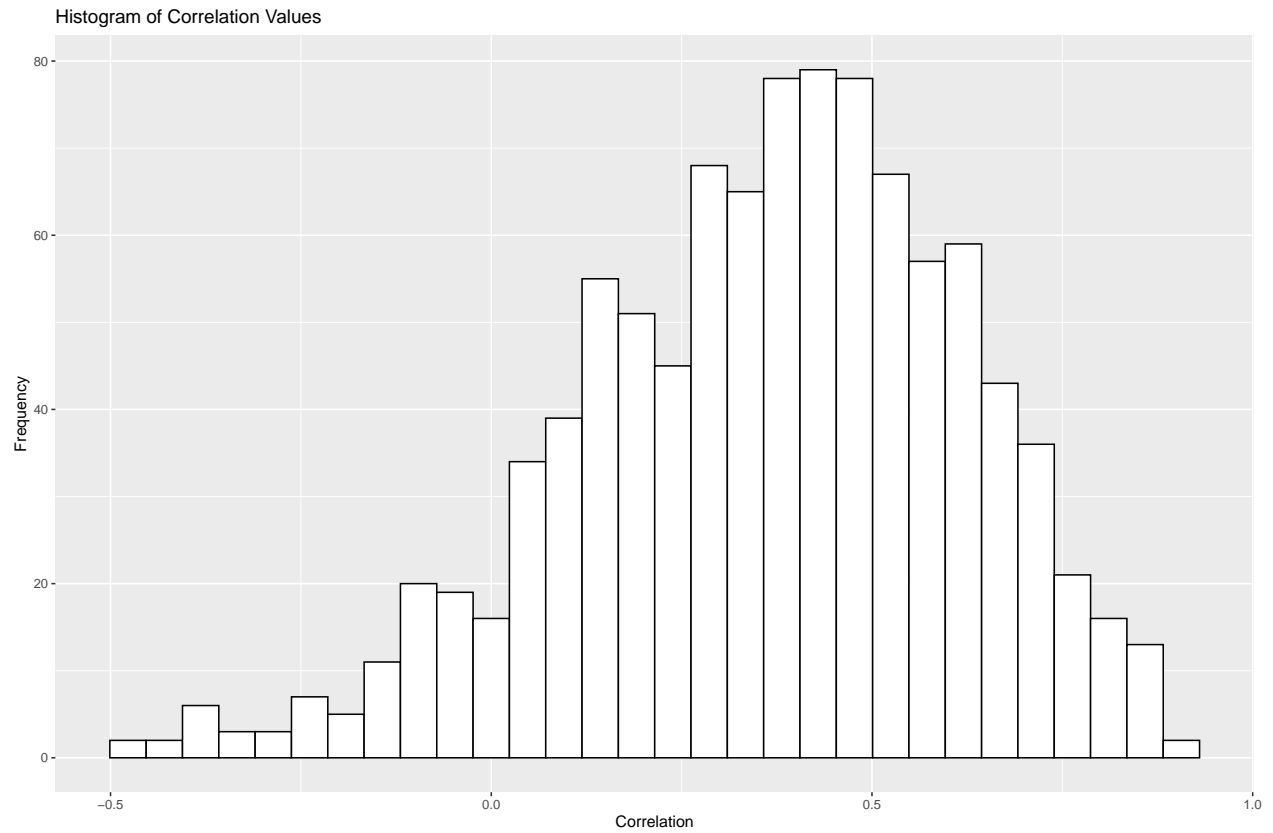
## Stacking on signature gene sets using repeated cross-validation

Ridge: 771 genes -> ROR-proliferation score

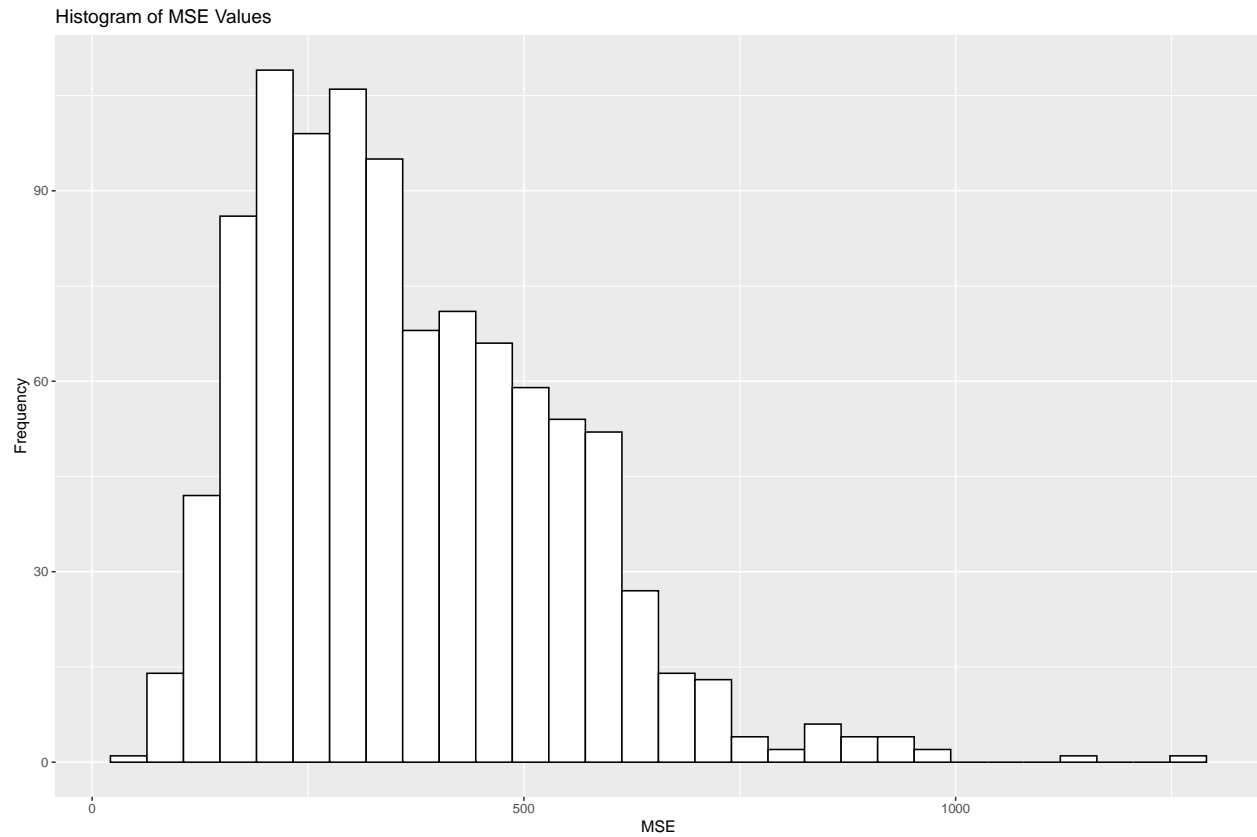
```

## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0
##
## CORRELATIONS RESULTS
## Mean: 0.363015
## Median: 0.3907333
## Variance: 0.06475058
## st.dev.: 0.2544613

```

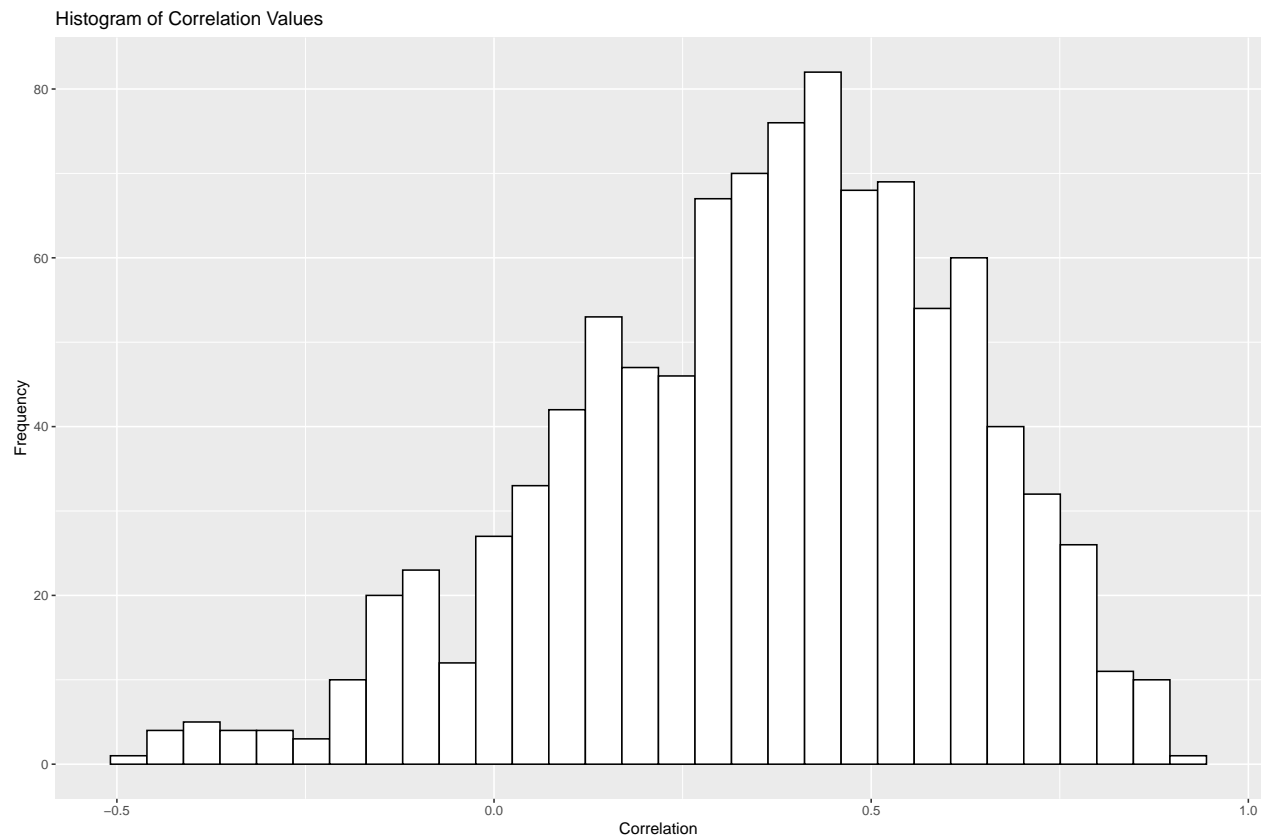


```
## MSE RESULTS
## Mean: 367.3704
## Median: 335.367
## Variance: 29532.74
## st.dev.: 171.8509
```

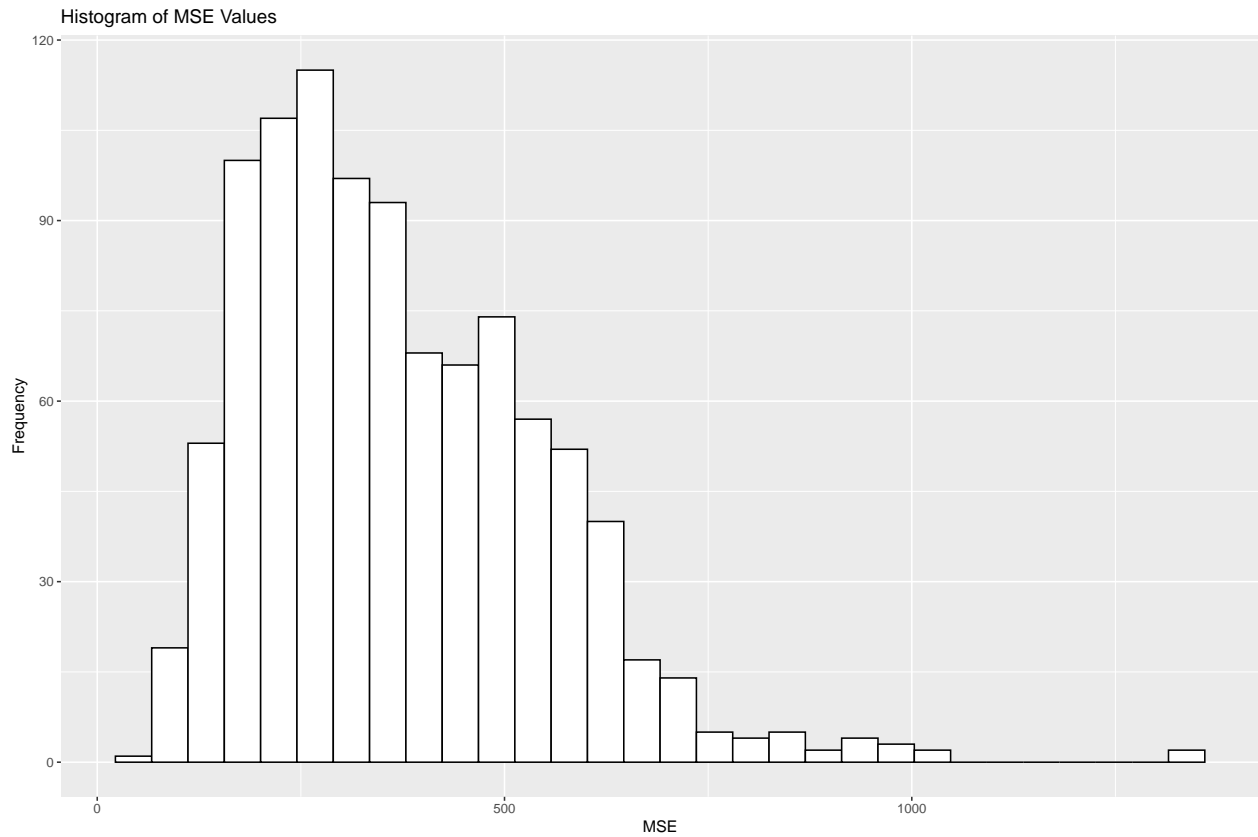


**Ridge: 771 genes -> ROR-proliferation score + interactions between PCs**

```
## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0
##
## CORRELATIONS RESULTS
## Mean: 0.3555283
## Median: 0.3864856
## Variance: 0.06877803
## st.dev.: 0.2622557
```

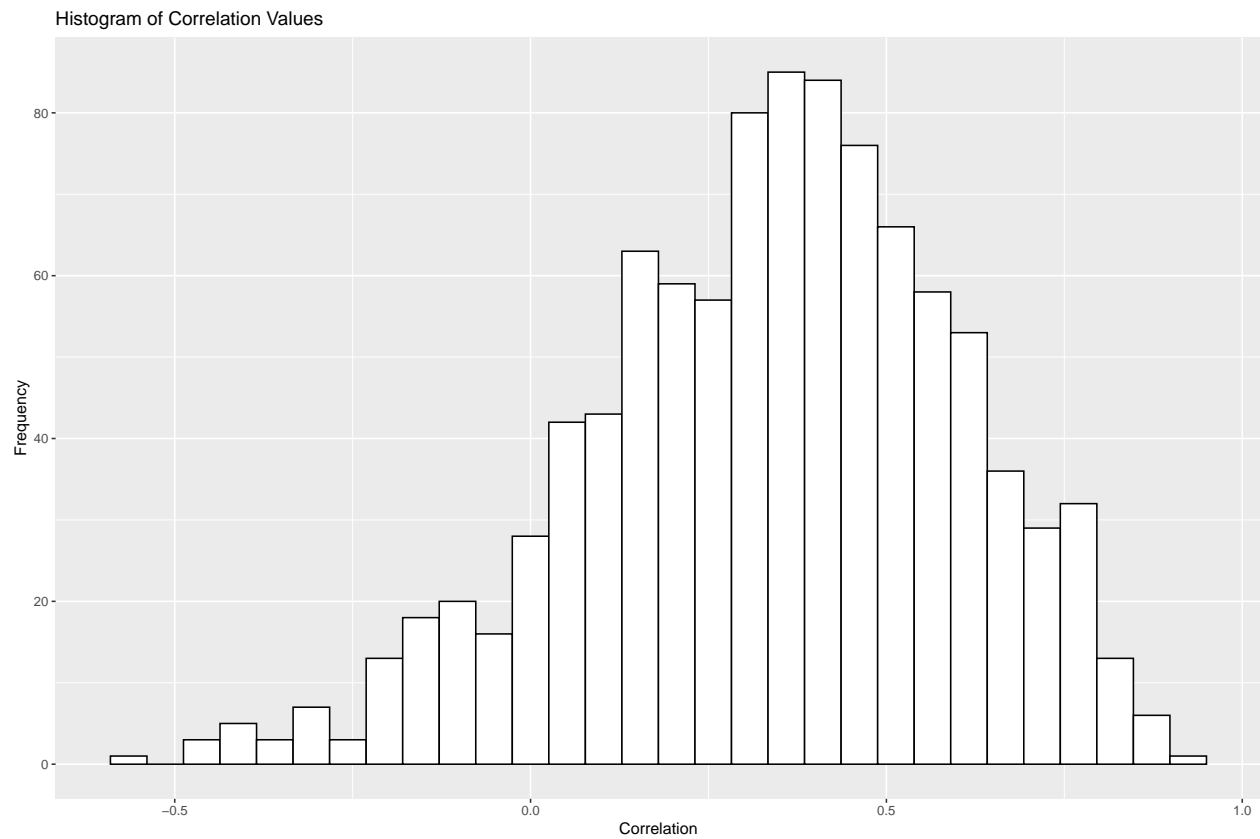


```
## MSE RESULTS
## Mean: 369.2144
## Median: 337.1152
## Variance: 31306.72
## st.dev.: 176.9371
```

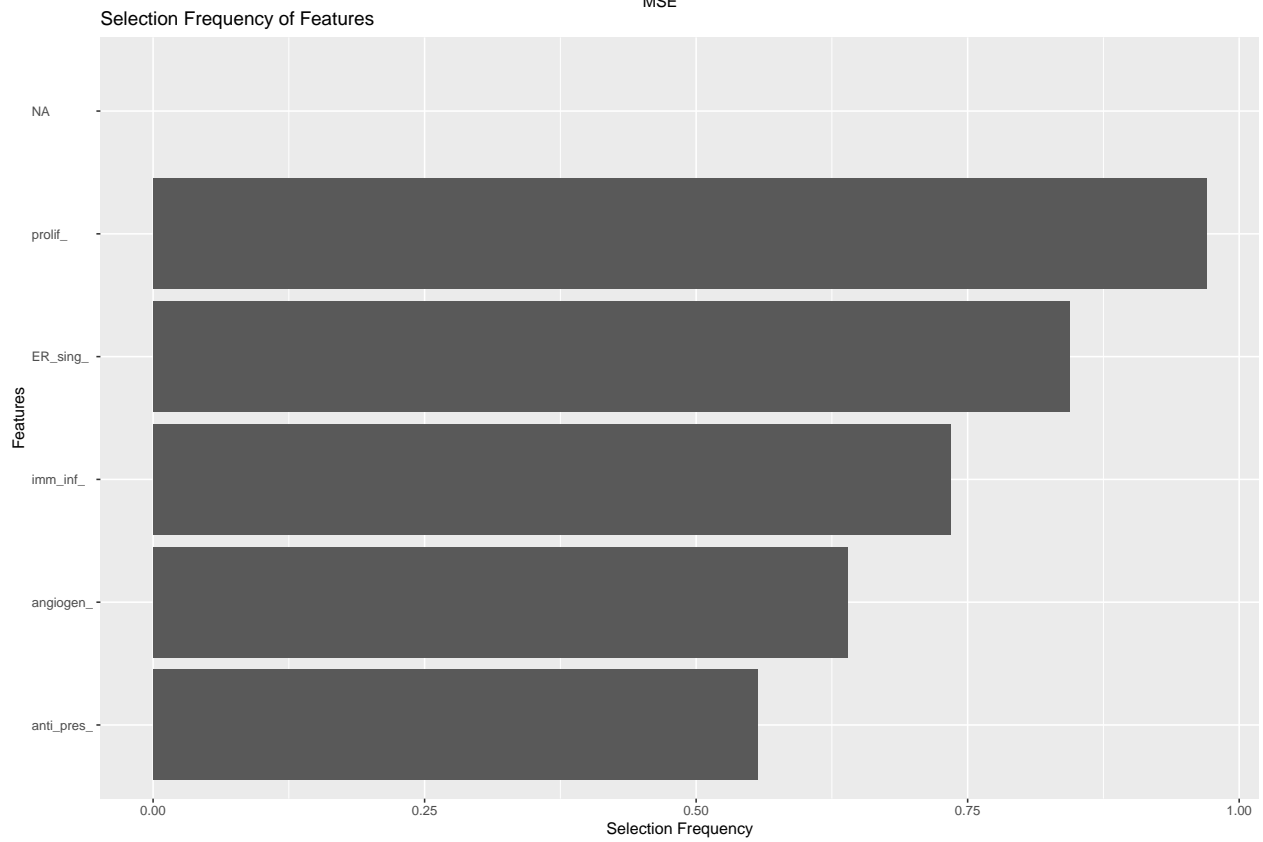
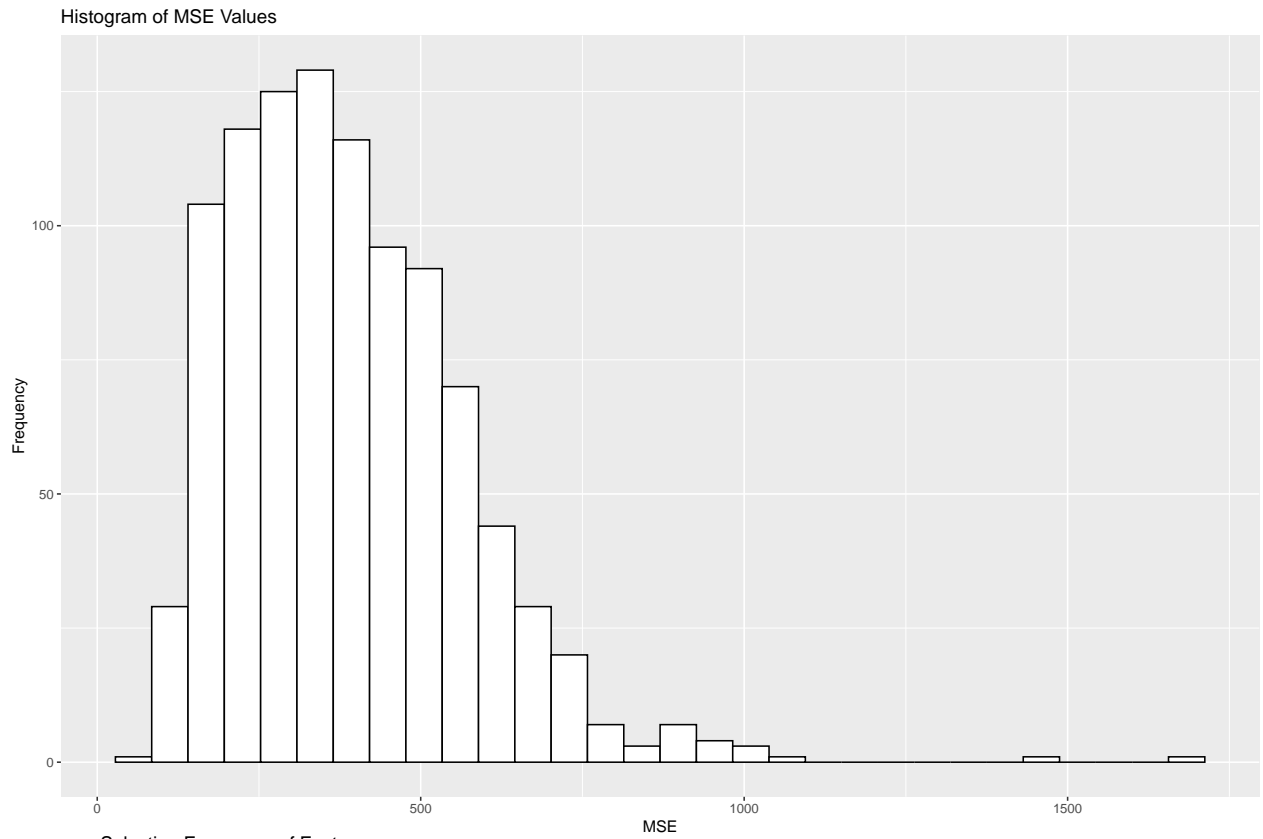


**Lasso: 771 genes -> ROR-proliferation score**

```
## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0
##
## CORRELATIONS RESULTS
## Mean: 0.3373612
## Median: 0.3601618
## Variance: 0.06786039
## st.dev.: 0.2605003
```



```
## MSE RESULTS
## Mean: 386.6455
## Median: 360.5423
## Variance: 32369.44
## st.dev.: 179.9151
```



##



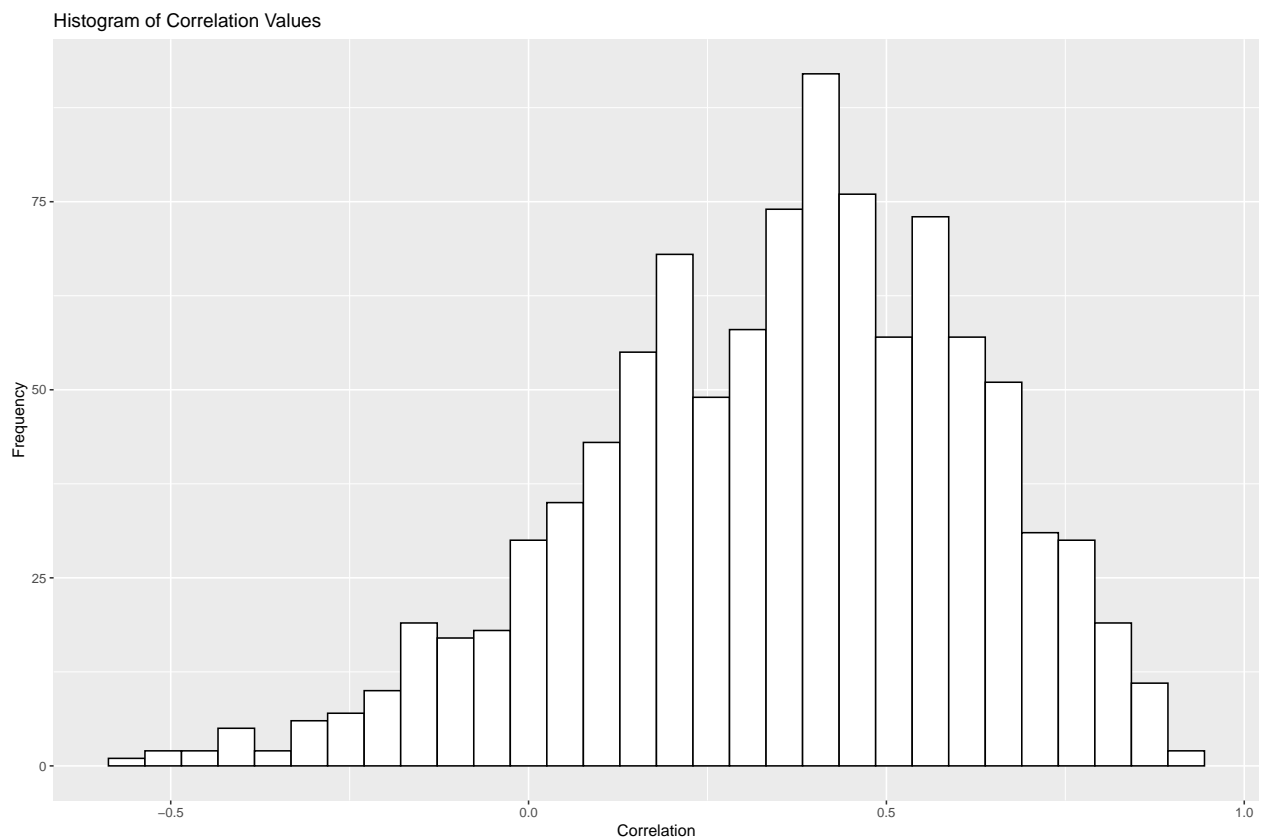
```
## Features selected 50% or more times:
## imm_inf_ prolif_ ER_sing_ anti_pres_ angiogen_
## Top 20 featrues:
## [1] "prolif_"      "ER_sing_"    "imm_inf_"    "angiogen_"  "anti_pres_"
## [6] NA            NA            NA            NA            NA
## [11] NA            NA            NA            NA            NA
## [16] NA            NA            NA            NA            NA
```

**Lasso: 771 genes -> ROR-proliferation score + interactions between PCs**

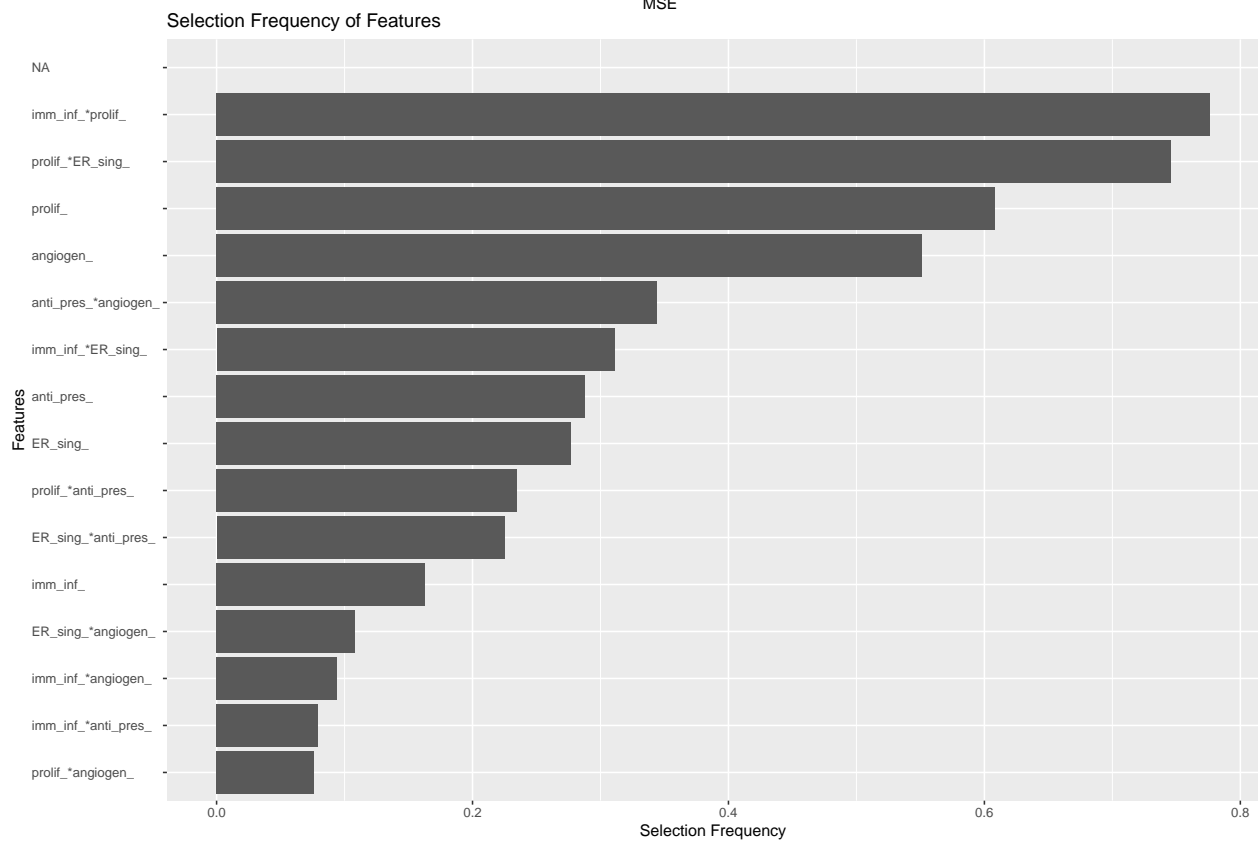
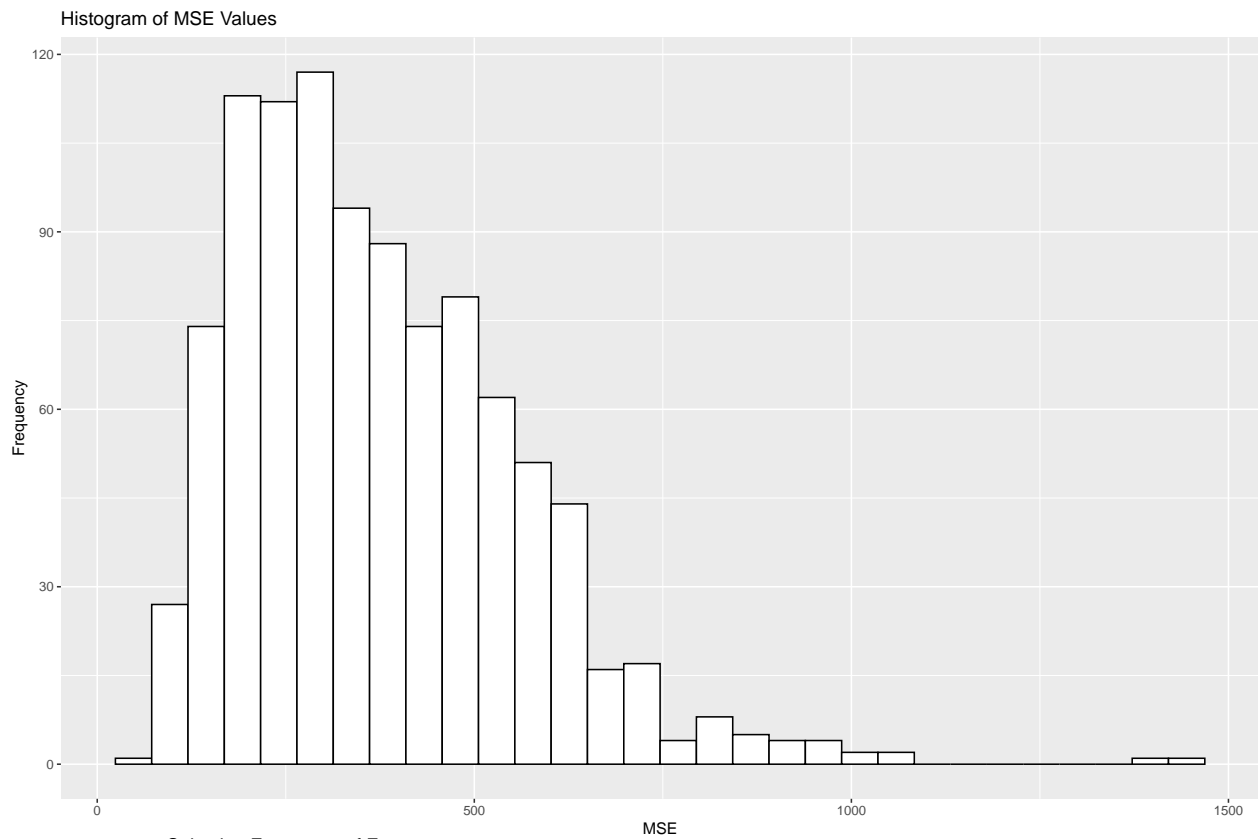
```
## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0
##
```

**## CORRELATIONS RESULTS**

```
## Mean: 0.3521323
## Median: 0.381805
## Variance: 0.07224413
## st.dev.: 0.2687827
```



```
## MSE RESULTS
## Mean: 373.2299
## Median: 341.6008
## Variance: 33334.83
## st.dev.: 182.5783
```



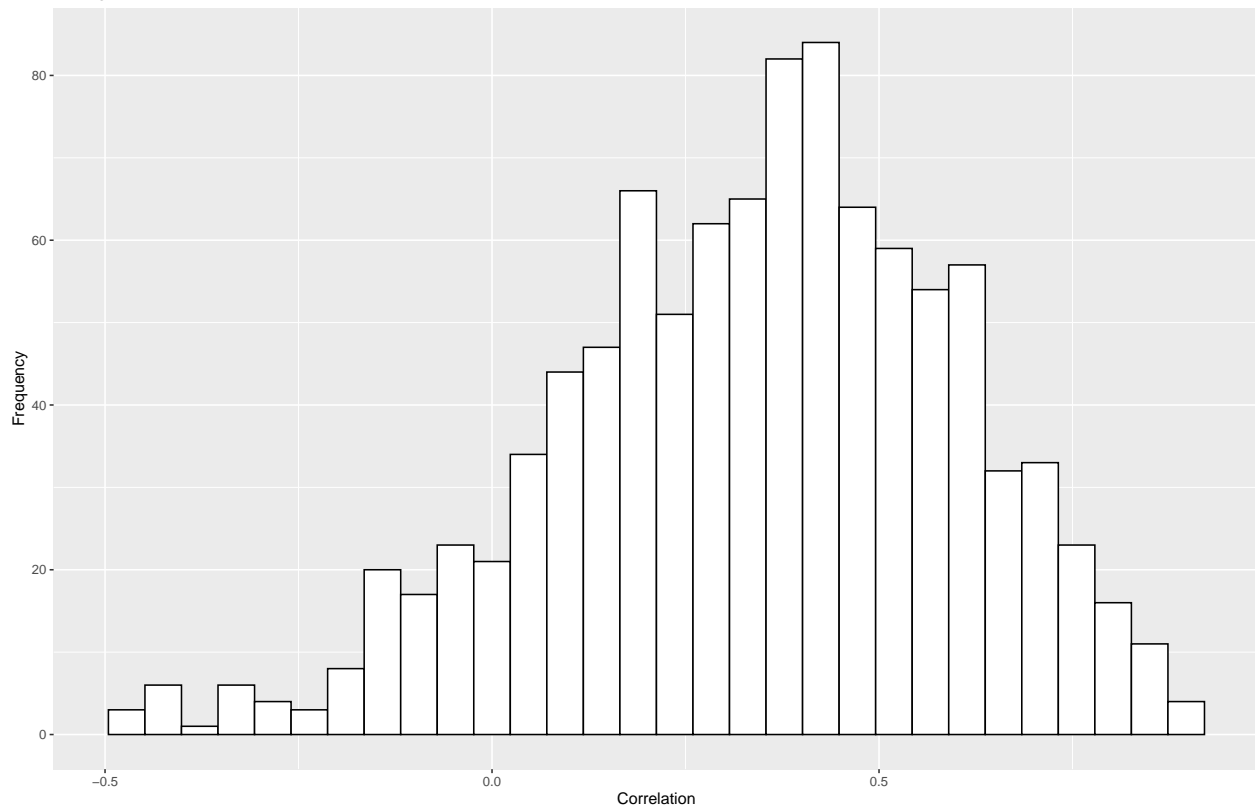
##

```
## Features selected 50% or more times:
## prolifer_ angiogen_ imm_inf_*prolif_ prolifer_*ER_sing_
## Top 20 features:
## [1] "imm_inf_*prolif_"      "prolif_*ER_sing_"    "prolif_"
## [4] "angiogen_"            "anti_pres_*angiogen_" "imm_inf_*ER_sing_"
## [7] "anti_pres_"           "ER_sing_"            "prolif_*anti_pres_"
## [10] "ER_sing_*anti_pres_"  "imm_inf_"            "ER_sing_*angiogen_"
## [13] "imm_inf_*angiogen_"   "imm_inf_*anti_pres_" "prolif_*angiogen_"
## [16] NA                      NA                     NA
## [19] NA                      NA                     NA
```

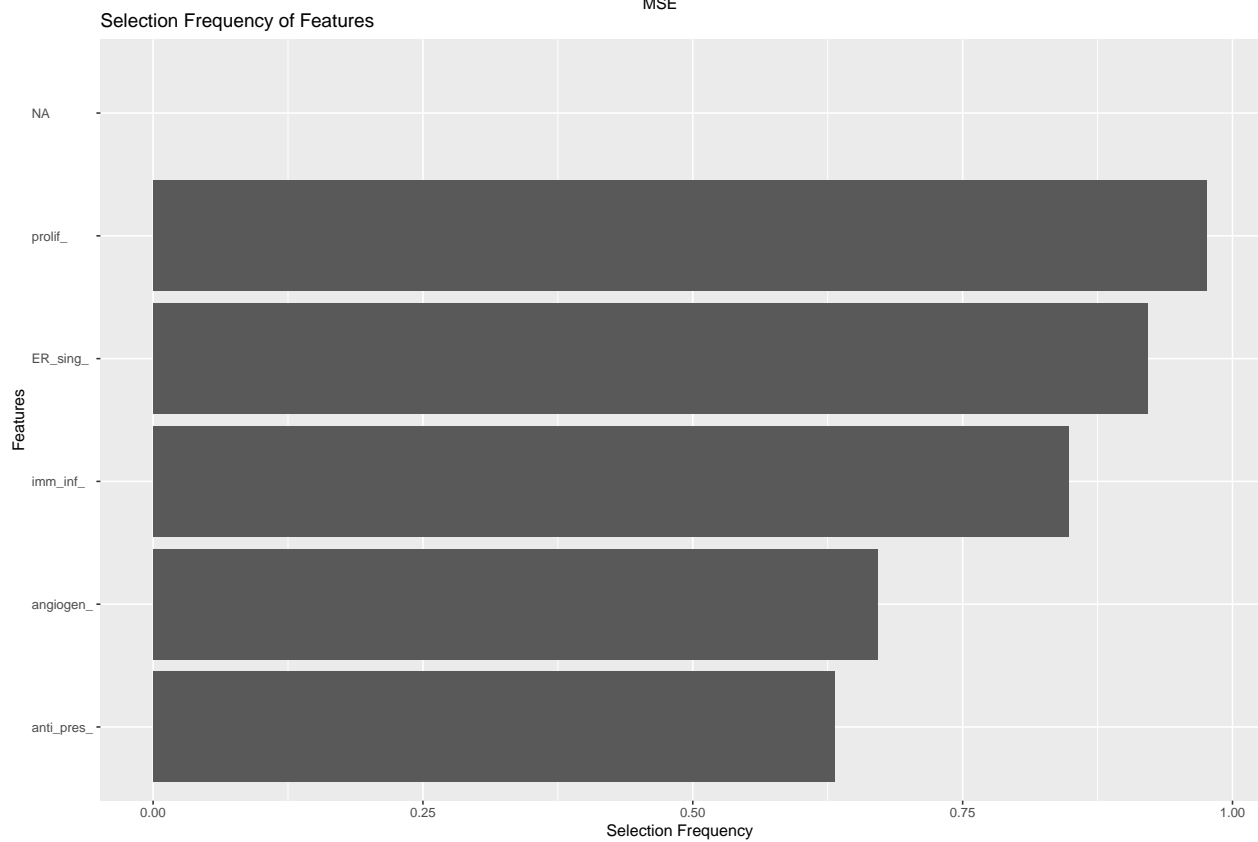
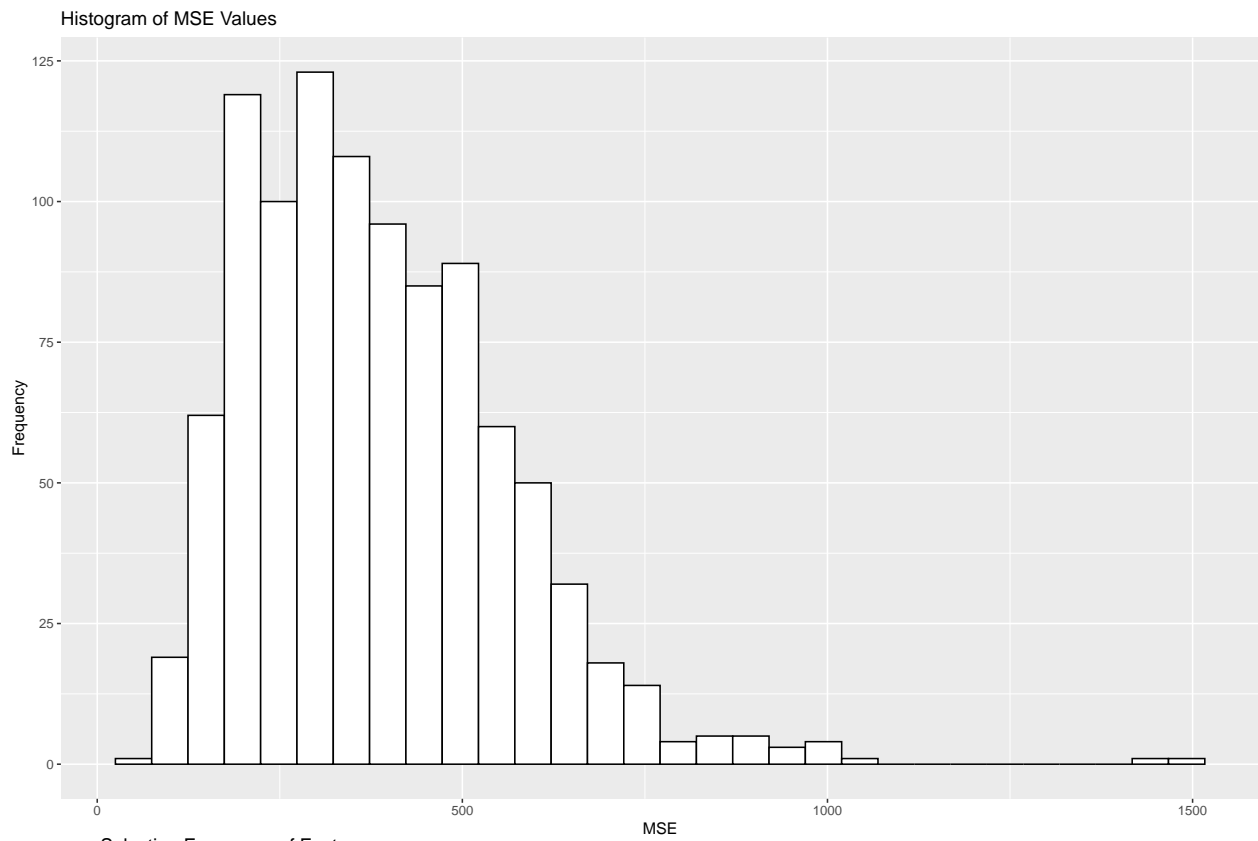
### ElasticNet: 771 genes -> ROR-proliferation score

```
## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0
##
## CORRELATIONS RESULTS
## Mean: 0.3417178
## Median: 0.3669518
## Variance: 0.06675737
## st.dev.: 0.2583745
```

Histogram of Correlation Values



```
## MSE RESULTS
## Mean: 383.7542
## Median: 356.8975
## Variance: 31468.03
## st.dev.: 177.3923
```



##

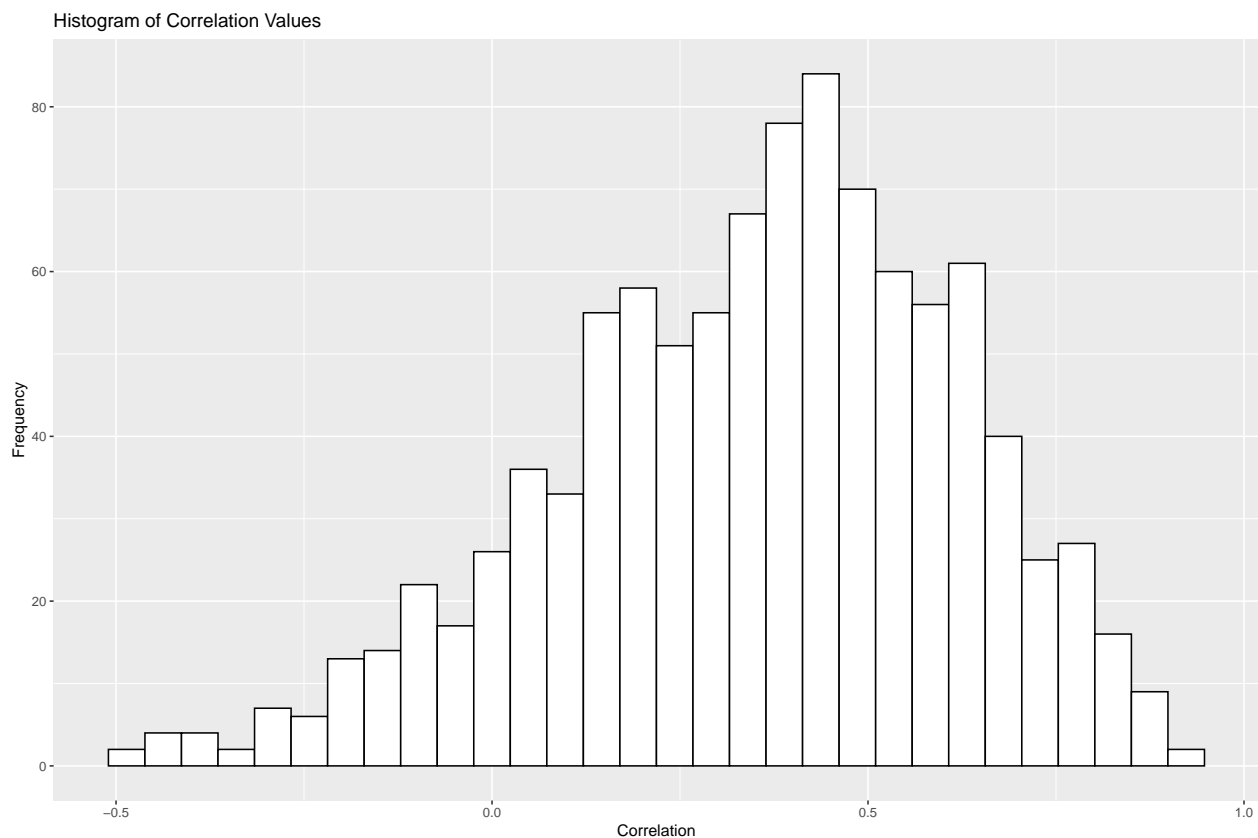
```
## Features selected 50% or more times:
## imm_inf_ prolif_ ER_sing_ anti_pres_ angiogen_
## Top 20 featrues:
## [1] "prolif_"      "ER_sing_"     "imm_inf_"     "angiogen_"    "anti_pres_"
## [6] NA             NA             NA             NA             NA
## [11] NA            NA            NA            NA            NA
## [16] NA            NA            NA            NA            NA
```

**ElasticNet: 771 genes -> ROR-proliferation score + interactions between PCs**

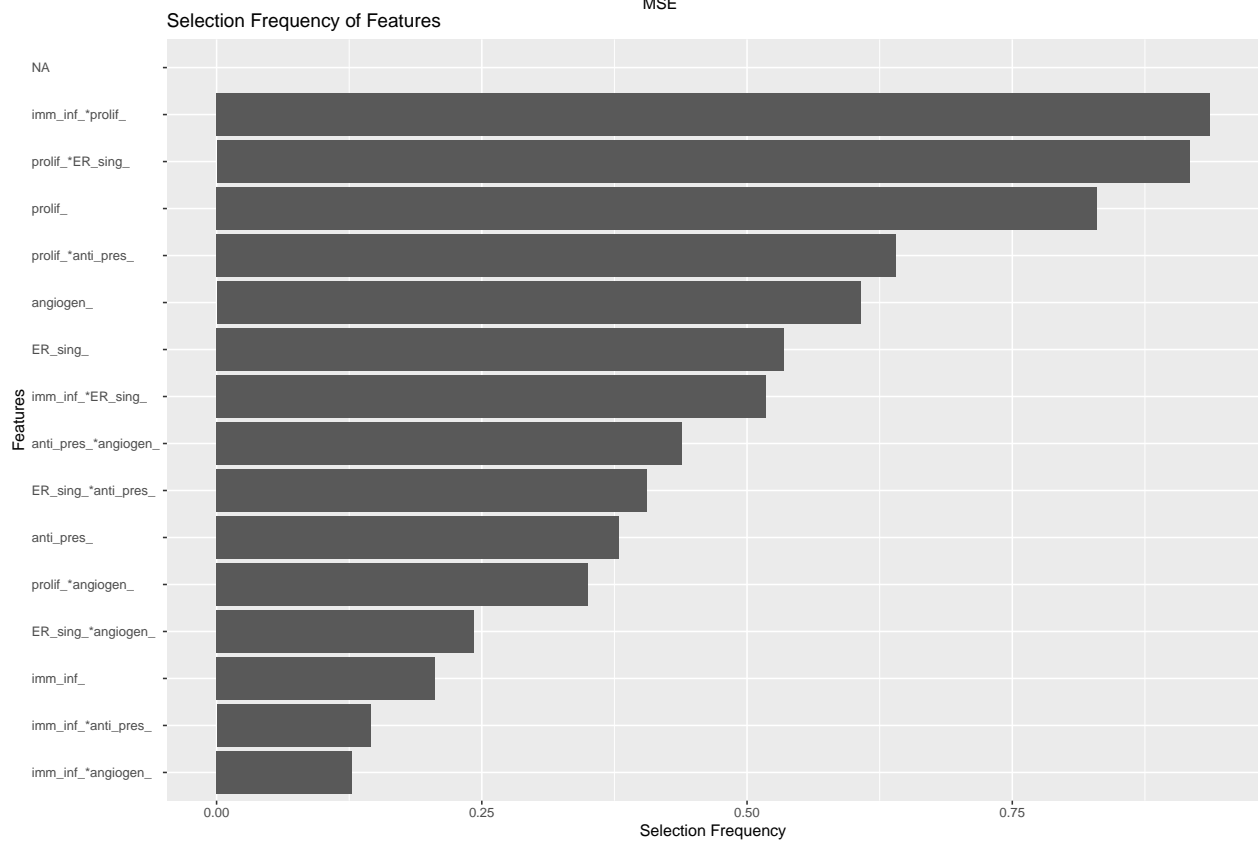
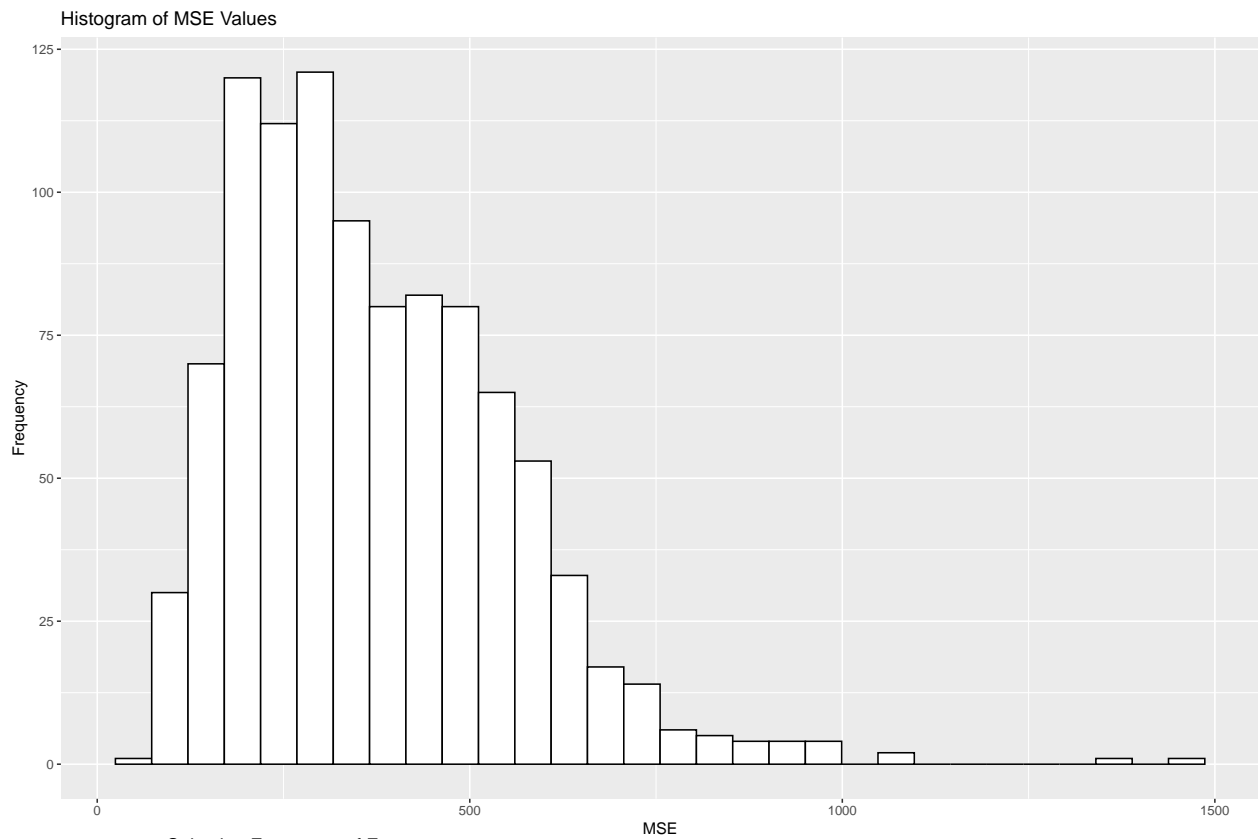
```
## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0
##
```

**## CORRELATIONS RESULTS**

```
## Mean: 0.353272
## Median: 0.3797595
## Variance: 0.07046161
## st.dev.: 0.2654461
```



```
## MSE RESULTS
## Mean: 371.1879
## Median: 339.6459
## Variance: 32238
## st.dev.: 179.5494
```



##

```
## Features selected 50% or more times:
## prolif_ ER_sing_ angiogen_ imm_inf_*prolif_ imm_inf_*ER_sing_ prolif_*ER_sing_ prolif_*anti_pres_
## Top 20 featrues:
## [1] "imm_inf_*prolif_"      "prolif_*ER_sing_"      "prolif_"
## [4] "prolif_*anti_pres_"    "angiogen_"             "ER_sing_"
## [7] "imm_inf_*ER_sing_"     "anti_pres_*angiogen_"  "ER_sing_*anti_pres_"
## [10] "anti_pres_"            "prolif_*angiogen_"     "ER_sing_*angiogen_"
## [13] "imm_inf_"              "imm_inf_*anti_pres_"    "imm_inf_*angiogen_"
## [16] NA                       NA                       NA
## [19] NA                       NA                       NA
```

### Summery results: Stacking ROR+proliferation score (repeated cross-validation)

Model	cor_mean	sd_cor	MSE_mean	MSE_sd
ridge	0.3630150	0.2544613	367.3704	171.8509
ridge_interac	0.3555283	0.2622557	369.2144	176.9371
lasso	0.3373612	0.2605003	386.6455	179.9151
lasso_interact	0.3521323	0.2687827	373.2299	182.5783
elastic	0.3417178	0.2583745	383.7542	177.3923
elastic_interact	0.3532720	0.2654461	371.1879	179.5494

## Post Lasso

not done

## Summery of all results

### Summery results: lasso proliferation score (bootstrap)

Model	cor_mean	sd_cor	MSE_mean	MSE_sd
lasso 6 genes	0.3498379	0.0631210	0.1492302	0.0124509
lasso 771 genes	0.7941413	0.0901070	0.0620913	0.0239813
Nodes	0.4144960	0.0642722	0.1479731	0.1916630
Residual additive	0.7835808	0.0854335	0.0638484	0.0213956
Residual multiplicative	0.7266736	0.0895236	0.0813415	0.0231428

### Summery results: lasso ROR+proliferation score (bootstrap)

Model	cor_mean	sd_cor	MSE_mean	MSE_sd
lasso 6 genes	0.1282306	0.0534128	378.0940	23.44024
lasso 771 genes	0.6968101	0.0995060	203.4080	61.34872
Nodes	0.2964169	0.0830696	417.6667	1027.06231
Residual additive	0.6925953	0.1092315	202.3235	61.04236
Residual multiplicative	0.5427757	0.1908061	291.0186	82.79231

### Summery results: lasso proliferation score (repeated cross-validation)

Model	cor_mean	sd_cor	MSE_mean	MSE_sd
lasso 6 genes	0.0919663	0.3068209	0.1655931	0.0718379
lasso 771 genes	0.4737037	0.2310209	0.0620913	0.0753056
Nodes	0.2842257	0.2768458	0.1560308	0.0762883
Residual additive	0.4633095	0.2227105	0.1331785	0.0654065
Residual multiplicative	0.4028471	0.2302632	0.1455819	0.0680617

**Summery results: lasso ROR+proliferation score (repeated cross-validation)**

Model	cor_mean	sd_cor	MSE_mean	MSE_sd
lasso 6 genes	-0.4822298	0.1724985	374.1519	144.1559
lasso 771 genes	0.0806237	0.2767153	393.8069	159.6451
Nodes	0.1806504	0.2854892	380.1157	164.5869
Residual additive	0.1642500	0.2788435	392.5436	158.8733
Residual multiplicative	-0.2145253	0.2512231	568.8063	208.5911

**Summery results: ridge 771 genes bootstrap and repeated cross-validation**

Model	cor_mean	sd_cor	MSE_mean	MSE_sd
prolif boot	0.8189568	0.0710276	0.0566524	0.0186773
ROR-prolif boot	0.7761924	0.0774688	156.0649552	44.1817261
prolif rep cross-val	0.5268342	0.2071537	0.1256548	0.0699318
ROR-prolif rep cross-val	0.0806237	0.2767153	393.8068910	159.6450765

**Summery results: elastic net 771 genes bootstrap and repeated cross-validation**

Model	cor_mean	sd_cor	MSE_mean	MSE_sd
prolif boot	0.8125591	0.0838975	0.0558955	0.0217032
ROR-prolif boot	0.7565123	0.0888143	164.4116160	52.7751849
prolif rep cross-val	0.4271890	0.2637029	0.1501025	0.0822400
ROR-prolif rep cross-val	0.2049341	0.3111969	427.3517412	186.2464725

**Summery results: Boosting with stumps 771 genes bootstrap and repeated cross-validation**

Model	cor_mean	sd_cor	MSE_mean	MSE_sd
prolif boot	0.7760479	0.0827829	0.0653710	0.0210015
ROR-prolif boot	0.7530515	0.0882432	165.1450271	51.8660843
prolif rep cross-val	0.2364594	0.2795041	0.1712618	0.0764014
ROR-prolif rep cross-val	0.1744792	0.3151549	394.2634498	171.6444924

**Summary using domain knowledge**

**Summery results: PCA ROR+proliferation score (repeated cross-validation)**



Model	cor_mean	sd_cor	MSE_mean	MSE_sd
ridge	0.3028091	0.2779432	364.5733	151.0208
ridge_interac	0.4505837	0.2404457	333.3975	151.6577
lasso	0.0784961	0.2856382	396.4902	160.1303
lasso_interact	0.4687056	0.2329426	321.0086	157.5895
elastic	0.0960693	0.2844609	392.3862	158.0853
elastic_interact	0.4749342	0.2335133	319.7269	157.8497

### Summery results: Stacking ROR+proliferation score (repeated cross-validation)

Model	cor_mean	sd_cor	MSE_mean	MSE_sd
ridge	0.3630150	0.2544613	367.3704	171.8509
ridge_interac	0.3555283	0.2622557	369.2144	176.9371
lasso	0.3373612	0.2605003	386.6455	179.9151
lasso_interact	0.3521323	0.2687827	373.2299	182.5783
elastic	0.3417178	0.2583745	383.7542	177.3923
elastic_interact	0.3532720	0.2654461	371.1879	179.5494

### Summery most interesting maybe

Response is just ROR+proliferation score, and only used repeated cross-validation.

Model	cor_mean	sd_cor	MSE_mean	MSE_sd
Lasso	0.0806236574665814	0.2767153	393.8069	159.6451
Ridge	0.0806236574665814	0.2767153	393.8069	159.6451
ElasticNet	0.204934145140861	0.3111969	427.3517	186.2465
Boosting	0.174479177155333	0.3151549	394.2634	171.6445
Residual (lasso/additive)	0.164249989278317	0.2788435	392.5436	158.8733
PCA on gene sets		NA	NA	NA
ridge	0.302809117868443	0.2779432	364.5733	151.0208
ridge_interac	0.450583687359656	0.2404457	333.3975	151.6577
lasso	0.0784961285212545	0.2856382	396.4902	160.1303
lasso_interact	0.468705571862351	0.2329426	321.0086	157.5895
elastic	0.0960692932769097	0.2844609	392.3862	158.0853
elastic_interact	0.474934188616362	0.2335133	319.7269	157.8497
Stacking on gene sets	NA	NA	NA	NA
ridge	0.363015012016748	0.2544613	367.3704	171.8509
ridge_interac	0.355528263391855	0.2622557	369.2144	176.9371
lasso	0.337361194772032	0.2605003	386.6455	179.9151
lasso_interact	0.352132288232874	0.2687827	373.2299	182.5783
elastic	0.341717815852986	0.2583745	383.7542	177.3923
elastic_interact	0.353272035127402	0.2654461	371.1879	179.5494