Milestone 2: Core results 01

Anders

25/1/2023

Data

One clinical trails 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 dived 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 then the signature genes; which I presume leads to some issue in modeling (as for clinical data too - see next sentence).

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.

Respones used

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 score based on expression level of some of the genes. Range: -8.035678 to 75.13174 ### Risk of relapse score with proliferation score (ROR-Prolif) A combined score based on expression level of more genes. Range: 1 to 97 (1-100).

The two scores involving ROR also have categorical variants containing: low, medium, high

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 lock at the graphs). The differentiation into two groups is done base 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 prolif

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 challanges

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. In addition to Correlation and MSE, 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

Results of individual modles:

Models tested

Lasso

Post Lasso

Residuals

Ridge

Elastic Net

Boosting with stumps as base learner

- mboost

- xgboost

PCA feature engineering

Stacking using different features in the base models

Synergistic learning

Lasso - Bootstrap

$6 \text{ genes} \rightarrow \text{proliferation score}$

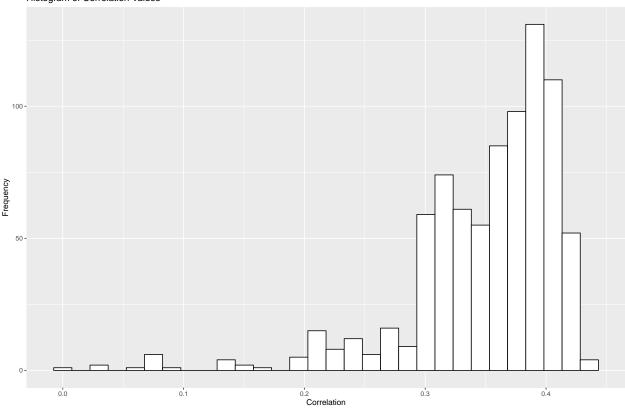
number of models fitted: 1000

Fraction of model fits with no selected genes: 0.182

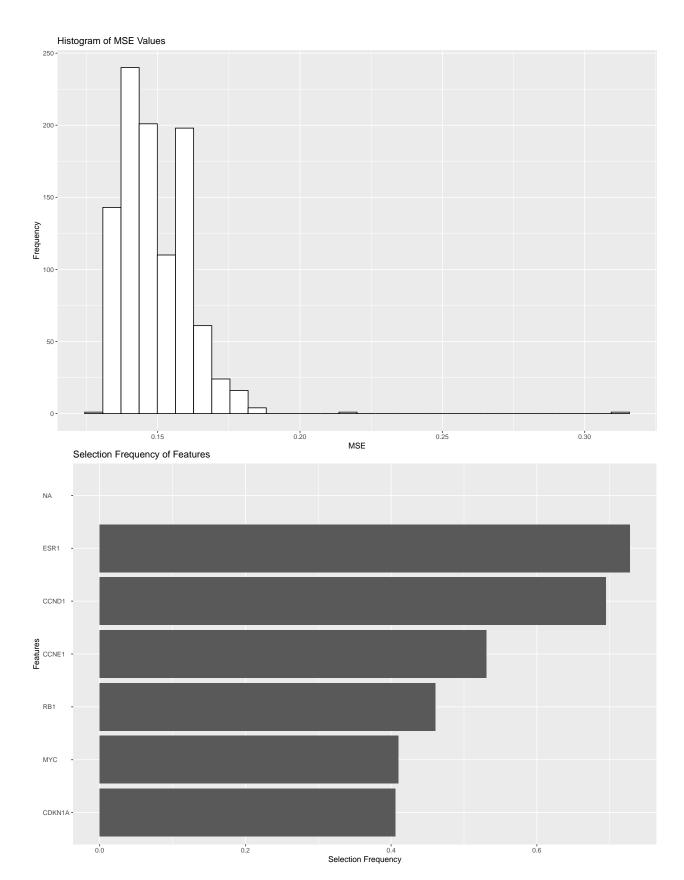
##

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 featrues:

[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

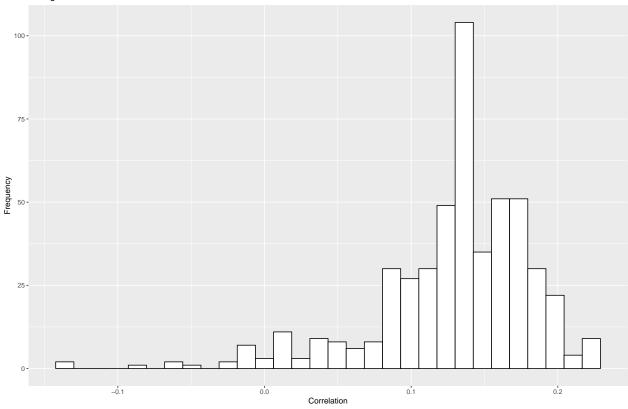
number of models fitted: 1000

Fraction of model fits with no selected genes: 0.495

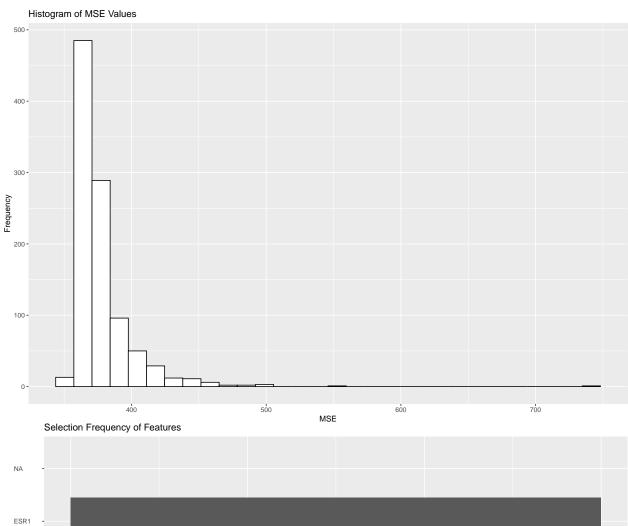
##

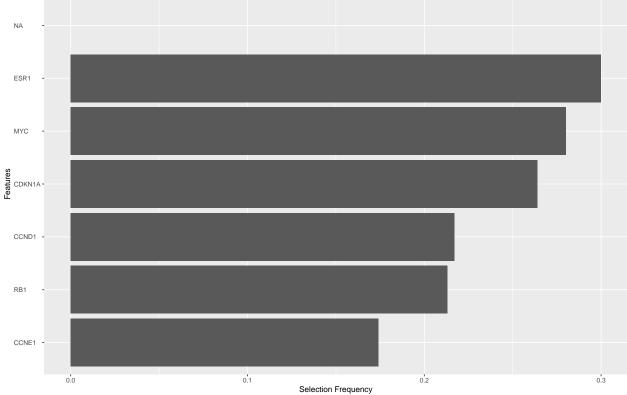
CORRELATIONS RESULTS
Mean: 0.1282306
Median: 0.1311715

Median: 0.1311715 ## Variance: 0.00285293 ## st.dev.: 0.05341282 Histogram of Correlation Values



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





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

771 genes -> proliferation score

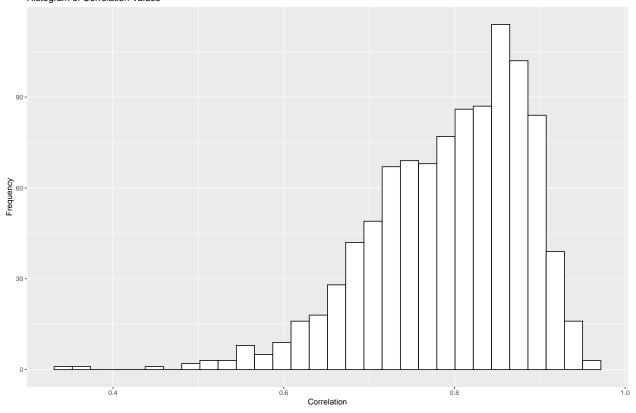
number of models fitted: 1000

Fraction of model fits with no selected genes: 0.002

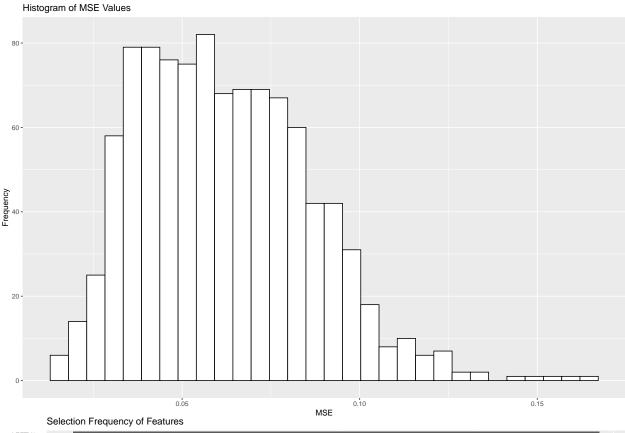
##

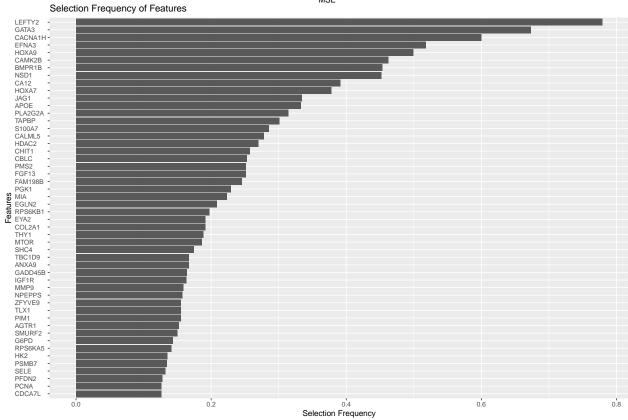
CORRELATIONS RESULTS
Mean: 0.7941413
Median: 0.8101886
Variance: 0.008119272
st.dev.: 0.090107

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

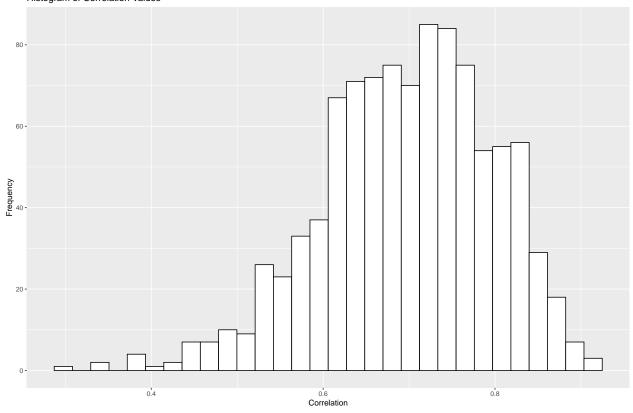
number of models fitted: 1000

 $\mbox{\tt \#\#}$ Fraction of model fits with no selected genes: 0.017

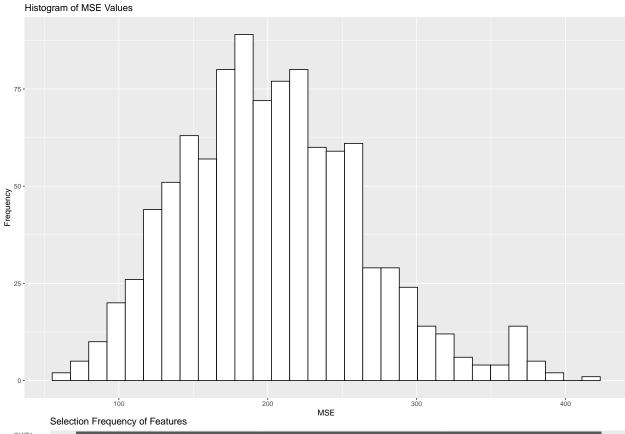
##

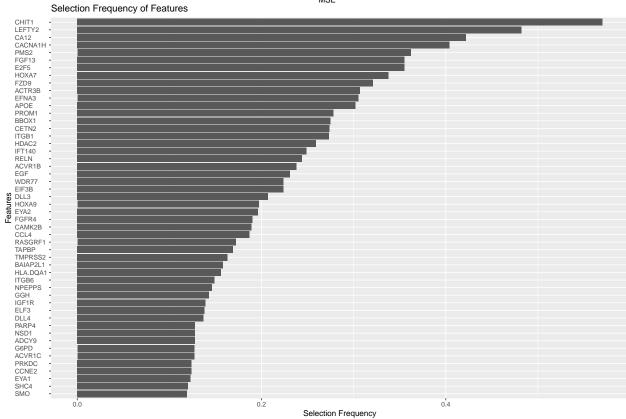
CORRELATIONS RESULTS
Mean: 0.6968101
Median: 0.7035889
Variance: 0.009901439
st.dev.: 0.09950598

Histogram of Correlation Values



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



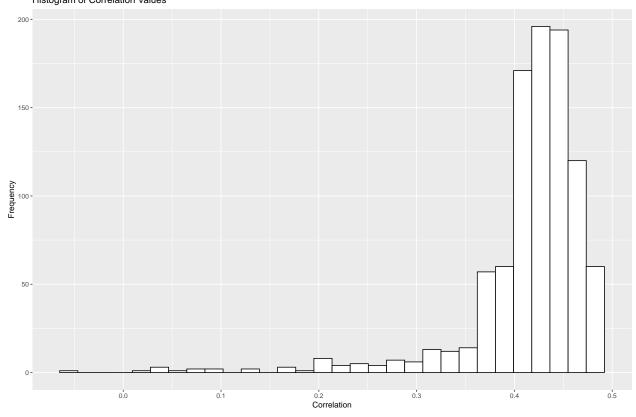


```
## Features selected 50% or more times:
## CHIT1
## Top 20 featrues:
## [1] "CHIT1"
                  "LEFTY2"
                            "CA12"
                                       "CACNA1H" "PMS2"
                                                           "E2F5"
                            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

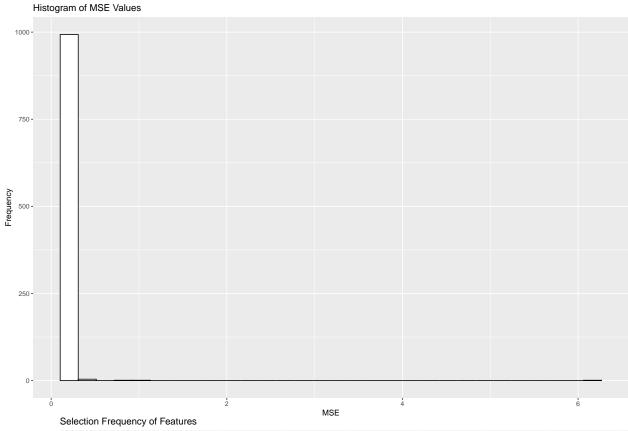
node values -> proliferation score

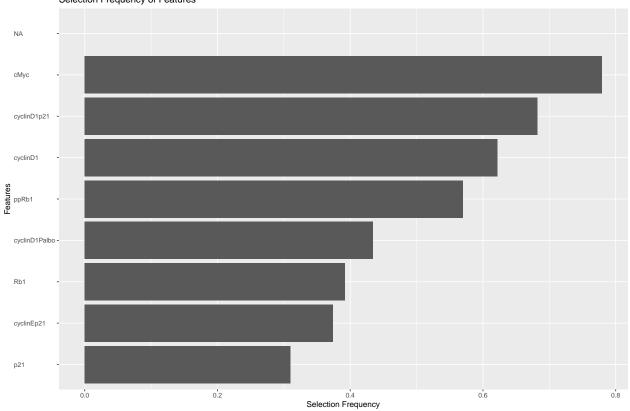
number of models fitted: 1000
Fraction of model fits with no selected genes: 0.053
##
CORRELATIONS RESULTS
Mean: 0.414496

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
## [13] NA
                        NA
                                         NA
                                                         NA
## [17] NA
                        NA
                                         NA
                                                         NA
```

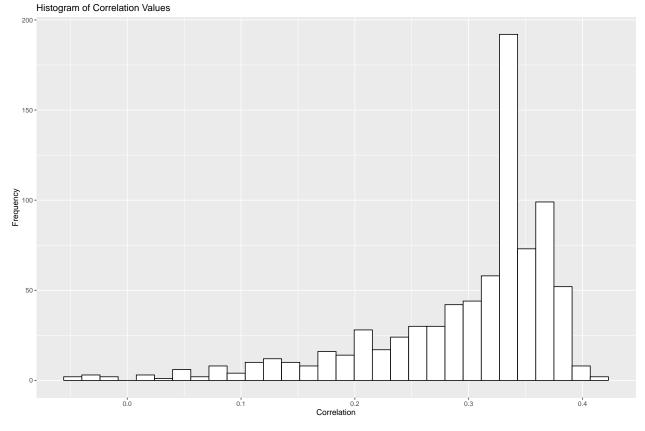
node values -> ROR-proliferation score

number of models fitted: 1000

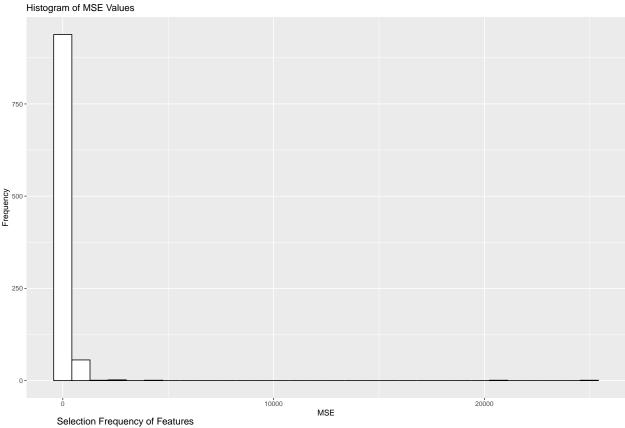
Fraction of model fits with no selected genes: 0.2

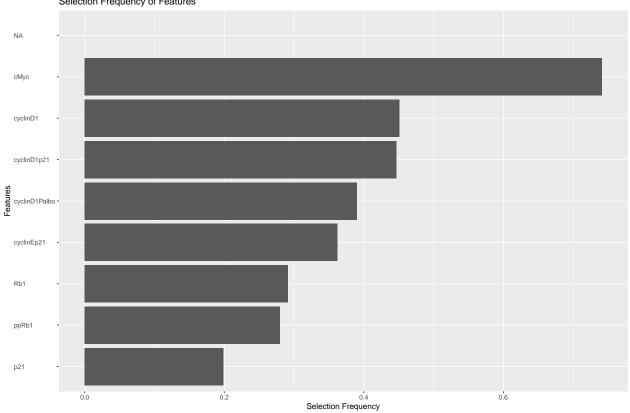
##

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"
                                                          "p21"
    [5] "cyclinEp21"
                         "Rb1"
                                          "ppRb1"
##
##
   [9] NA
                         NA
                                         NA
                                                          NA
## [13] NA
                         NA
                                         NA
                                                          NA
## [17] NA
                         NA
                                         NA
                                                          NA
```

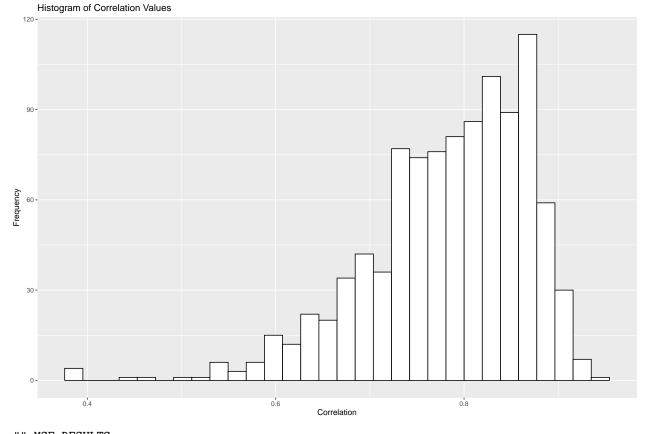
Mechanistic + Residuals -> proliferation score (additive)

number of models fitted: 1000

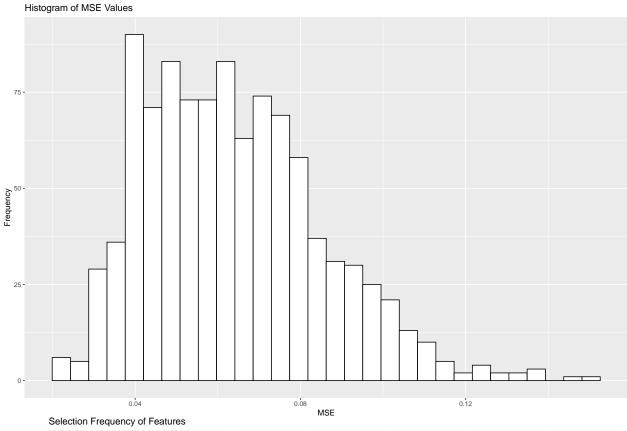
Fraction of model fits with no selected genes: 0

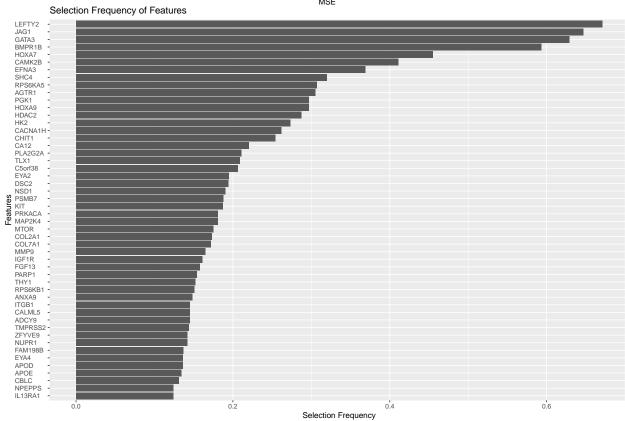
##

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

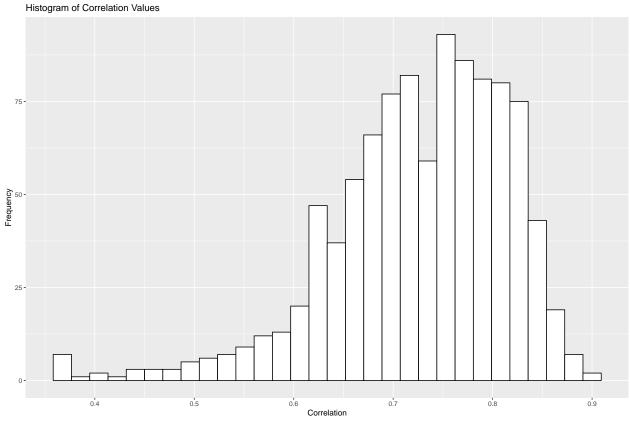




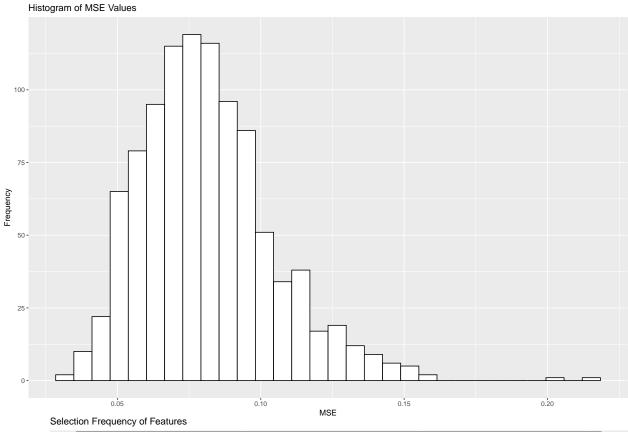
```
## Features selected 50% or more times:
## BMPR1B GATA3 JAG1 LEFTY2
## Top 20 featrues:
  [1] "LEFTY2" "JAG1"
                            "GATA3"
                                      "BMPR1B"
                                                 "HOXA7"
                                              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

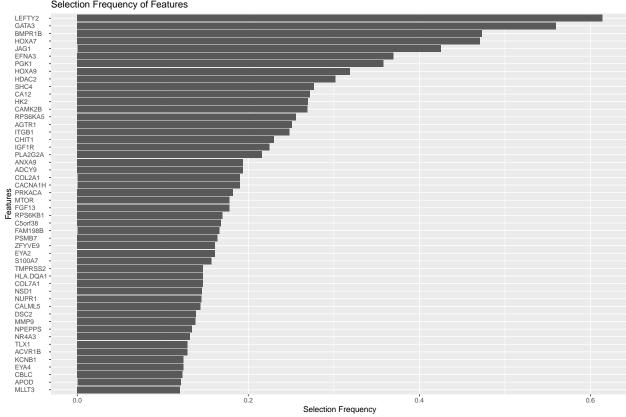
$Mechanistic + Residuals -> proliferation\ score\ (multiplicative)$

```
## 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

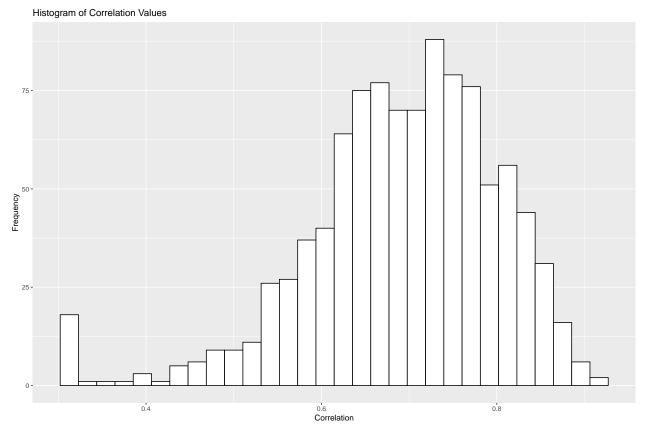




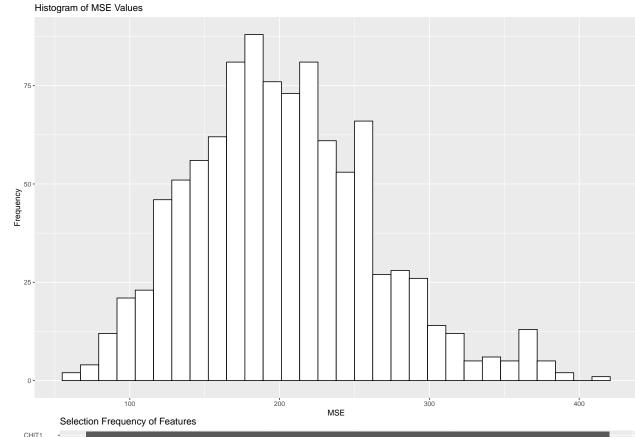
```
## Features selected 50% or more times:
## GATA3 LEFTY2
## Top 20 featrues:
  [1] "LEFTY2"
                  "GATA3"
                            "BMPR1B"
                                       "HOXA7"
                                                 "JAG1"
                                       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

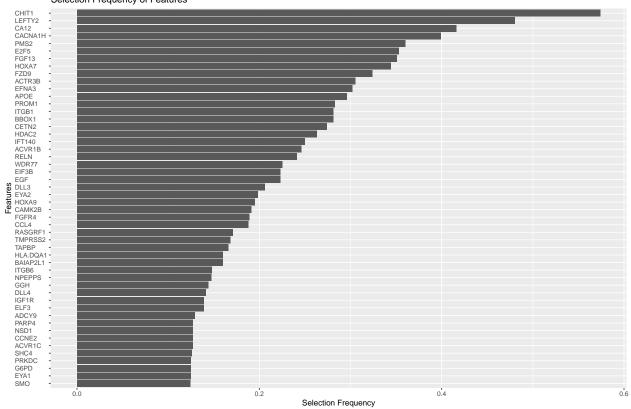
Mechnaistic + Residuals -> ROR-proliferation score (additive)

```
## 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

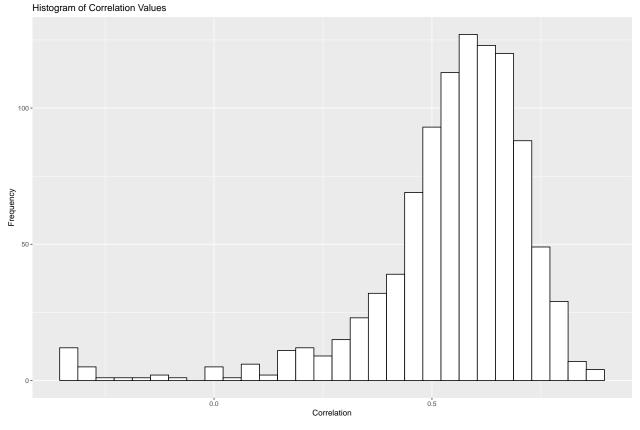




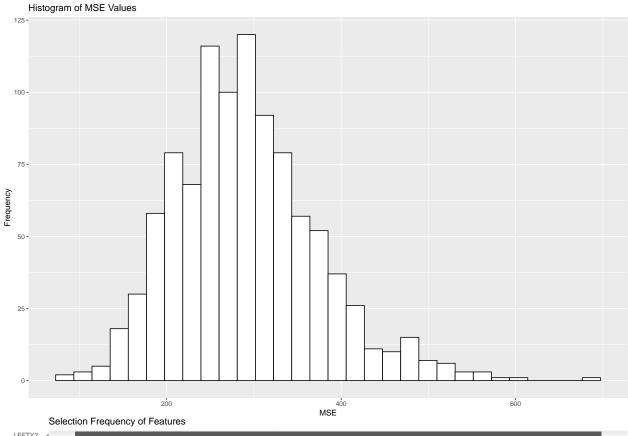
```
## Features selected 50% or more times:
## CHIT1
## Top 20 featrues:
  [1] "CHIT1"
                  "LEFTY2"
                            "CA12"
                                       "CACNA1H" "PMS2"
                                                           "E2F5"
                             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

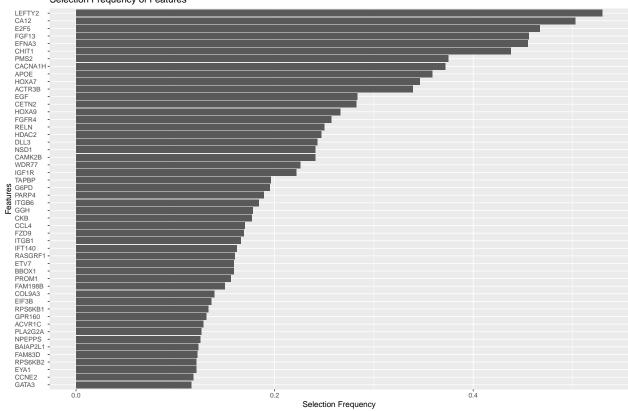
Mechnaistic + Residuals -> ROR-proliferation score (multiplicative)

```
## 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"
                                                 "EGF"
                                                                      "HOXA9"
                             "HOXA7"
                                       "ACTR3B"
                                                            "CETN2"
                  "RELN"
## [15] "FGFR4"
                             "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

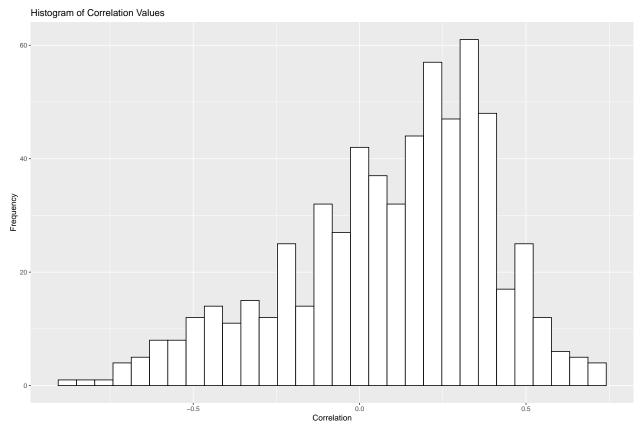
200 repeats of five fold cross-validation ~### 6 genes -> proliferation score

number of models fitted: 1000

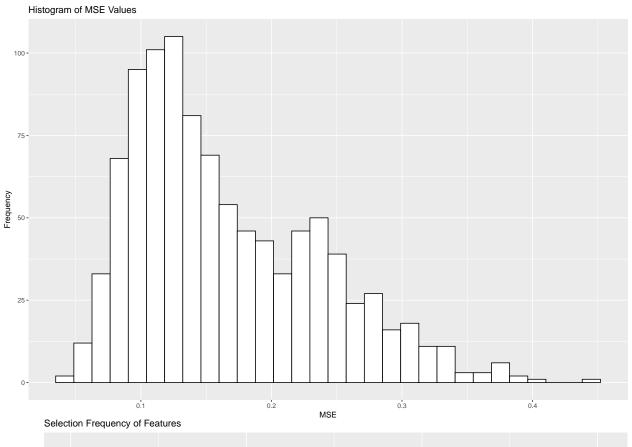
Fraction of model fits with no selected genes: 0.373

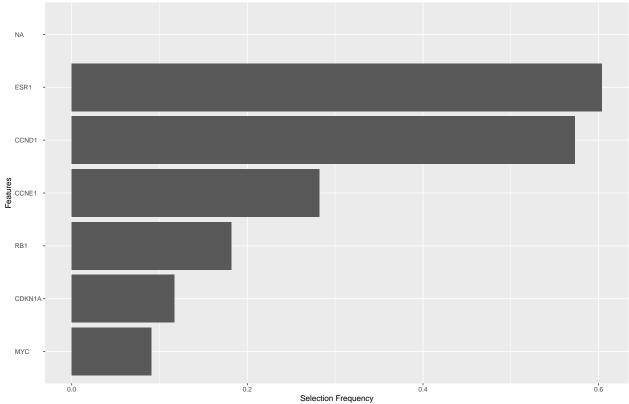
##

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

NA

6 genes -> ROR_proliferation score

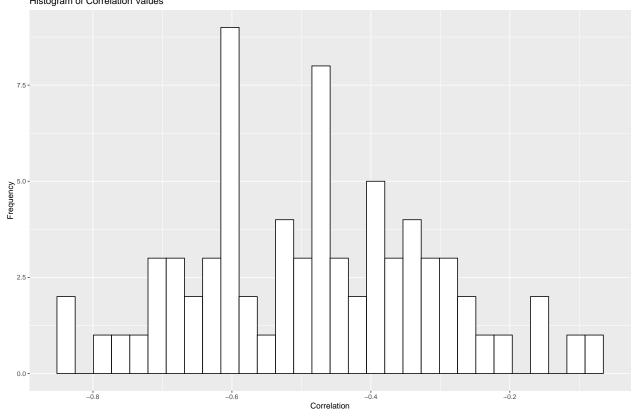
NA

number of models fitted: 1000
Fraction of model fits with no selected genes: 0.926
##
CORRELATIONS RESULTS
Mean: -0.4822298
Median: -0.4810641

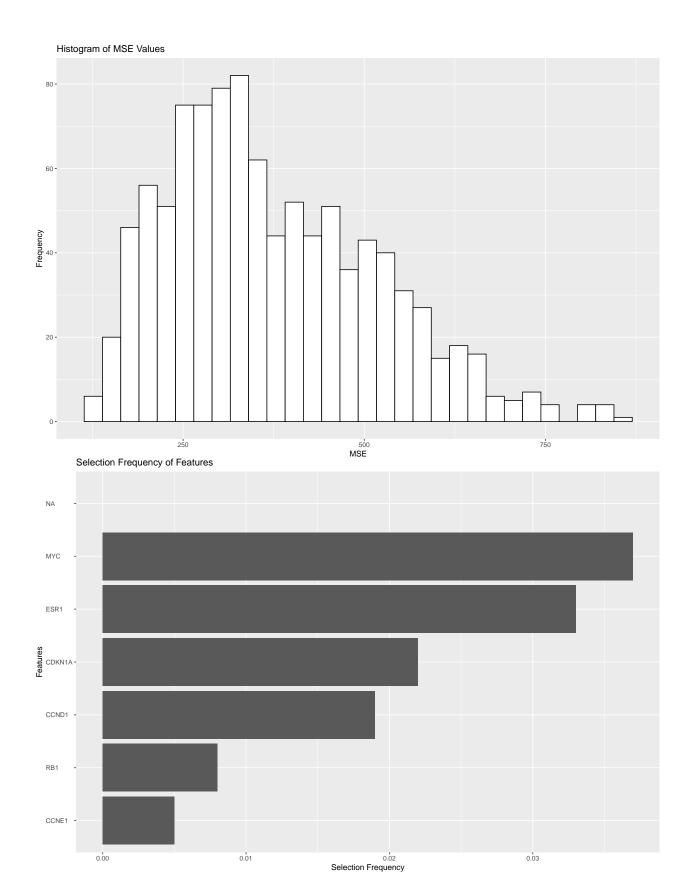
NA

Variance: 0.02975572
st.dev.: 0.1724985
Histogram of Correlation Values

[17] NA



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

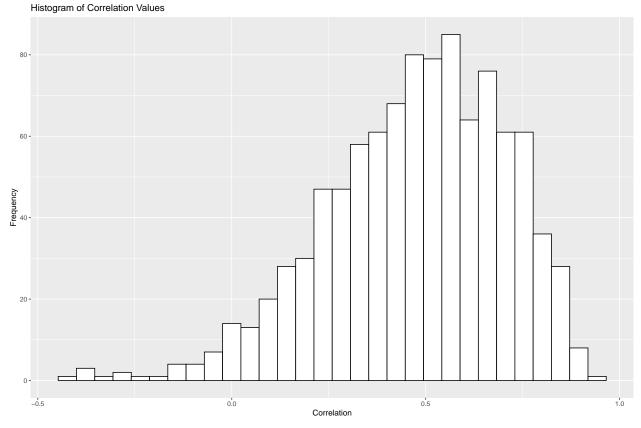


```
## Features selected 50% or more times:
##
## Top 20 featrues:
  [1] "MYC"
                 "ESR1"
                          "CDKN1A" "CCND1"
                                            "RB1"
                                                      "CCNE1"
                                          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

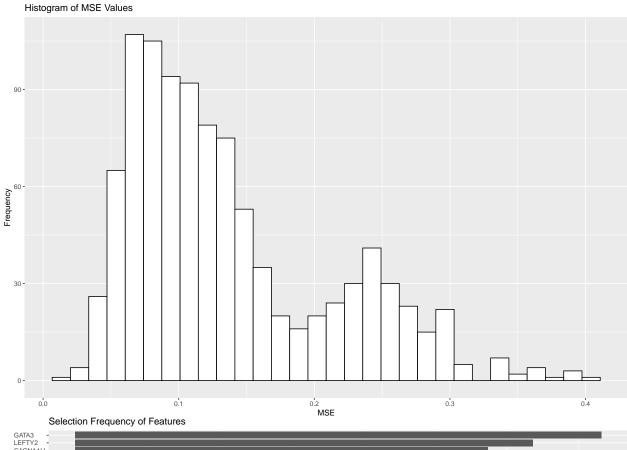
771 genes -> proliferation score

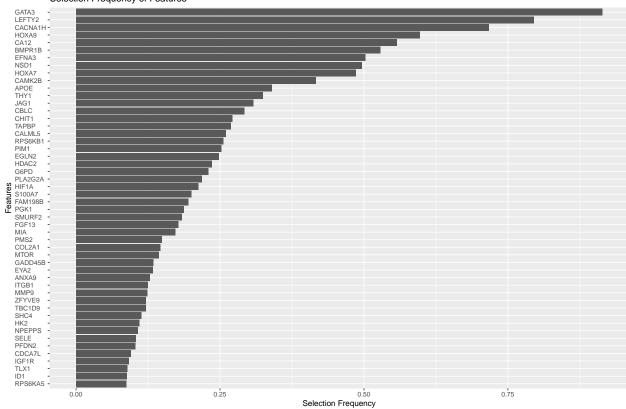
number of models fitted: 1000
Fraction of model fits with no selected genes: 0.011
##
CORRELATIONS RESULTS

Mean: 0.4737037 ## Median: 0.4959203 ## Variance: 0.05337068 ## st.dev.: 0.2310209



MSE RESULTS
Mean: 0.1376002
Median: 0.1154157
Variance: 0.005670929
st.dev.: 0.07530557

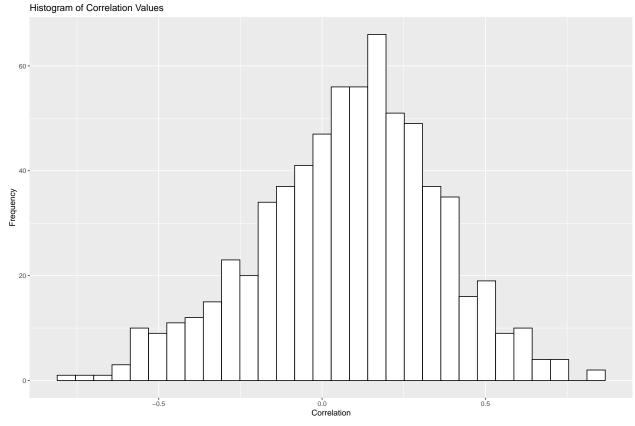




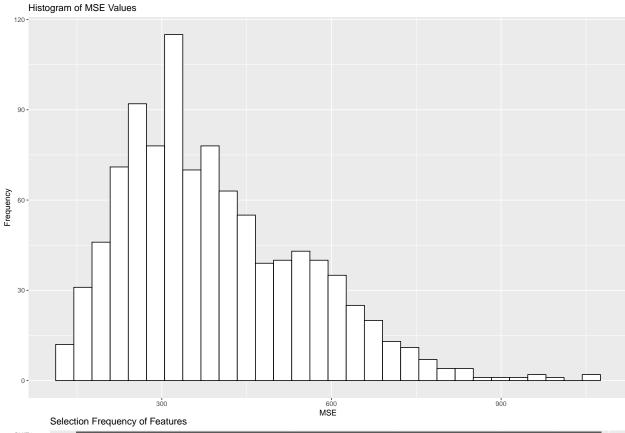
```
## Features selected 50% or more times:
## BMPR1B CA12 CACNA1H EFNA3 GATA3 HOXA9 LEFTY2
## Top 20 featrues:
## [1] "GATA3"
                  "LEFTY2"
                            "CACNA1H" "HOXA9"
                                                 "CA12"
                                            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

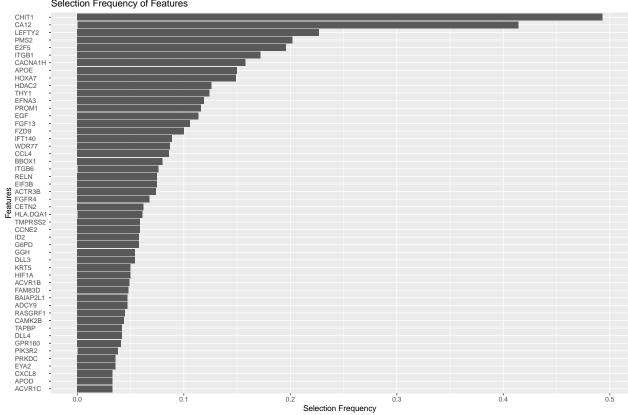
771 genes -> ROR-proliferation score

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



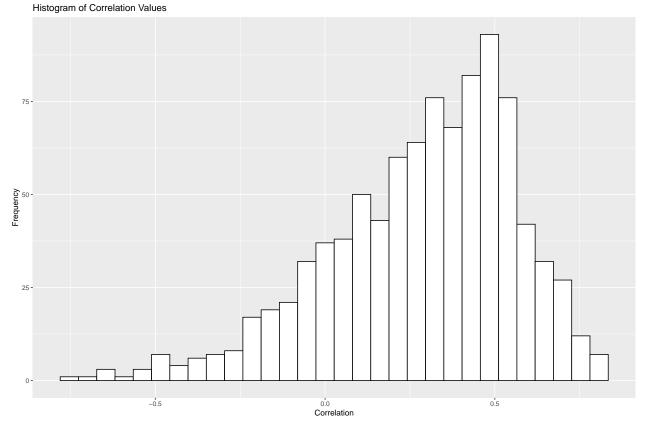


```
## Features selected 50% or more times:
##
## Top 20 featrues:
                  "CA12"
  [1] "CHIT1"
                             "LEFTY2"
                                       "PMS2"
                                                 "E2F5"
                                                            "ITGB1"
                                                                      "CACNA1H"
## [8] "APOE"
                             "HDAC2"
                                                                      "EGF"
                  "HOXA7"
                                       "THY1"
                                                 "EFNA3"
                                                            "PROM1"
## [15] "FGF13"
                  "FZD9"
                             "IFT140" "WDR77"
                                                 "CCL4"
                                                            "BBOX1"
```

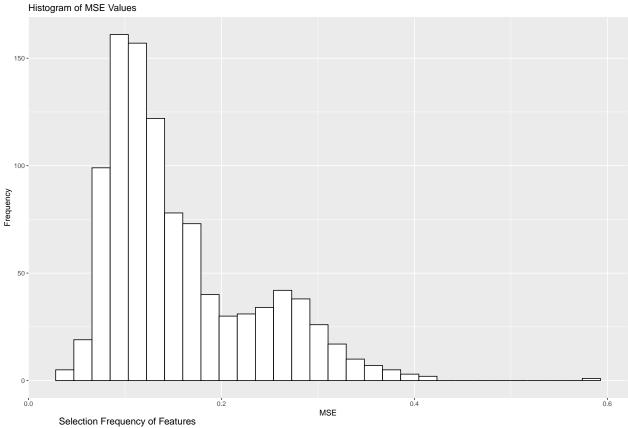
${\bf node\ values\ \text{--}>\ proliferation\ score}$

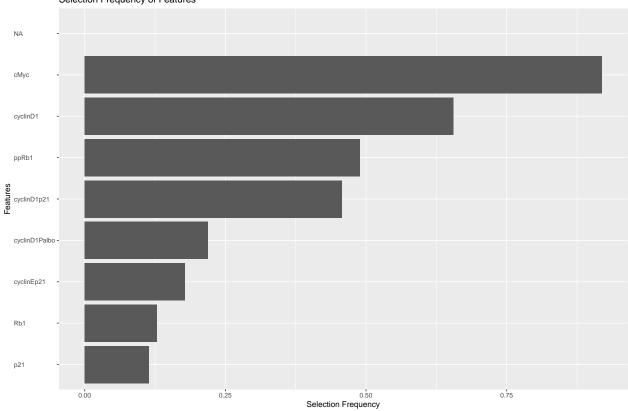
number of models fitted: 1000
Fraction of model fits with no selected genes: 0.063
##
CORRELATIONS RESULTS
Mean: 0.2842257
Median: 0.3249779

Variance: 0.07664357 ## st.dev.: 0.2768458



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"
                                                          "p21"
    [5] "cyclinD1Palbo" "cyclinEp21"
                                         "Rb1"
##
   [9] NA
                        NA
                                         NA
                                                          NA
## [13] NA
                        NA
                                         NA
                                                          NA
## [17] NA
                        NA
                                                         NA
                                         NA
```

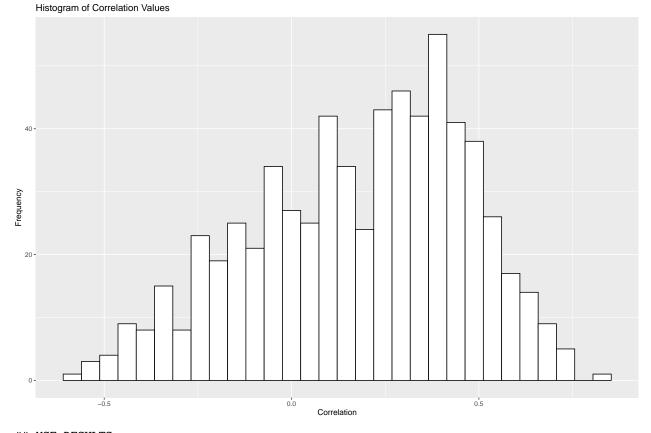
node values \rightarrow ROR-proliferation score

number of models fitted: 1000

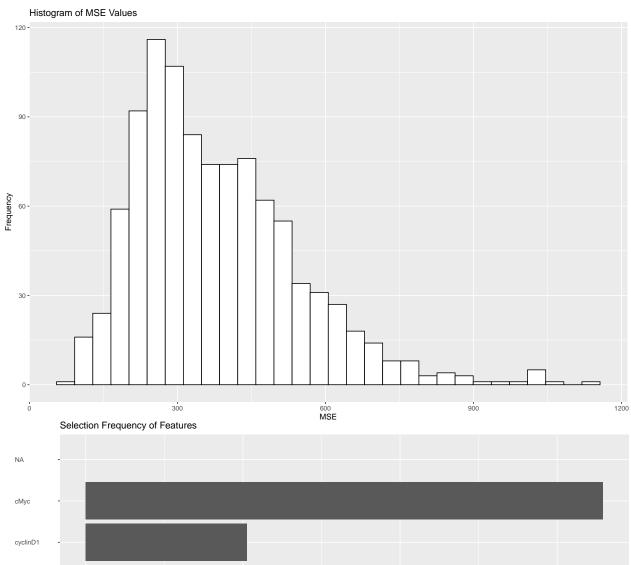
Fraction of model fits with no selected genes: 0.341

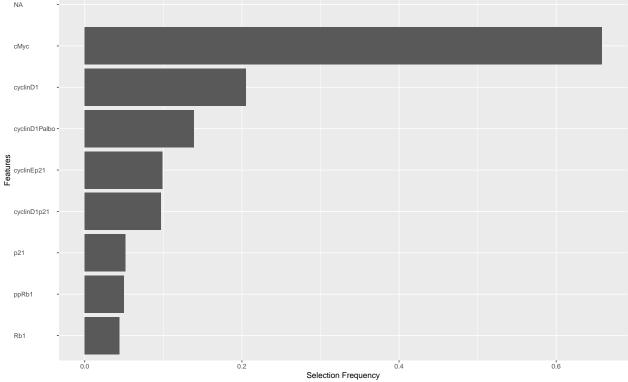
##

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



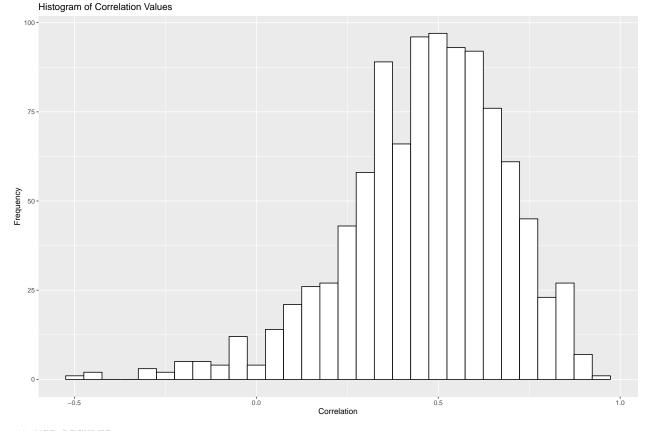


```
## Features selected 50% or more times:
## cMyc
## Top 20 featrues:
   [1] "cMyc"
                         "cyclinD1"
                                         "cyclinD1Palbo" "cyclinEp21"
    [5] "cyclinD1p21"
                         "p21"
                                         "ppRb1"
      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

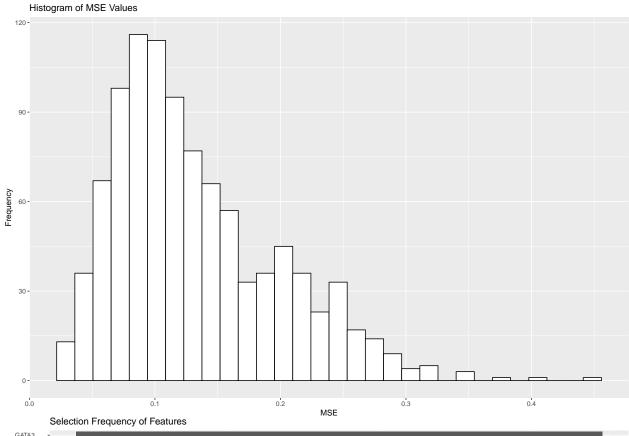
Mechanistic + Residuals -> proliferation score (additive)

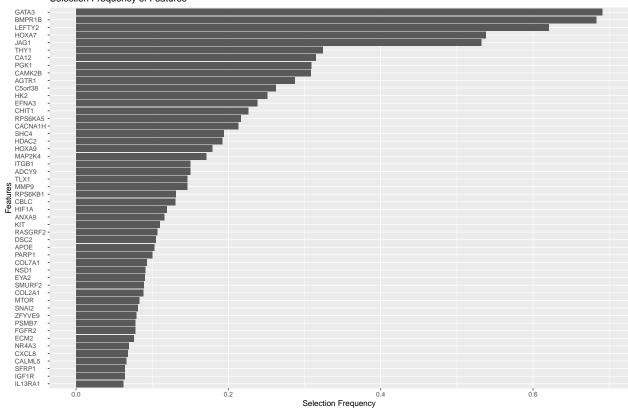
number of models fitted: 1000
Fraction of model fits with no selected genes: 0
##

CORRELATIONS RESULTS
Mean: 0.4633095
Median: 0.4870052
Variance: 0.04959996
st.dev.: 0.2227105



MSE RESULTS
Mean: 0.1331785
Median: 0.1164927
Variance: 0.004278014
st.dev.: 0.06540653



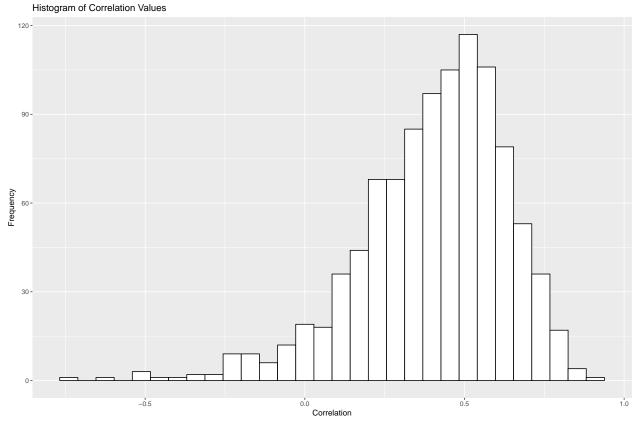


##

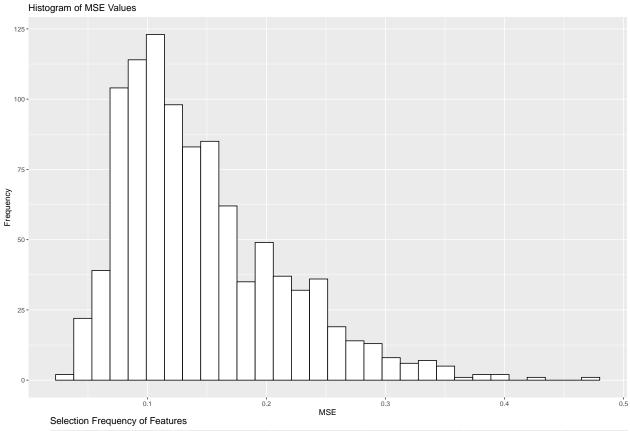
```
## Features selected 50% or more times:
## BMPR1B GATA3 HOXA7 JAG1 LEFTY2
## Top 20 featrues:
## [1] "GATA3"
                  "BMPR1B"
                            "LEFTY2"
                                      "HOXA7"
                                                 "JAG1"
                     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

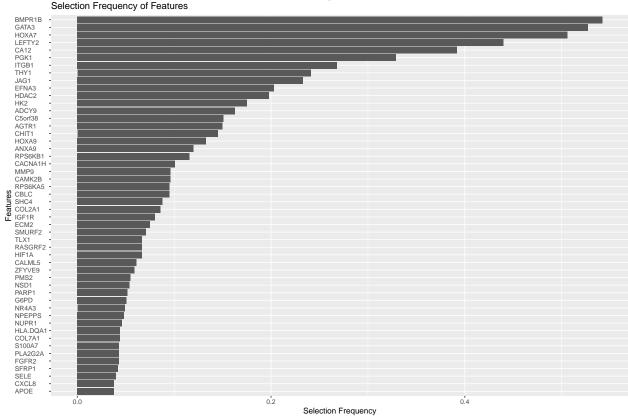
Mechanistic + Residuals -> proliferation score (multiplicative)

```
## 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





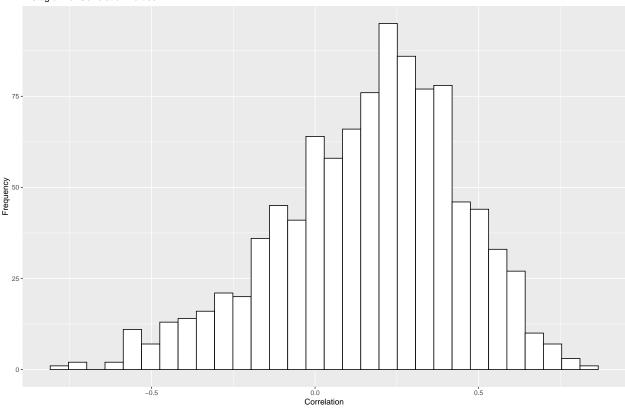
##

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

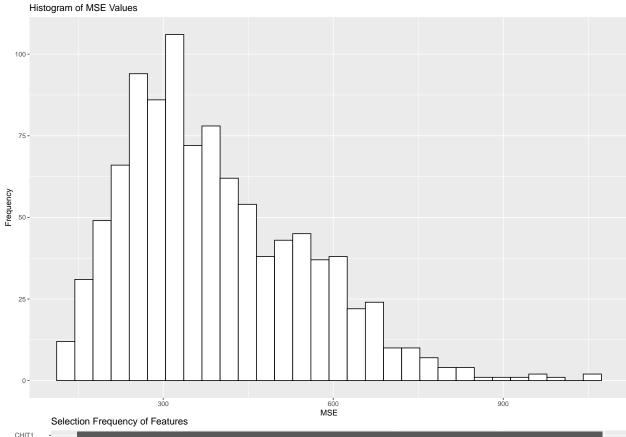
Mechnaistic + Residuals -> ROR-proliferation score (additive)

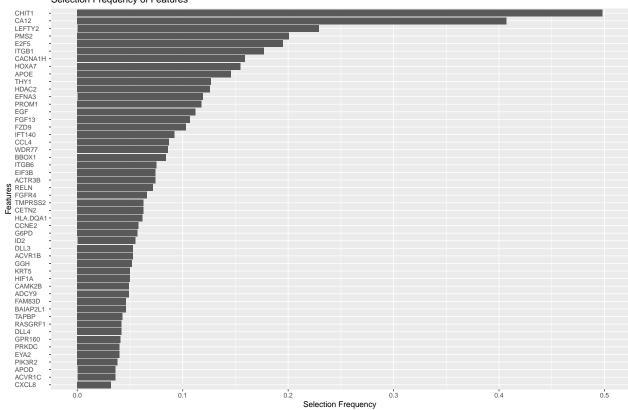
number of models fitted: 1000
Fraction of model fits with no selected genes: 0
##
CORRELATIONS RESULTS
Mean: 0.16425
Median: 0.198308
Variance: 0.07775369

st.dev.: 0.2788435
Histogram of Correlation Values



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



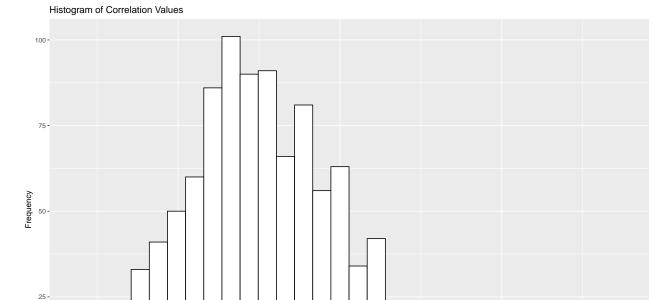


##

```
## Features selected 50% or more times:
##
## Top 20 featrues:
                  "CA12"
   [1] "CHIT1"
                             "LEFTY2"
                                       "PMS2"
                                                  "E2F5"
                                                            "ITGB1"
                                                                       "CACNA1H"
   [8] "HOXA7"
                   "APOE"
                             "THY1"
                                                                       "EGF"
                                        "HDAC2"
                                                  "EFNA3"
                                                            "PROM1"
## [15] "FGF13"
                  "FZD9"
                             "IFT140"
                                       "CCL4"
                                                  "WDR77"
                                                            "BBOX1"
```

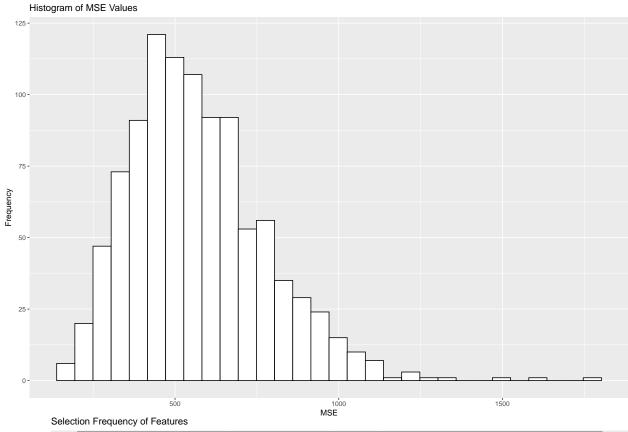
Mechnaistic + Residuals -> ROR-proliferation score (multiplicative)

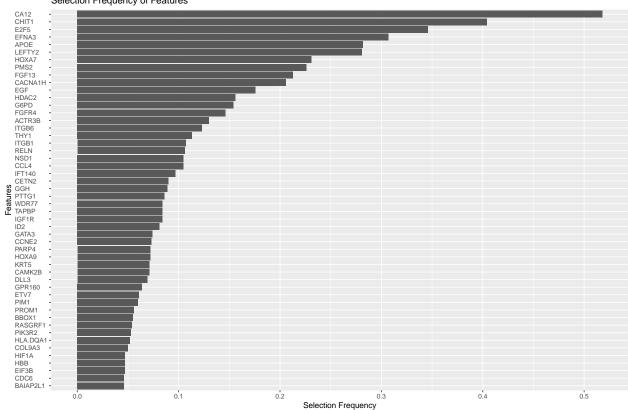
```
## number of models fitted: 1000
## Fraction of model fits with no selected genes: 0
##
## CORRELATIONS RESULTS
## Mean: -0.2145253
## Median: -0.2415987
## Variance: 0.06311304
## st.dev.: 0.2512231
```



MSE RESULTS
Mean: 568.8063
Median: 541.2023
Variance: 43510.24
st.dev.: 208.5911

Correlation





##

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

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

Model	cor_mean	sd_cor	${\rm MSE_mean}$	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)

cor_mean	sd_cor	${\rm MSE_mean}$	MSE_sd
-0.4822298	0.1724985	374.1519	144.1559
0.0806237	0.2767153	393.8069	159.6451
0.1806504	0.2854892	380.1157	164.5869
0.1642500	0.2788435	392.5436	158.8733
-0.2145253	0.2512231	568.8063	208.5911
	-0.4822298 0.0806237 0.1806504 0.1642500	-0.4822298 0.1724985 0.0806237 0.2767153 0.1806504 0.2854892 0.1642500 0.2788435	-0.4822298 0.1724985 374.1519 0.0806237 0.2767153 393.8069 0.1806504 0.2854892 380.1157 0.1642500 0.2788435 392.5436

Ridge bootstrap

771 genes -> proliferation score

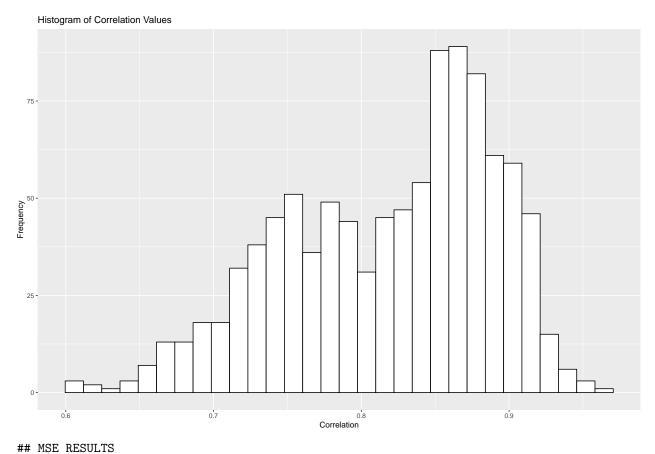
```
## number of models fitted: 1000
```

Fraction of model fits with no selected genes: 0

##

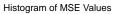
CORRELATIONS RESULTS

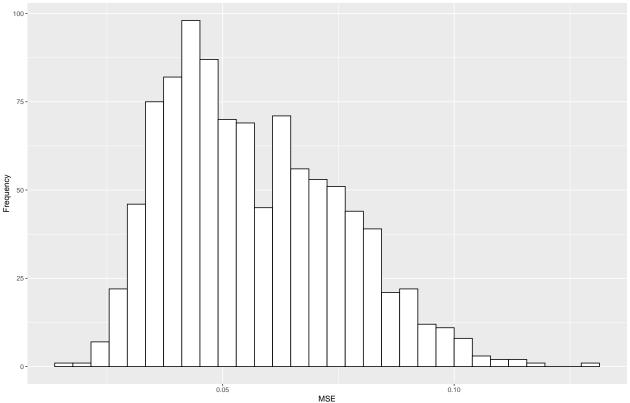
Mean: 0.8189568 ## Median: 0.8355063 ## Variance: 0.005044925 ## st.dev.: 0.07102764



Mse Results ## Mean: 0.05665241 ## Median: 0.0532761

Variance: 0.0003488416 ## st.dev.: 0.0186773





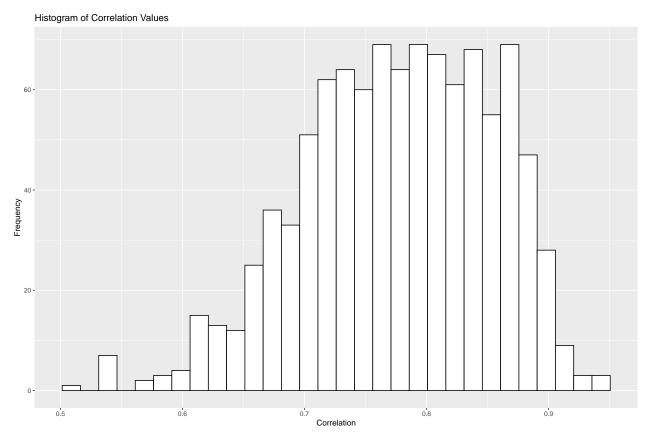
771 genes -> ROR-proliferation score

number of models fitted: 1000

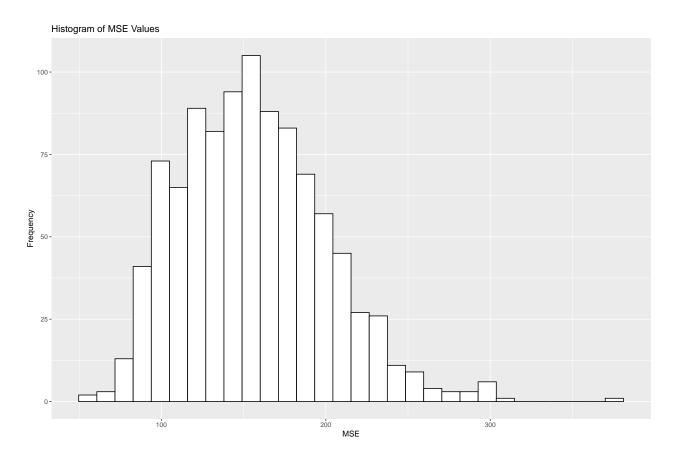
 $\mbox{\tt \#\#}$ Fraction of model fits with no selected genes: 0

##

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
```

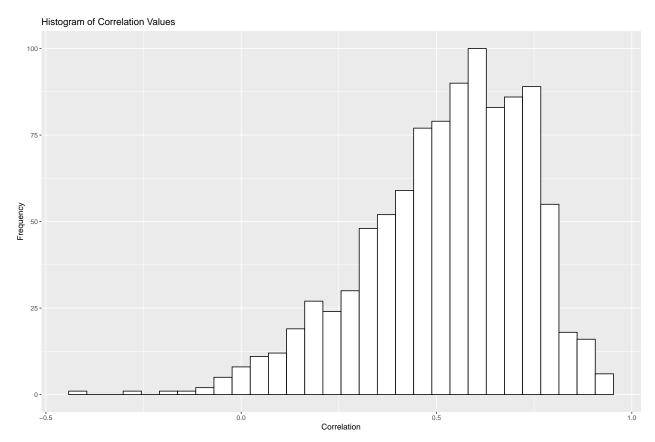
number of models fitted: 1000

Fraction of model fits with no selected genes: 0

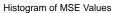
##

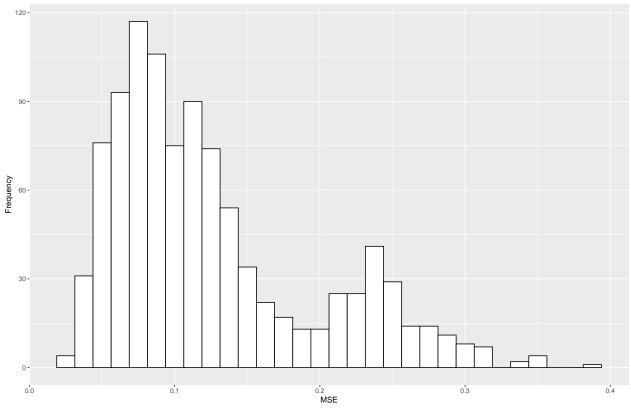
CORRELATIONS RESULTS
Mean: 0.5268342
Median: 0.5562175

Variance: 0.04291266 ## st.dev.: 0.2071537



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





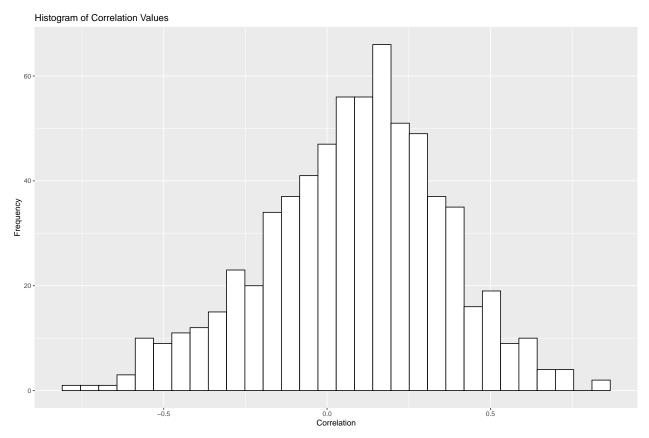
771 genes -> ROR-proliferation score

number of models fitted: 1000

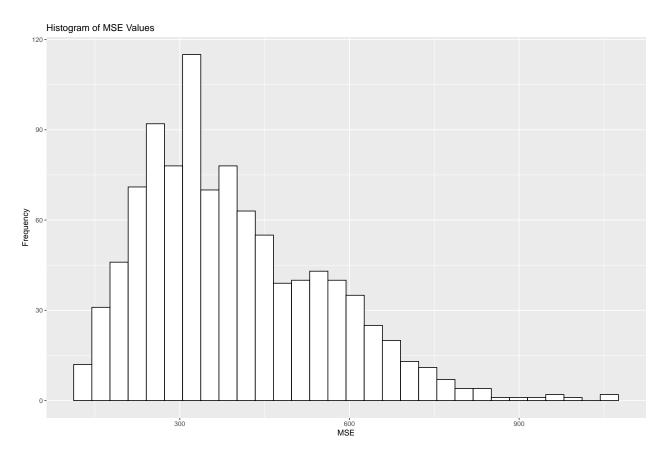
 $\mbox{\tt \#\#}$ Fraction of model fits with no selected genes: 0.321

##

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

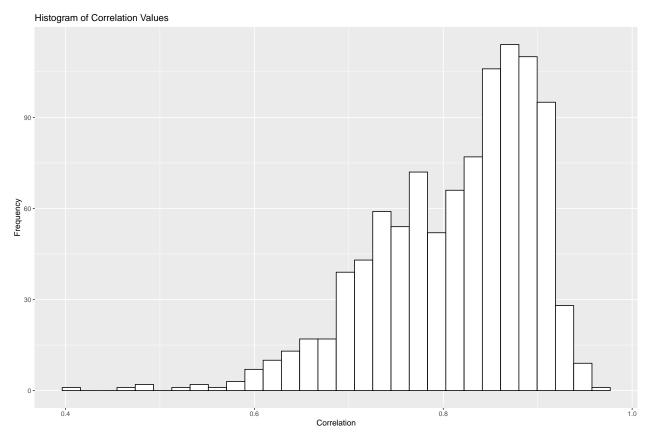
number of models fitted: 1000

Fraction of model fits with no selected genes: 0

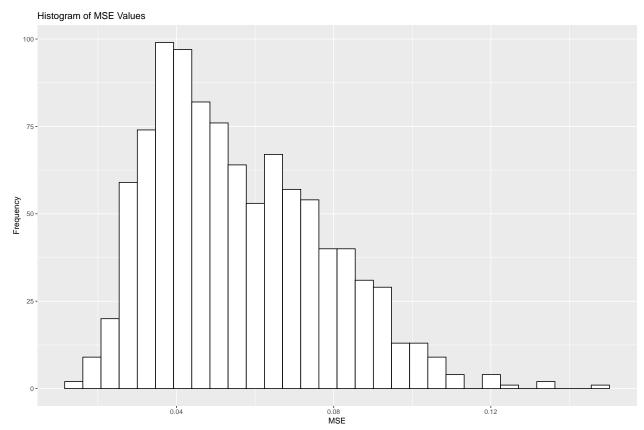
##

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



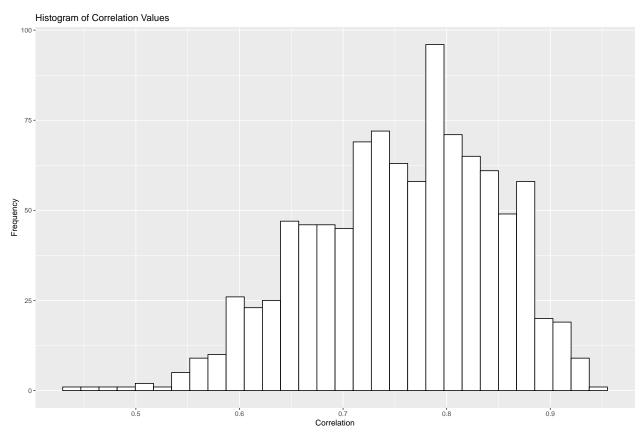
771 genes -> ROR-proliferation score

number of models fitted: 1000

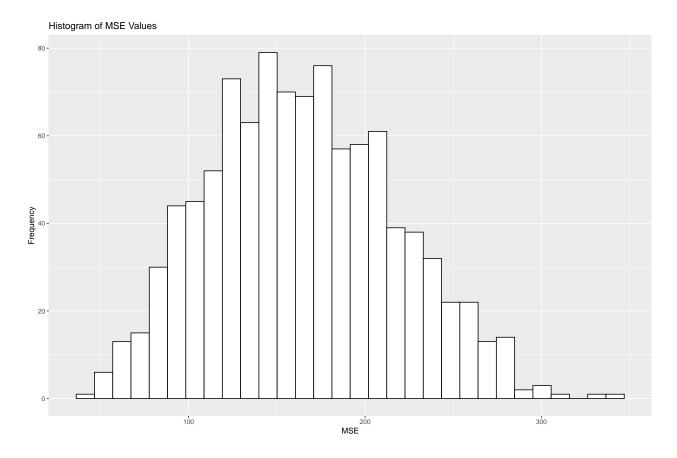
 $\mbox{\tt \#\#}$ Fraction of model fits with no selected genes: 0

##

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

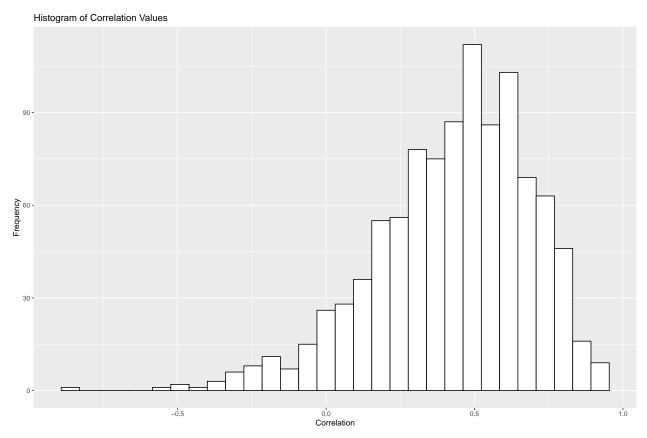
Fraction of model fits with no selected genes: 0

##

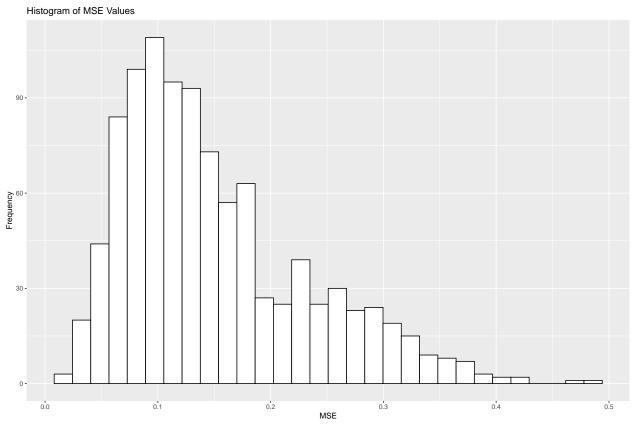
CORRELATIONS RESULTS

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



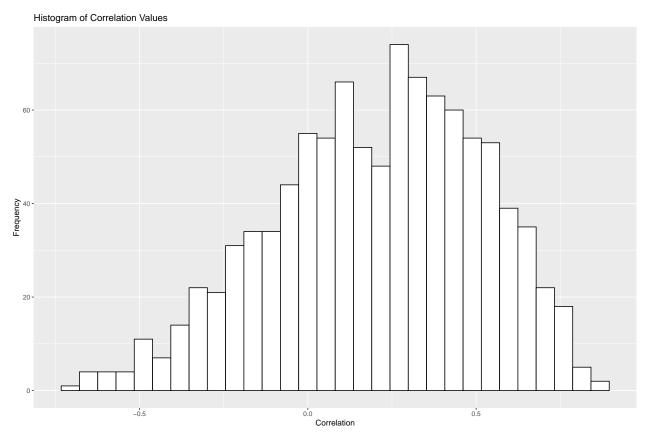
771 genes -> ROR-proliferation score

number of models fitted: 1000

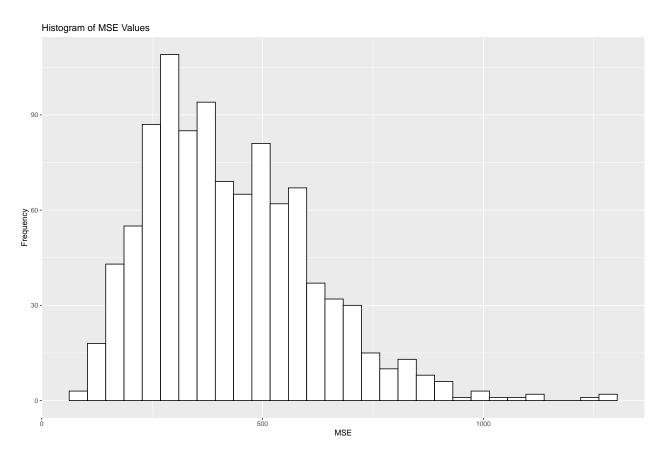
 $\mbox{\tt \#\#}$ Fraction of model fits with no selected genes: 0.002

##

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

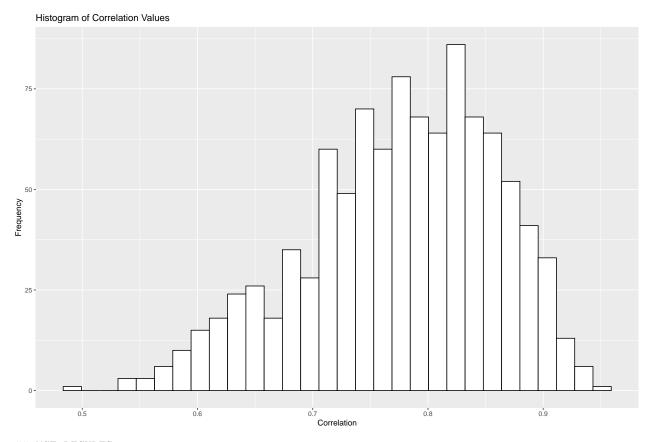
number of models fitted: 1000

Fraction of model fits with no selected genes: 0

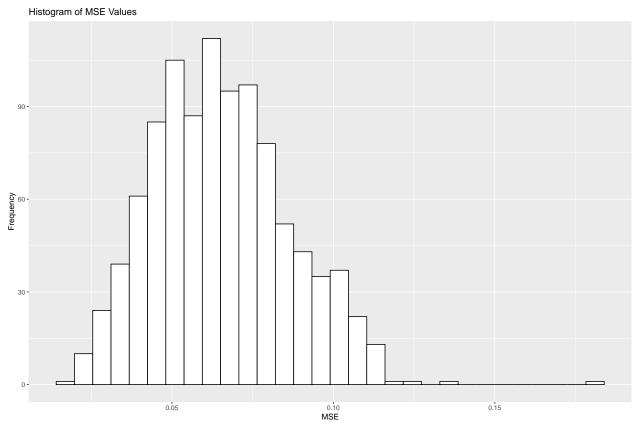
##

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



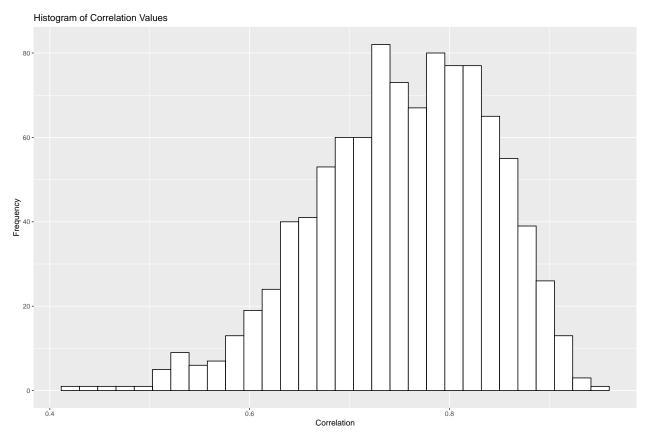
771 genes -> ROR-proliferation score

number of models fitted: 1000

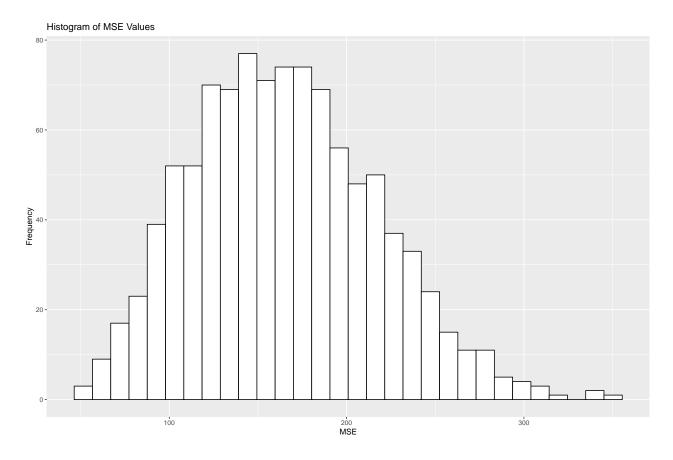
 $\mbox{\tt \#\#}$ Fraction of model fits with no selected genes: 0

##

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

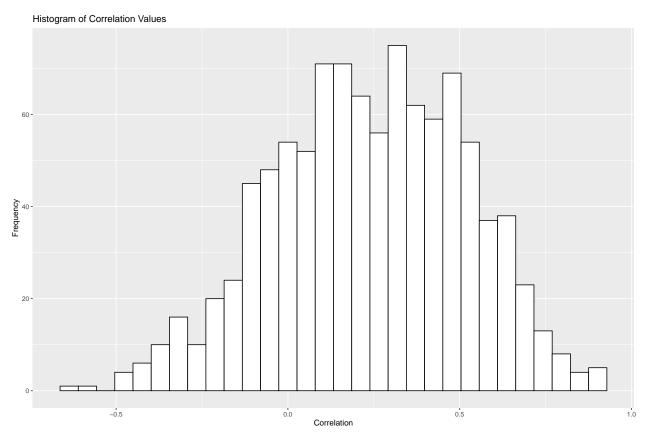
number of models fitted: 1000

Fraction of model fits with no selected genes: 0

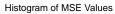
##

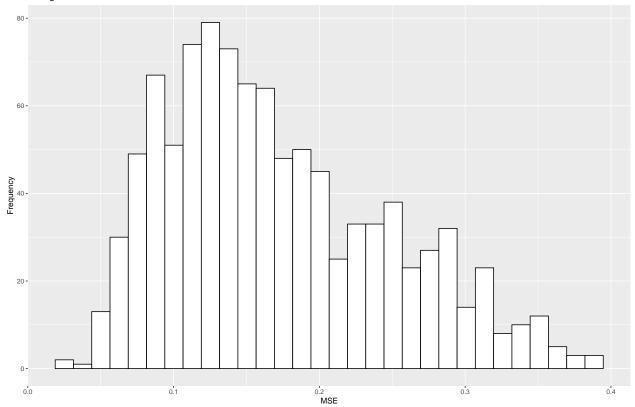
CORRELATIONS RESULTS ## Mean: 0.2364594

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





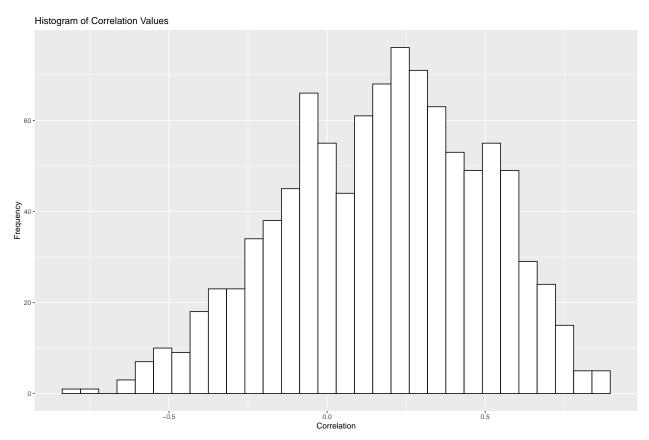
771 genes -> ROR-proliferation score

number of models fitted: 1000

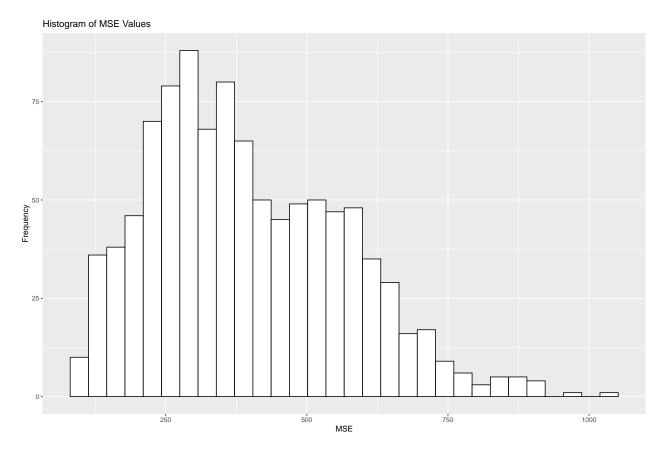
 $\mbox{\tt \#\#}$ Fraction of model fits with no selected genes: 0

##

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, cross-validation

Ridge: 771 genes -> ROR-proliferation score

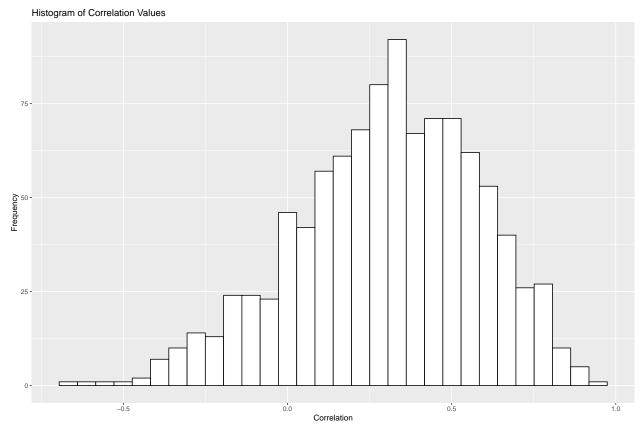
number of models fitted: 1000

 $\mbox{\tt \#\#}$ Fraction of model fits with no selected genes: 0

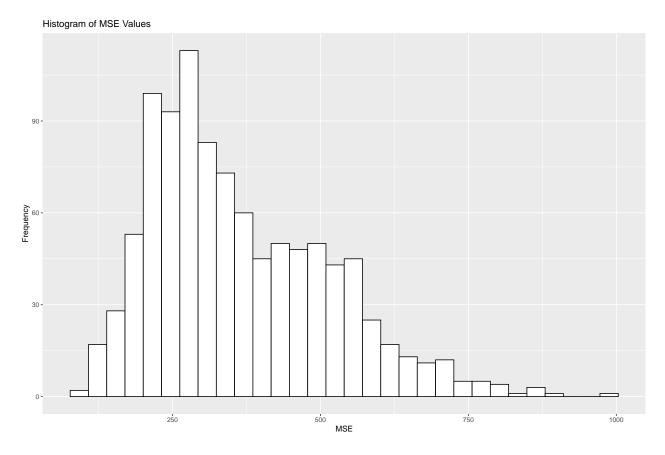
##

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

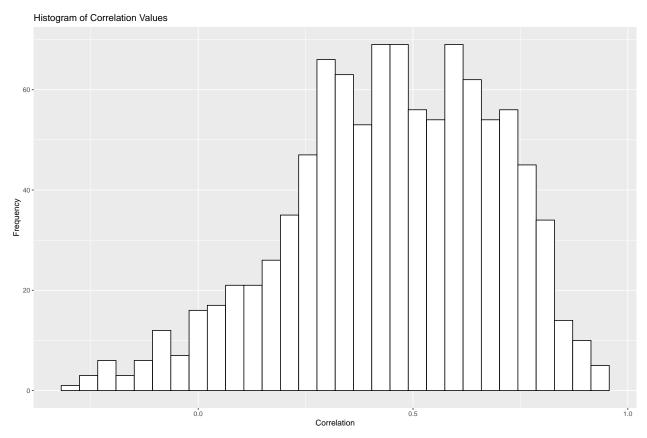
number of models fitted: 1000

Fraction of model fits with no selected genes: 0

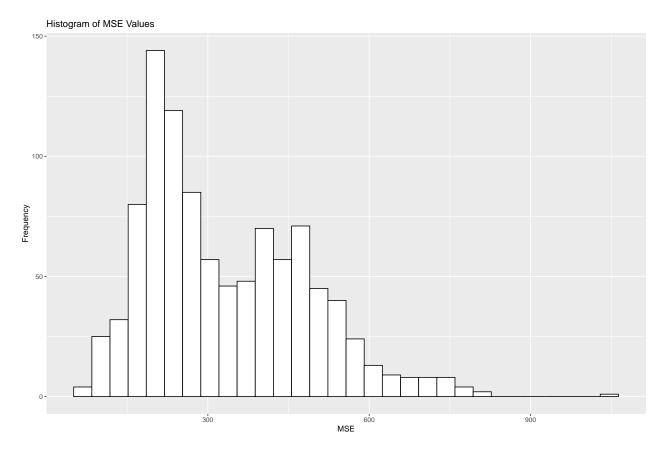
##

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



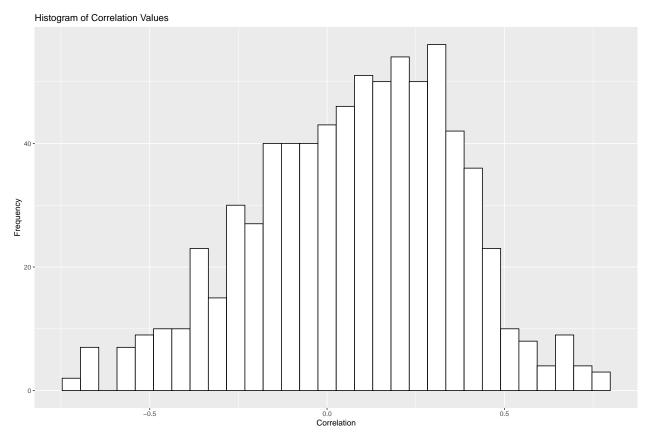
Lasso: 771 genes -> ROR-proliferation score

number of models fitted: 1000

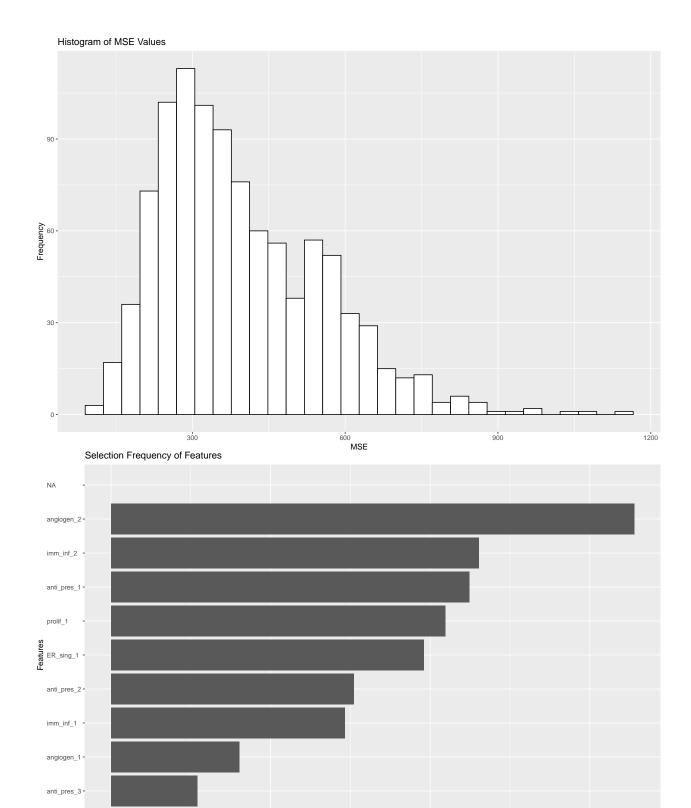
Fraction of model fits with no selected genes: 0.251

##

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



prolif_2

0.0

Selection Frequency

0.4

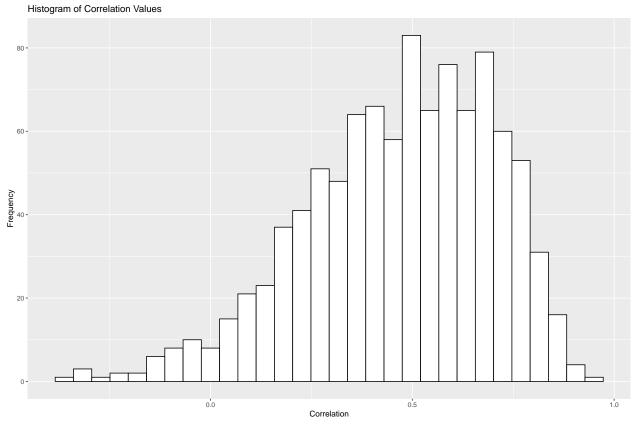
0.6

0.2

```
## 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 NA
## [16] NA NA NA NA NA
```

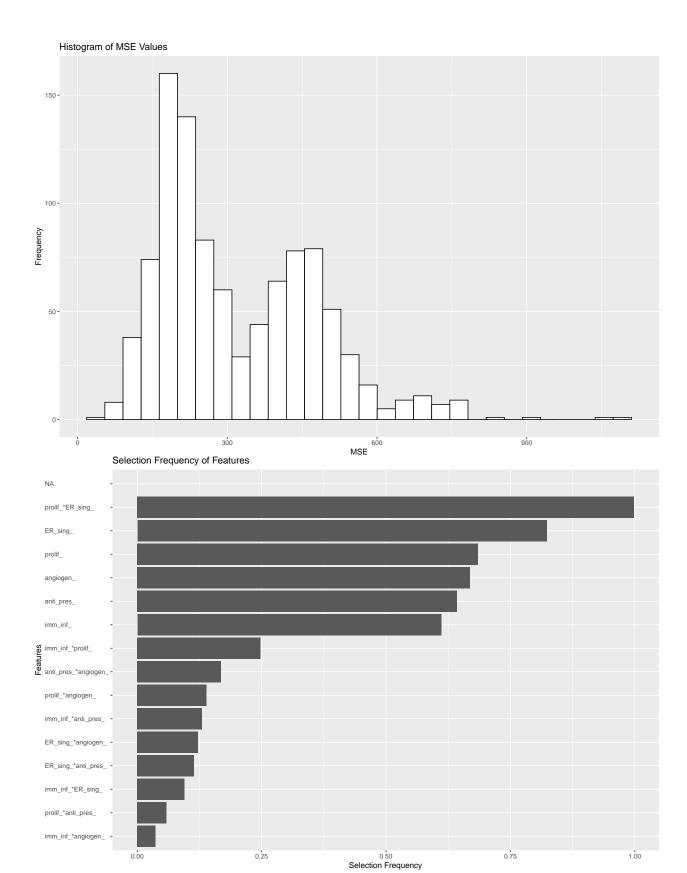
Lasso: 771 genes -> ROR-proliferation score + interactions between PCs

```
## 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
```



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

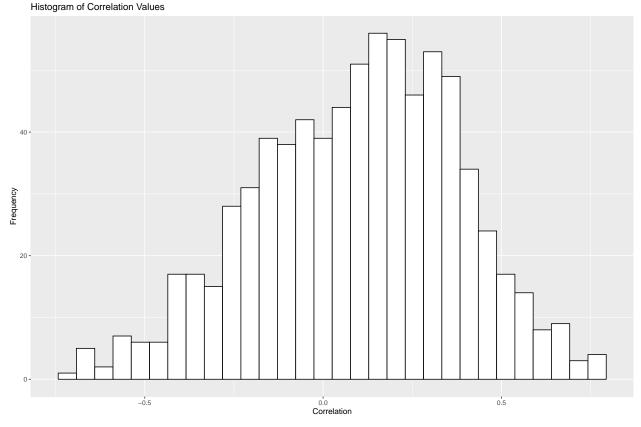
st.dev.: 0.2329426



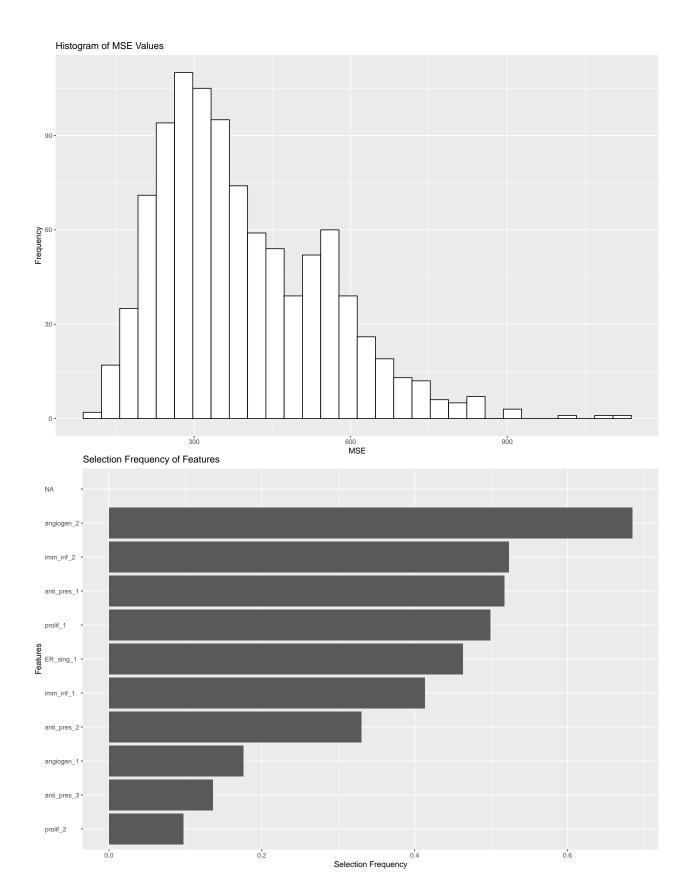
```
## Features selected 50% or more times:
## imm_inf_ prolif_ ER_sing_ anti_pres_ angiogen_ prolif_*ER_sing_
## Top 20 featrues:
  [1] "prolif_*ER_sing_"
                               "ER_sing_"
                                                       "prolif_"
   [4] "angiogen_"
                  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



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

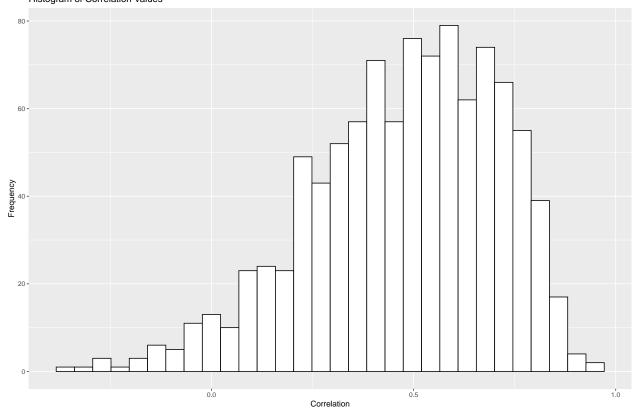


```
## Features selected 50% or more times:
## imm_inf_2 anti_pres_1 angiogen_2
## Top 20 featrues:
  [1] "angiogen_2"
                     "imm_inf_2"
                                   "anti_pres_1" "prolif_1"
                                                               "ER_sing_1"
             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

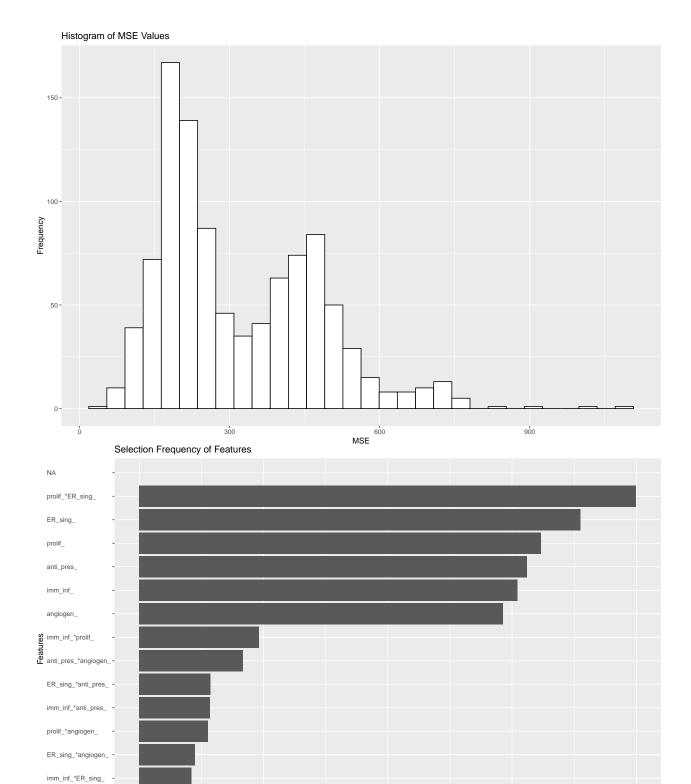
ElasticNet: 771 genes -> ROR-proliferation score + interactions between PCs

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 Histogram of Correlation Values



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



prolif_*anti_pres_ imm_inf_*angiogen_

0.00

0.25

0.50 Selection Frequency 0.75

```
## 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
## [19] NA
                               NA
```

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

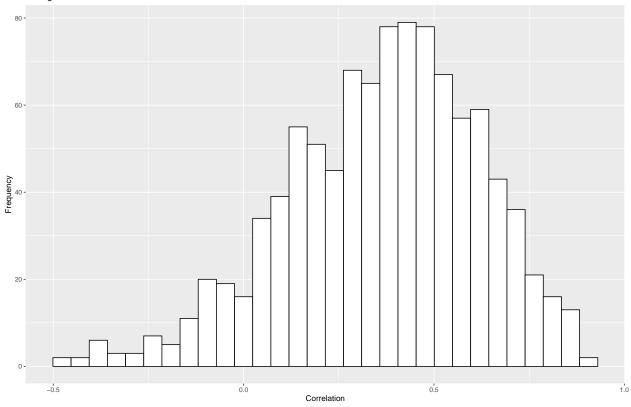
Model	cor_mean	sd_cor	MSE_mean	MSE_sd
ridge	0.3028091	0.2779432	364.5733	151.0208
$ridge_interac$	0.4505837	0.2404457	333.3975	151.6577
lasso	0.0784961	0.2856382	396.4902	160.1303
lasso_interact	0.4687056	0.2329426	321.0086	157.5895
elastic	0.0960693	0.2844609	392.3862	158.0853
$elastic_interact$	0.4749342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

Stacking on signature gene sets, cross-validation

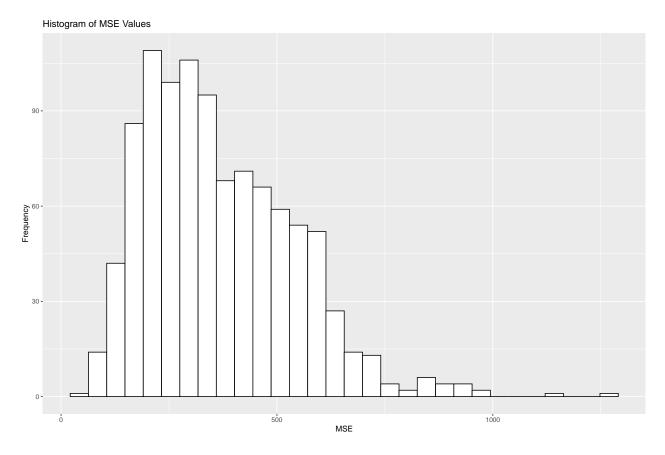
Ridge: 771 genes -> ROR-proliferation score

```
## 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

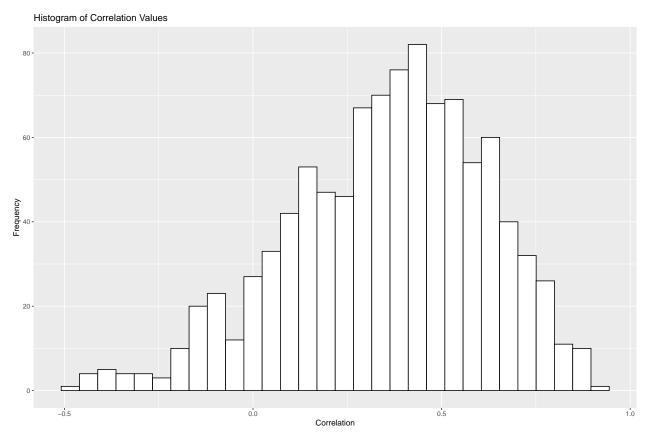
number of models fitted: 1000

Fraction of model fits with no selected genes: 0

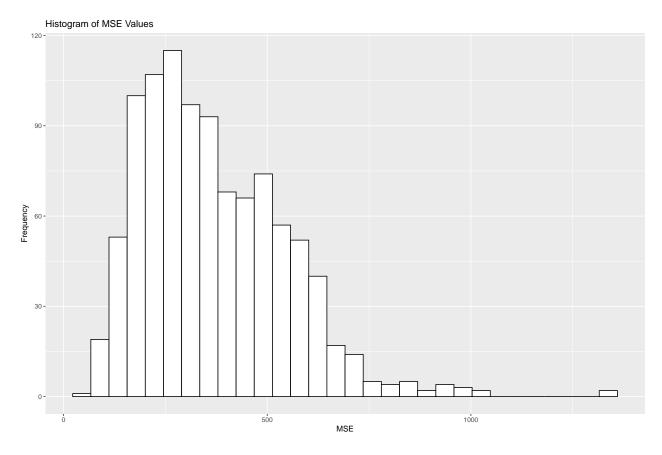
##

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

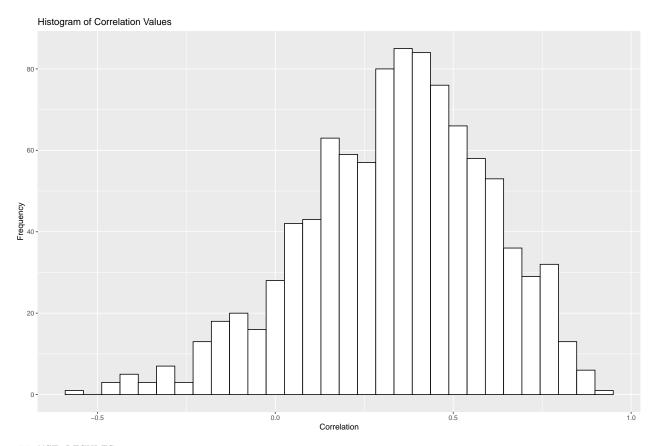
Fraction of model fits with no selected genes: 0

##

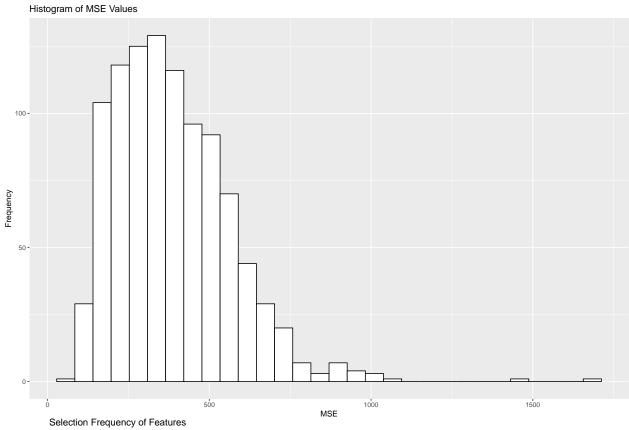
CORRELATIONS RESULTS

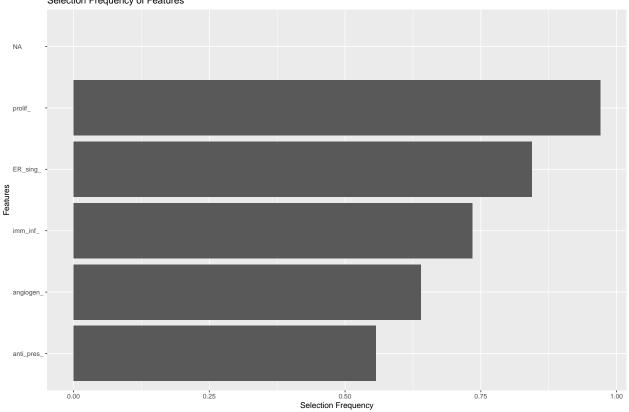
Mean: 0.3373612 ## Median: 0.3601618 ## Variance: 0.06786039

st.dev.: 0.2605003



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



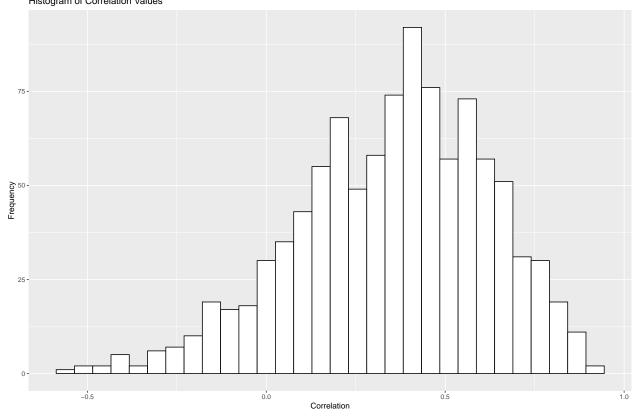


```
## Features selected 50% or more times:
## imm_inf_ prolif_ ER_sing_ anti_pres_ angiogen_
## Top 20 featrues:
   [1] "prolif_"
                     "ER_sing_"
                                   "imm_inf_"
                                                "angiogen_" "anti_pres_"
##
   [6] NA
     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

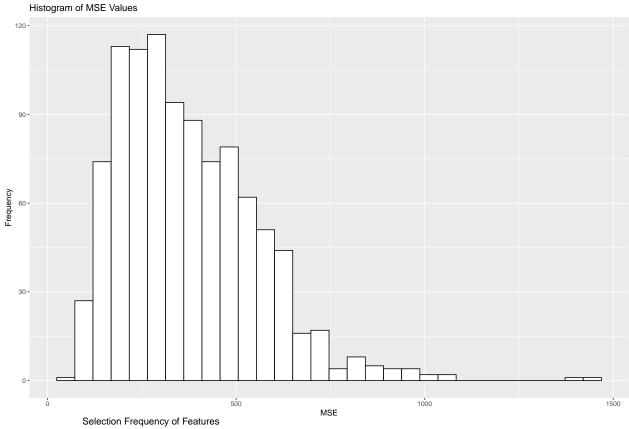
Lasso: 771 genes -> ROR-proliferation score + interactions between PCs

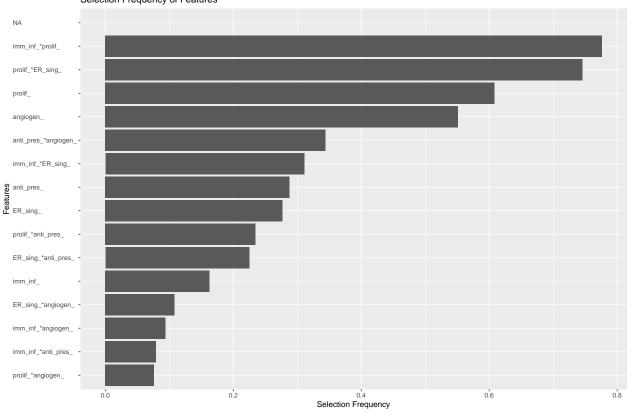
number of models fitted: 1000
Fraction of model fits with no selected genes: 0
##
CORRELATIONS RESULTS

Mean: 0.3521323 ## Median: 0.381805 ## Variance: 0.07224413 ## st.dev.: 0.2687827 Histogram of Correlation Values



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

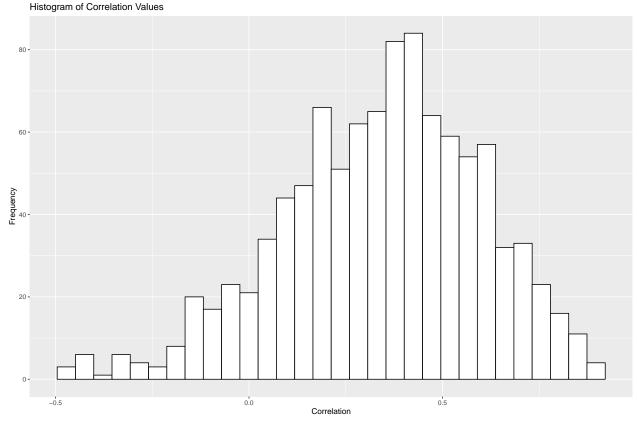




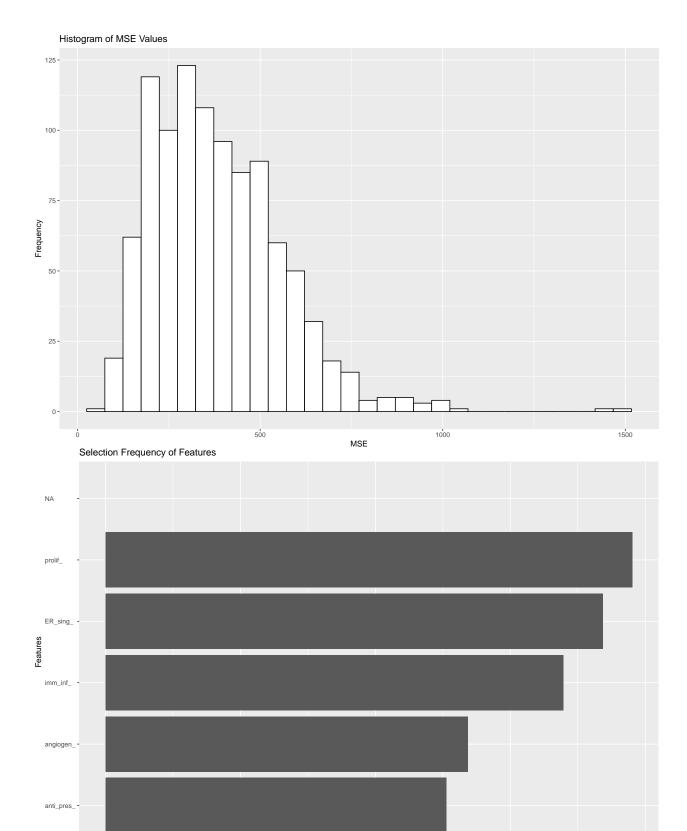
```
## Features selected 50% or more times:
## prolif_ angiogen_ imm_inf_*prolif_ prolif_*ER_sing_
## Top 20 featrues:
  [1] "imm_inf_*prolif_"
                                "prolif_*ER_sing_"
                                                       "prolif_"
                                "anti_pres_*angiogen_"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

ElasticNet: 771 genes \rightarrow 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



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



0.00

0.25

0.50 Selection Frequency

0.75

```
## 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
## [11] NA
                     NA
                                   NA
                                                NA
                                                              NA
## [16] NA
                     NA
                                   NA
                                                NA
                                                              NA
```

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

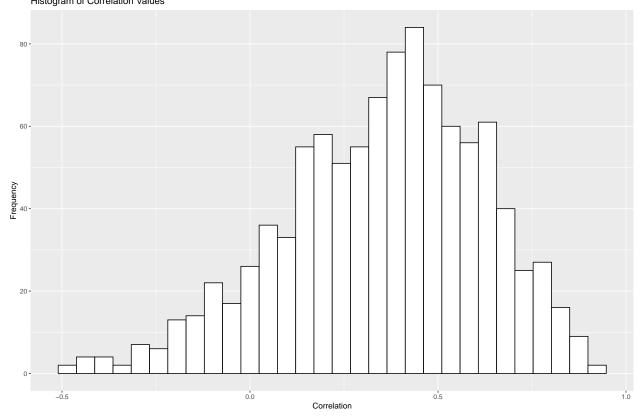
number of models fitted: 1000

 $\mbox{\tt \#\#}$ Fraction of model fits with no selected genes: 0

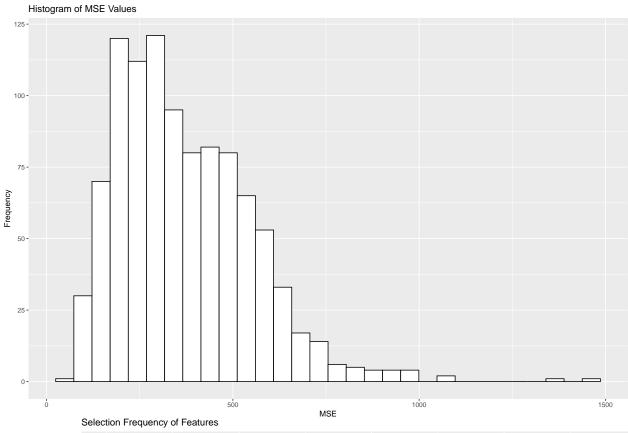
##

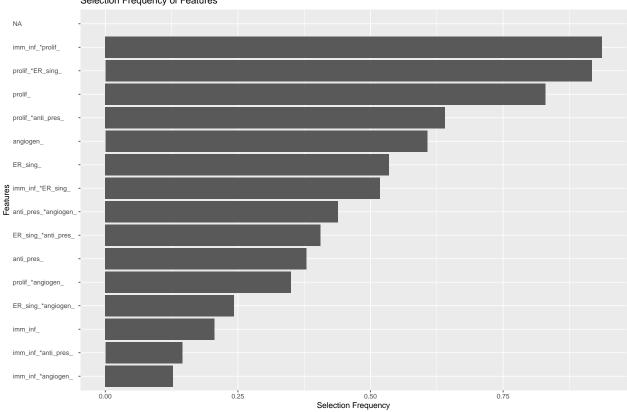
CORRELATIONS RESULTS

Mean: 0.353272
Median: 0.3797595
Variance: 0.07046161
st.dev.: 0.2654461
Histogram of Correlation Values



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_"
                               "prolif_*angiogen_"
## [10] "anti_pres_"
                                                     "ER_sing_*angiogen_"
                               "imm_inf_*anti_pres_" "imm_inf_*angiogen_"
## [13] "imm_inf_"
## [16] NA
## [19] 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	${\rm MSE_mean}$	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	${\rm MSE_mean}$	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

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

Model	cor_mean	sd_cor	MSE_mean	MSE_sd
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