Supplemental data

## Article

## Machine Learning Models Identify Molecules Active Against the Ebola Virus *In Vitro*

## Sean Ekins1,2,3\*, Joel S. Freundlich4, Alex M. Clark5, Manu Anantpadma6, Robert A. Davey6 and Peter B. Madrid7

## 1 Collaborations in Chemistry, 5616 Hilltop Needmore Road, Fuquay-Varina, NC 27526, USA.

## 2 Collaborations Pharmaceuticals Inc, 5616 Hilltop Needmore Road, Fuquay-Varina, NC 27526, USA.

## 3Collaborative Drug Discovery, 1633 Bayshore Highway, Suite 342, Burlingame, CA 94010, USA

## 4 Departments of Pharmacology & Physiology and Medicine, Center for Emerging and Reemerging Pathogens, UMDNJ – New Jersey Medical School, 185 South Orange Avenue Newark, NJ 07103, USA.

## 5 Molecular Materials Informatics, Inc., 1900 St. Jacques #302, Montreal H3J 2S1, Quebec, Canada

## 6 Texas Biomedical Research Institute, San Antonio, TX 78227, USA.

## 7 SRI International, 333 Ravenswood Avenue, Menlo Park, CA 94025, USA.

\* To whom correspondence should be addressed. Sean Ekins, E-mail address: ekinssean@yahoo.com, Phone: +1 215-687-1320 Twitter: @collabchem

**Supplemental data S1. Pseudotype bayesian model**

|  |  |
| --- | --- |
|

|  |
| --- |
| ROC score is 0.847 (leave-one-out).Best cutoff for this model is 0.812. |

 |
|

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|

|  |
| --- |
| **5-Fold Cross-Validation Result** |
| **Model Name** | **ROC Score** | **ROC Rating** | **True Positive** | **False Negative** | **False Positive** | **True Negative** | **Sensitivity** | **Specificity** | **Concordance** |
| Ebola pseudoviral N868 | 0.846 | Good | 39 | 2 | 176 | 651 | 0.951 | 0.787 | 0.795 |

 |
| C:\Users\sean\Documents\Discovery Studio\Results\CreateBayesianModel_2014_10_15_193044_538\Output\Report\images\image4602195027874986580.pngLeave out 50% x 100 fold cross validation

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| External\_ROC\_Score | Internal\_ROC\_Score | Concordance | Specificity | Sensitivity |
| 0.82 | 0.82 | 79.98 | 80.52 | 68.90 |
| 0.05 | 0.04 | 7.60 | 8.39 | 12.40 |

 |

 |

 |

**Supplemental data S2. EBOV replication Bayesian**

|  |  |
| --- | --- |
|

|  |
| --- |
| ROC score is 0.858 (leave-one-out).Best cutoff for this model is 6.770.See ModelDescription.html for more detailed information about this model. |

 |
|

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|

|  |
| --- |
| **5-Fold Cross-Validation Result** |
| **Model Name** | **ROC Score** | **ROC Rating** | **True Positive** | **False Negative** | **False Positive** | **True Negative** | **Sensitivity** | **Specificity** | **Concordance** |
| Ebola EBOV rep N868 USES CHLOROQUINE AND TOREMIFENE | 0.867 | Good | 19 | 1 | 239 | 609 | 0.950 | 0.718 | 0.724 |

 |
|  |

 |

 |

Leave out 50% x 100 fold cross validation

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| External\_ROC\_Score | Internal\_ROC\_Score | Concordance | Specificity | Sensitivity |
| 0.84 | 0.85 | 75.66 | 75.81 | 67.67 |
| 0.05 | 0.05 | 13.57 | 14.26 | 21.07 |

**Supplemental Data S3. SVM output file for Pseudotype model**

FitSummary

Call:

svm(formula = form, data = xy, type = type, kernel = tolower("Radial"),

 gamma = gamma, cost = cost, probability = prob, fitted = TRUE,

 epsilon = epsilon, nu = nu, coef0 = coef0, degree = degree, scale = TRUE)

Parameters:

 SVM-Type: C-classification

 SVM-Kernel: radial

 cost: 2

 gamma: 0.007352941

Number of Support Vectors: 307

 ( 266 41 )

Number of Classes: 2

Levels:

 0 1

Cross-validation results (5-fold):

 Gamma Cost ROC Score Best

1 0.007353 1 0.7538

2 0.007353 2 0.7598 \*\*\*

Contingency Table (best CV model):

 Predicted

Actual 0 1

 0 823 4

 1 41 0

All-data model results (non-cross-validated):

Settings used:

 Gamma Cost

 0.007352941 2

ROC Score: 0.9997

Contingency Table (all-data model):

 Predicted

Actual 0 1

 0 827 0

 1 13 28

FitPlot

 Binary Property

**Supplemental Data S4. SVM output file for EBOV replication model**

FitSummary

Call:

svm(formula = form, data = xy, type = type, kernel = tolower("Radial"),

 gamma = gamma, cost = cost, probability = prob, fitted = TRUE,

 epsilon = epsilon, nu = nu, coef0 = coef0, degree = degree, scale = TRUE)

Parameters:

 SVM-Type: C-classification

 SVM-Kernel: radial

 cost: 2

 gamma: 0.007352941

Number of Support Vectors: 222

 ( 202 20 )

Number of Classes: 2

Levels:

 0 1

Cross-validation results (5-fold):

 Gamma Cost ROC Score Best

1 0.007353 1 0.7235

2 0.007353 2 0.7263 \*\*\*

Contingency Table (best CV model):

 Predicted

Actual 0 1

 0 845 3

 1 20 0

All-data model results (non-cross-validated):

Settings used:

 Gamma Cost

 0.007352941 2

ROC Score: 1

Contingency Table (all-data model):

 Predicted

Actual 0 1

 0 848 0

 1 5 15

FitPlot

 Binary Property

**Supplemental Data S6. Predictions for Ebola activity using Open Bayesian models in the MMDS app.** Higher scores are more likely to be active.

****

**Supplemental Data S7. High content screening images illustrating inhibition of Ebola and cytotoxic concentration.**

****