In [112]:
```
import pandas as pd
import matplotlib.pyplot as plt
import seaborn as sns
import numpy as np

from sklearn.linear_model import Lasso
from sklearn.neighbors import KNeighborsRegressor

from sklearn.decomposition import PCA
from sklearn.cluster import KMeans

from sklearn.model_selection import train_test_split
from sklearn.model_selection import cross_val_score
from sklearn.model_selection import LeaveOneOut
from sklearn.model_selection import KFold

from sklearn.metrics import accuracy_score
from sklearn.metrics import roc_curve, auc

%matplotlib inline
sns.set(rc={'figure.figsize':(11.7,8.27)})
sns.set_style("whitegrid")
```

DATASET 1 DATA EXLORATION:

In [2]:
```
# read in dataset 1:

df = pd.read_csv('../data/dream_data/SubCh1_TrainingData.csv')
df.head()
```

Out[2]:

	Sample_Name	Isolate	Timepoint	Treatment	BioRep	MAL1.465720.465873.bc..rv..	MAL1.4828
0	isolate_01.24HR.DHA.BRep1	isolate_01	24HR	DHA	BRep1	0.008286	
1	isolate_01.24HR.DHA.BRep2	isolate_01	24HR	DHA	BRep2	-0.872028	
2	isolate_01.24HR.UT.BRep1	isolate_01	24HR	UT	BRep1	0.039480	
3	isolate_01.24HR.UT.BRep2	isolate_01	24HR	UT	BRep2	0.125177	
4	isolate_01.6HR.DHA.BRep1	isolate_01	6HR	DHA	BRep1	1.354956	

5 rows × 5546 columns

In [3]:
```
# quick look at whats in the df:
print("Dataframe 1 shape: ", df.shape)
print("Na values in df: ", df.isna().sum().sum())
```

```
Dataframe 1 shape:  (272, 5546)
Na values in df:  0
```

In [4]:
```
dfmean = df.groupby(["Isolate", "Timepoint", "Treatment"], as_index=False).mean()
dfmean.head()
```

Out[4]:

	Isolate	Timepoint	Treatment	MAL1.465720.465873.bc..rv..	MAL1.48287.48430....kr...can	MAL1.562126.56224
0	isolate_01	24HR	DHA	-0.431871	-1.464025	-'
1	isolate_01	24HR	UT	0.082329	-1.377065	-'
2	isolate_01	6HR	DHA	0.568441	-1.603999	-(
3	isolate_01	6HR	UT	1.154536	-1.583729	-'
4	isolate_02	24HR	DHA	0.146128	-1.584068	-'

5 rows × 5544 columns

In [5]:
```
# Normalize expression data across each gene:
df_norm = pd.concat([dfmean.iloc[:,:3], dfmean.iloc[:,3:-1].apply(lambda x: (x - n
p.mean(x))/np.std(x))], axis = 1)
df_norm.insert(3, 'DHA_IC50', dfmean[['DHA_IC50']])
df_norm.head()
```

Out[5]:

	Isolate	Timepoint	Treatment	DHA_IC50	MAL1.465720.465873.bc..rv..	MAL1.48287.48430....kr...can	MAL1.5
0	isolate_01	24HR	DHA	2.177	-1.572063	0.149176	
1	isolate_01	24HR	UT	2.177	-0.114184	0.392518	
2	isolate_01	6HR	DHA	2.177	1.264062	-0.242517	
3	isolate_01	6HR	UT	2.177	2.925783	-0.185794	
4	isolate_02	24HR	DHA	1.697	0.066701	-0.186743	

5 rows × 5544 columns

In [6]:
```
## make masks to call unperturbed and perturbed samples individually

mask_dha = dfmean['Treatment'] == 'DHA'
mask_ut = dfmean['Treatment'] == 'UT'
```

In [7]:
```
## calculate mean and st.dev expression for each gene for DHA and UT samples seper
ately -- append to end of each column

idx_rename = {'mean':'dha_mean','std':'dha_std'}
compare_dha = df_norm[mask_dha].agg(['mean', 'std'])
compare_dha.rename(index = idx_rename, inplace = True)

idx_rename = {'mean':'ut_mean','std':'ut_std'}
compare_ut = df_norm[mask_ut].agg(['mean','std'])
compare_ut.rename(index = idx_rename, inplace = True)


compare = pd.concat([compare_dha, compare_ut], sort = False).drop("DHA_IC50", axis
= 1)
```

In [8]:
```
## sanity check:
print("Normalized dataframe shape: ", df_norm.shape)
print("Comparison dataframe shape: ", compare.shape)

## checks out!
```

```
Normalized dataframe shape:  (120, 5544)
Comparison dataframe shape:  (4, 5540)
```

In [9]:
```
# run a welchs t-test to evaluate the difference in expression levels between trea
ted and untreated for each gene
# (function runs across each column in the dataframe)

def welch_t_test(col):
    return (
        (col.loc['dha_mean'] - col.loc['ut_mean']) /
        np.sqrt(
            col.loc['dha_std']**2/mask_dha.sum() + col.loc['ut_std']**2/mask_ut.su
m()
        )
    )
```

In [10]:
```
idx_rename = {0:'dha_mean', 1:'dha_std', 2:'ut_mean', 3:'ut_std', 4:'ttest'}

compare = compare.append(compare.apply(welch_t_test), ignore_index = True, sort =
False)
compare.rename(index = idx_rename, inplace = True)
#compare.sort_values(by = "ttest", axis = 1, inplace = True)
```

In [11]:
```
# builds mask for top 50 and top 100 differentially expressed genes between pertur
bed and unperterbed samples
sample_idx = ["Isolate", "Timepoint", "Treatment", "DHA_IC50"]
top50 = pd.concat([compare.loc['ttest'].nlargest(n = 25, keep = 'all'),
                   compare.loc['ttest'].nsmallest(n = 25, keep = 'all')], axis =
0)
top100 = pd.concat([compare.loc['ttest'].nlargest(n = 50, keep = 'all'),
                   compare.loc['ttest'].nsmallest(n = 50, keep = 'all')], axis =
0)
```

In [12]:
```
# make dfs with these top 50 and 100 genes
df50 = pd.concat([df_norm[sample_idx], df_norm[top50.index]], axis = 1)
df100 = pd.concat([df_norm[sample_idx], df_norm[top100.index]], axis = 1)
```

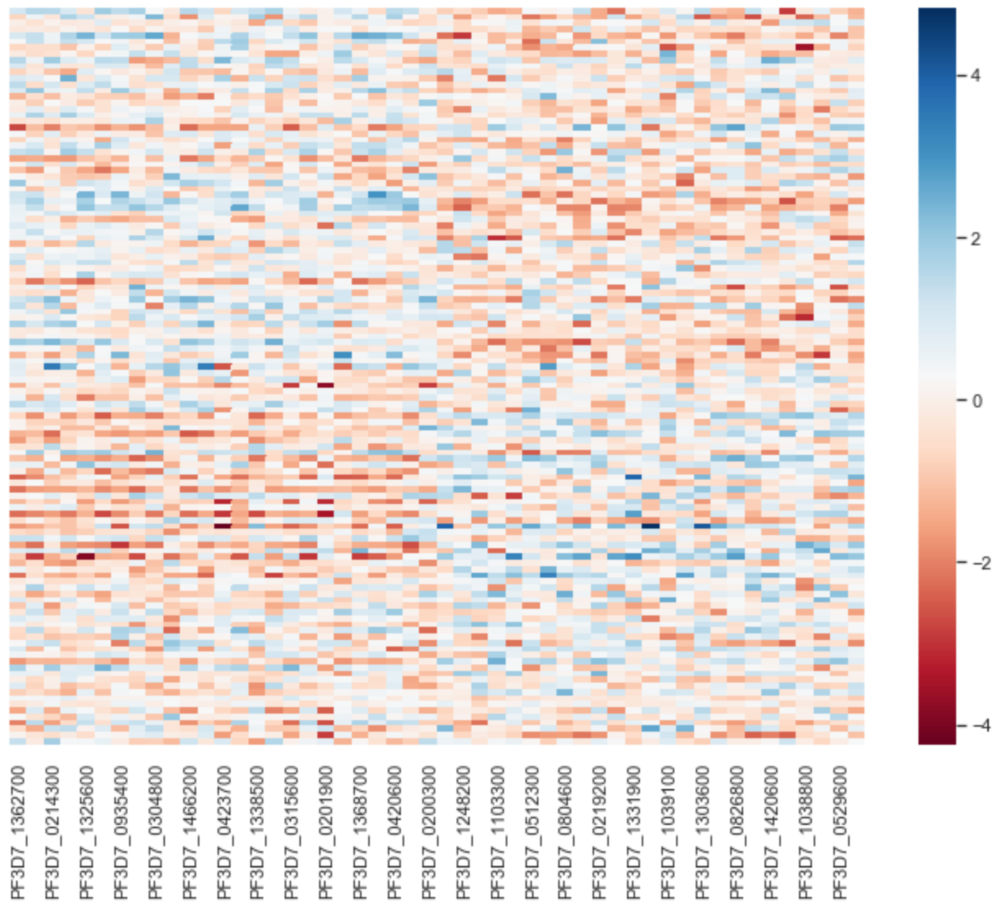
In [13]:
```
## save a list of these top 50 genes
ds1_top50 = top50.index
```

In [14]:
```
# save a list of these top 50 genes
pd.DataFrame(df50.columns[4:]).to_csv("correlation_features_ch1.csv")
```

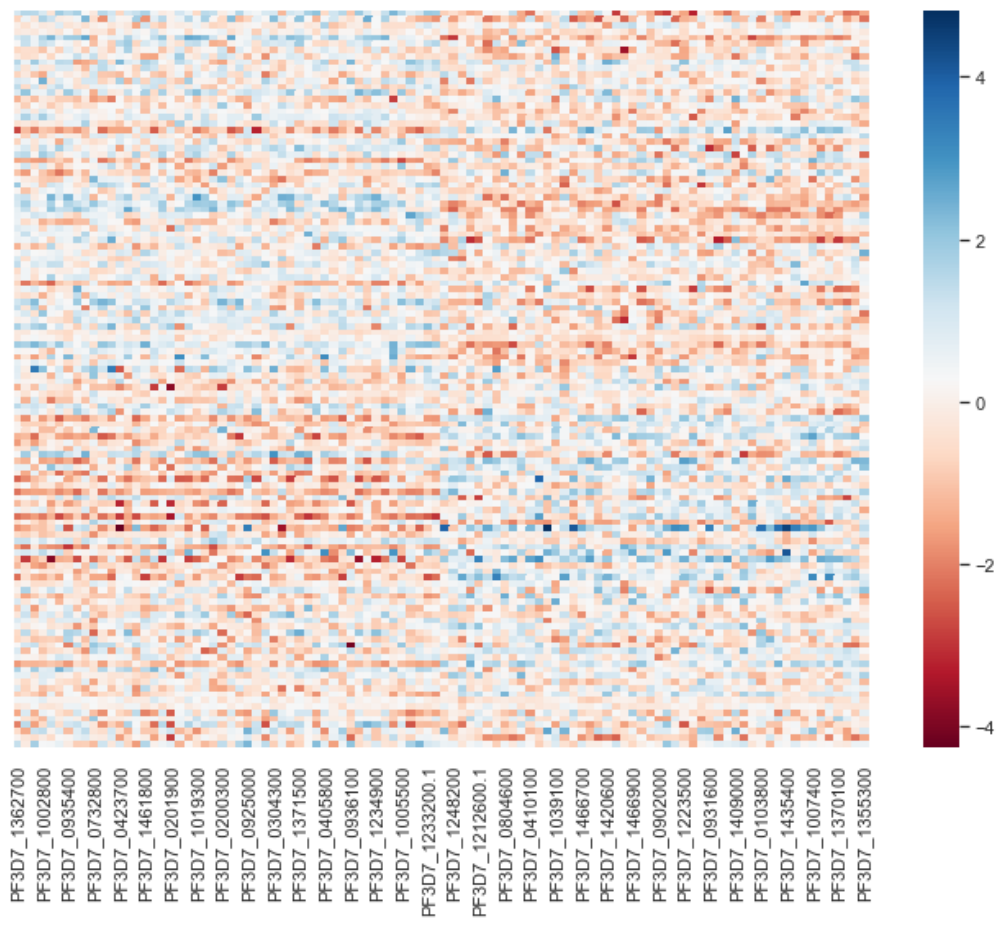
In [15]:
```
# sanity check
print("Top 50 differentially expressed genes: ", df50.shape)
print("Top 100 differentially expressed genes: ", df100.shape)
```

```
Top 50 differentially expressed genes:  (120, 54)
Top 100 differentially expressed genes:  (120, 104)
```

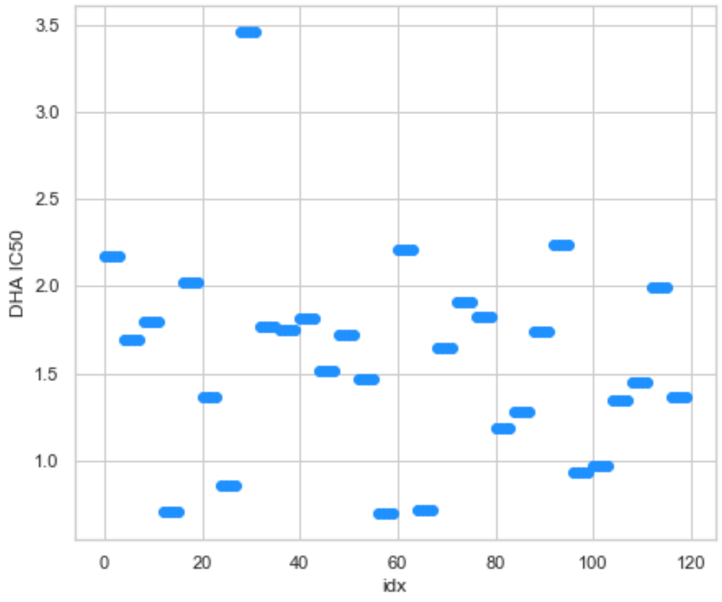
In [16]:
```
## plot the top 50 df with samples seperated by treatment condition

sns.heatmap(pd.concat([df50[df50["Treatment"] == "DHA"].drop(sample_idx, axis =
1),
                       df50[df50["Treatment"] == "UT"].drop(sample_idx, axis =
1)]),
            yticklabels=False, cmap = 'RdBu')
plt.show()
#df_group = df_norm.set_index('Sample_Name').groupby(['Timepoint','Treatment','Iso
late'])
```



In [17]:
```
## plot the top 50 df with samples seperated by treatment condition

sns.heatmap(pd.concat([df100[df100["Treatment"] == "DHA"].drop(sample_idx, axis =
1),
                       df100[df100["Treatment"] == "UT"].drop(sample_idx, axis =
1)]),
            yticklabels=False, cmap = 'RdBu')
plt.show()
```



In [18]:
```
## Take a look at outcome variable: DHA IC50:

plt.figure(figsize = (7,6))
plt.scatter(dfmean.index, dfmean['DHA_IC50'], color = "dodgerblue")
plt.xlabel("idx")
plt.ylabel("DHA IC50")
plt.show()
```



In [19]:
```
df["DHA_IC50"].var()
```

Out[19]:
```
0.28559082812242237
```

DATASET 1 MODELING:

In [20]:
```
# convert timepoint column into integer
def time_convert(i):
    if i == "24HR":
        time = 24
    else:
        time = 6
    return time


dfmean["Timepoint"] = dfmean["Timepoint"].apply(time_convert)
```

In [21]:
```
# encode perturbation variable:
dfmean["Treatment"] = dfmean["Treatment"].astype('category').cat.codes
```

```
In [167]: # make numpy objects:
          features = dfmean.iloc[:,1:-1].to_numpy()
          labels = dfmean["DHA_IC50"].to_numpy()

          # sanity check:
          print("Feature frame size: ", features.shape)
          print("Label frame size: ", labels.shape)


          # split data into training and test set -- here I held 25% as my test set
          x_train, x_test, y_train, y_test = train_test_split(features, labels, test_size=0.
          25, random_state=1)

          print(x_train.shape)
          print(x_test.shape)
          print(y_train.shape)
          print(y_test.shape)
```

```
Feature frame size:  (120, 5542)
Label frame size:  (120,)
(90, 5542)
(30, 5542)
(90,)
(30,)
```

Try out a bunch of models:

```
In [23]: ## L1 regression (Lasso):
         from sklearn import linear_model

         lasso = linear_model.Lasso(alpha=0.5, max_iter = 500).fit(x_train, y_train)
         lasso.score(x_test, y_test)
```

```
Out[23]: -0.001428799782112744
```

```
In [24]: ## L2 regression cross-validated model (Ridge):
         from sklearn.linear_model import RidgeCV

         ll2 = RidgeCV(alphas=(0.1, 1.0, 10.0)).fit(x_train, y_train)
         ll2.score(x_test, y_test) ## this returns an r2 score

         # Ridge(alpha=1.0, copy_X=True, fit_intercept=True, max_iter=None,
         #       normalize=False, random_state=None, solver='auto', tol=0.001)
```

```
Out[24]: -1.0259340432439599
```

```
In [25]: ## Bayesian ridge:
         from sklearn.linear_model import BayesianRidge

         b_ridge = linear_model.BayesianRidge(n_iter = 500).fit(x_train, y_train)
         b_ridge.score(x_test, y_test)
```

```
Out[25]: -1.1615634282366218
```

In [26]:
```
## SVM model:
from sklearn.svm import SVR

SVR = SVR(kernel = "rbf", gamma='scale', C=5.0, epsilon=0.1).fit(x_train, y_train)
print(SVR.score(x_test, y_test))  ## this returns an r2 score
y_pred = SVR.predict(x_test)


#scores = cross_val_score(rfr, feature_train, label_train, cv=10, scoring='r2')
```

```
-0.35967127073700866
```

In [29]:
```
## SVM tuning function:
from sklearn.svm import SVR
from sklearn.model_selection import GridSearchCV

def svr_model(X, y):
    # Perform Grid-Search
    gsc = GridSearchCV(
        estimator=SVR(),
        param_grid={
            'kernel': ('rbf', 'linear', 'sigmoid'),
            'gamma': ('scale','auto'),
            'C': (0.5, 1, 10),
        },
        cv=5, verbose=0, n_jobs=-1)

    grid_result = gsc.fit(X, y)
    best_params = grid_result.best_params_

    svr = SVR(kernel=best_params["kernel"],
              gamma=best_params["gamma"],
              C=best_params["C"]) # Perform K-Fold CV
    score = cross_val_score(svr, X, y, cv=10).mean()

    return score, best_params

svr_model(features, labels)
```

Out[29]:
```
(-1.361556910181731, {'C': 0.5, 'gamma': 'auto', 'kernel': 'rbf'})
```

In [30]:
```
## SVM model:

svr = SVR(kernel = "rbf", gamma='auto', C=0.5).fit(x_train, y_train)
print(svr.score(x_test, y_test) ) ## this returns an r2 score
```

```
-0.05300284029875746
```

In [32]:
```
len(svr.support_)
```

Out[32]:
```
83
```

In [33]:
```
## KNN tuning function:
from sklearn.neighbors import KNeighborsRegressor

def knr_model(X, y):
    # Perform Grid-Search
    gsc = GridSearchCV(
        estimator=KNeighborsRegressor(),
        param_grid={
            'n_neighbors': range(2,12),
            'weights': ('uniform', 'distance'),
        },
        cv=5, verbose=0, n_jobs=-1)

    grid_result = gsc.fit(X, y)
    best_params = grid_result.best_params_

    knr = KNeighborsRegressor(n_neighbors=best_params["n_neighbors"], weights=best
_params["weights"]) # Perform K-Fold CV
    score = cross_val_score(knr, X, y, cv=10).mean()

    return score, best_params

knr_model(features, labels)
```

Out[33]:
```
(-1.7928478626876347, {'n_neighbors': 11, 'weights': 'distance'})
```

In [34]:
```
## KNN model:
from sklearn.neighbors import KNeighborsRegressor

knr = KNeighborsRegressor(n_neighbors=11).fit(x_train, y_train)
print(knr.score(x_test, y_test) ) ## this returns an r2 score
y_pred = knr.predict(x_test)
```

```
-0.11130066152266505
```

In [39]:
```
# random forest first swing at parameters:
from sklearn.ensemble import RandomForestRegressor

rfr = RandomForestRegressor(n_estimators = 100, max_features = "sqrt",
                            max_depth = 8,
                            bootstrap = True).fit(x_train, y_train)

print("Test data r2 score: ", rfr.score(x_test, y_test)) ## this returns an r2 sco
re

y_pred = rfr.predict(x_test)
```

```
Test data r2 score:  -0.147795477333l5024
```

In [36]:
```
## random forest tuning function:

def rfr_model(X, y):
    # Perform Grid-Search
    gsc = GridSearchCV(
        estimator=RandomForestRegressor(),
        param_grid={
            'max_depth': range(3,10),
            'n_estimators': (25, 50, 100, 250),
            'max_features': ("auto", "sqrt")
        },
        cv=5, scoring='neg_mean_squared_error',
        verbose=0, n_jobs=-1)

    grid_result = gsc.fit(X, y)
    best_params = grid_result.best_params_

    rfr = RandomForestRegressor(max_depth=best_params["max_depth"], n_estimators=b
est_params["n_estimators"],
                                random_state=False, verbose=False) # Perform K-Fol
d CV
    score = cross_val_score(rfr, X, y, cv=10, scoring='neg_mean_absolute_error').m
ean()

    return score, best_params

rfr_model(features, labels)
```

Out[36]:
```
(-0.46528672747362754,
 {'max_depth': 8, 'max_features': 'sqrt', 'n_estimators': 100})
```

In [37]:
```
## look at random forest regression feature importances!!

print("Number of features in fitted model: ", rfr.n_features_)
print("Feature Importances: ", rfr.feature_importances_)
```

```
Number of features in fitted model:  5542
Feature Importances:  [0. 0. 0. ... 0. 0. 0.]
```

In [38]:
```
np.count_nonzero(rfr.feature_importances_)
```

Out[38]:
```
1434
```

Above models didn't generate a single positive R2 value. Trying feature selection next

In [40]:
```
# start with top 50 most important random forest features:

# select features:
top50_rforestA = df.drop(["Sample_Name", "Isolate", "BioRep", "DHA_IC50"],
                         axis = 1).columns[np.argsort(rfr.feature_importances_)[549
2:5542]]


# apply to x_train and x_test data:
x_train_rf50 = x_train[:,np.argsort(rfr.feature_importances_)[5492:5542]]
x_test_rf50 = x_test[:,np.argsort(rfr.feature_importances_)[5492:5542]]

print(x_train_rf50.shape)
print(x_test_rf50.shape)
print(y_train.shape)
print(y_test.shape)
```

```
(90, 50)
(30, 50)
(90,)
(30,)
```

In [41]:
```
## L1 regression (Lasso):

lasso = linear_model.Lasso(alpha=0.5, max_iter = 500).fit(x_train_rf50, y_train)
lasso.score(x_test_rf50, y_test)
```

Out[41]:
```
-0.001428799782112744
```

In [42]:
```
## L2 regression cross-validated model (Ridge):

ll2 = RidgeCV(alphas=(0.1, 1.0, 10.0)).fit(x_train_rf50, y_train)
ll2.score(x_test_rf50, y_test) ## this returns an r2 score

# Ridge(alpha=1.0, copy_X=True, fit_intercept=True, max_iter=None,
#       normalize=False, random_state=None, solver='auto', tol=0.001)
```

Out[42]:
```
-0.15068131298017873
```

In [43]:
```
## Bayesian ridge:

b_ridge = linear_model.BayesianRidge(n_iter = 500).fit(x_train_rf50, y_train)
b_ridge.score(x_test_rf50, y_test)
```

Out[43]:
```
-0.002701207686544249
```

In [44]:
```
## run SVR model tuning function:
svr_model(x_train_rf50, y_train)
```

Out[44]:
```
(-0.19879435844896845, {'C': 0.5, 'gamma': 'scale', 'kernel': 'rbf'})
```

In [45]:
```
## SVM model:

svr = SVR(kernel = "rbf", gamma='auto', C=0.5).fit(x_train_rf50, y_train)
print(svr.score(x_test_rf50, y_test) ) ## this returns an r2 score
```

```
-0.03246442015633799
```

In [46]:
```
## run KNN model tuning function:
knr_model(x_train_rf50, y_train)
```

Out[46]:
```
(-0.24883513448795452, {'n_neighbors': 11, 'weights': 'uniform'})
```

```
In [47]: ## KNN model:

         knr = KNeighborsRegressor(n_neighbors=11, weights = "distance").fit(x_train_rf50,
         y_train)
         print(knr.score(x_test_rf50, y_test) ) ## this returns an r2 score

         -0.16067113252896292
```

```
In [48]: from sklearn.metrics import mean_absolute_error

         mean_absolute_error(y_test, y_pred)

Out[48]: 0.5250768245990801
```

```
In [49]: ## run random forest model tuning:
         rfr_model(x_train_rf50, y_train)

Out[49]: (-0.4312482312476809,
          {'max_depth': 3, 'max_features': 'sqrt', 'n_estimators': 25})
```

```
In [52]: # random forest model:

         rfr = RandomForestRegressor(n_estimators = 50,
                                     max_depth = 3,
                                     max_features = "sqrt",
                                     bootstrap = True).fit(x_train_rf50, y_train)

         print("Test data r2 score: ", rfr.score(x_test_rf50, y_test)) ## this returns an r
         2 score

         Test data r2 score:  -0.20695264342083752
```

```
In [53]: mean_absolute_error(y_test, y_pred)

Out[53]: 0.5250768245990801
```

Random forest selected features didn't generate any positive R2 scores either. Next Trying out recursive features selection:

```
In [168]: ## recursive feature selection:
          from sklearn.feature_selection import RFE

          # Create the RFE object and rank each feature
          #rf = RandomForestRegressor(n_estimators = 100, bootstrap = True, max_features = '
          sqrt')
          b_ridge = linear_model.BayesianRidge(n_iter = 500)

          rfs100 = RFE(estimator=b_ridge, step=20, n_features_to_select = 100).fit(features,
          labels)

          rfs100.n_features_

Out[168]: 100
```

```
In [169]: ## save names of top 100 features selected by rfe for model 1

          m1_rfe_features = dfmean.iloc[:,1:-1].columns[rfs100.support_]
```

In [55]:
```
# generate feature array with top 100 feautures:

features_rfs100 = features[:,rfs100.support_]

print("Feature frame size: ", features_rfs100.shape)
print("Label frame size: ", labels.shape)
```

```
Feature frame size:  (120, 100)
Label frame size:  (120,)
```

In [56]:
```
# sanity check:
print("Feature frame size: ", features.shape)
print("Label frame size: ", labels.shape)

# split data into training and test set -- continue holding out 25% as test set
x_train_rfs100, x_test_rfs100, y_train_rfs100, y_test_rfs100 = train_test_split(
    features[:,rfs100.support_],
    labels,
    test_size=0.25)

print(x_train_rfs100.shape)
print(x_test_rfs100.shape)
print(y_train_rfs100.shape)
print(y_test_rfs100.shape)
```

```
Feature frame size:  (120, 5542)
Label frame size:  (120,)
(90, 100)
(30, 100)
(90,)
(30,)
```

In [57]:
```
## L1 regression (Lasso):

lasso = linear_model.Lasso(alpha=0.5, max_iter = 500).fit(x_train_rfs100, y_train_
rfs100)
lasso.score(x_test_rfs100, y_test_rfs100)
```

Out[57]:
```
-0.007587957228985642
```

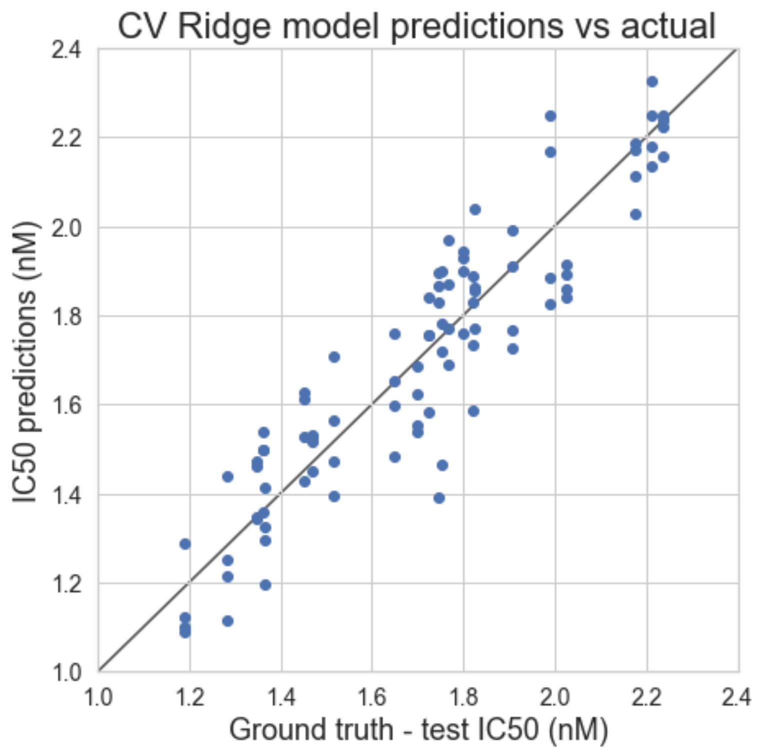
In [58]:
```
## take a look at predictors as well as R2 score from model generated with cross v
alidation
## (cross validated models are build on the complete dataset)

from sklearn.model_selection import cross_val_predict
from sklearn.linear_model import Ridge

ridge = linear_model.Ridge(alpha = 0.1)
y_pred = cross_val_predict(ridge, features_rfs100, labels, cv=5)
score = cross_val_score(ridge, features_rfs100, labels, cv=5).mean()
```

In [59]:
```
print(score)
print(mean_absolute_error(labels, y_pred))
```

```
0.8976431818845458
0.10946002410955051
```

GENERATED A POSITIVE R2 SCORE!

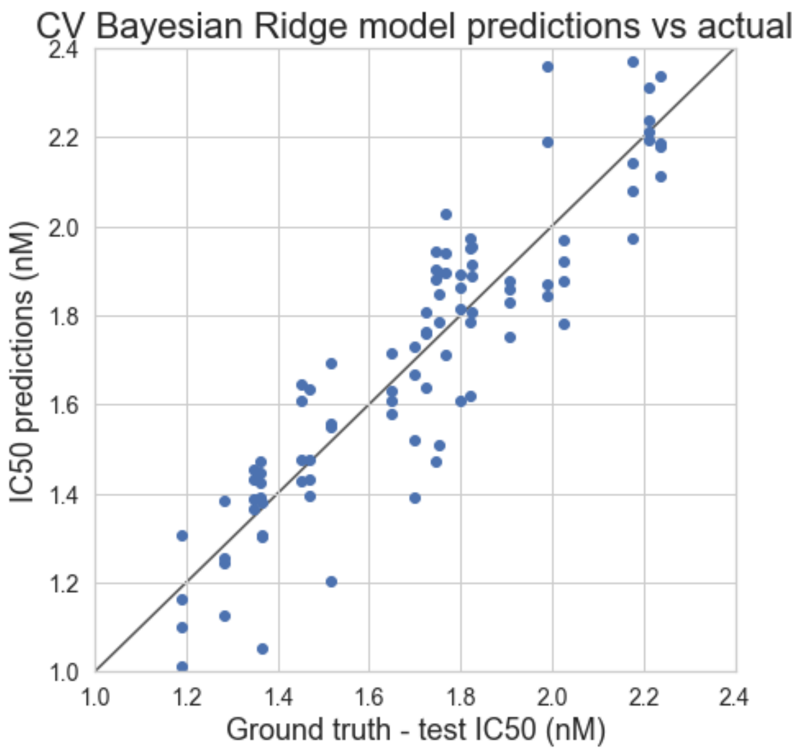
In [60]:
```
x = np.linspace(0,4,10)
plt.figure(figsize = (7, 7))
plt.scatter(labels, y_pred)
plt.plot(x, x, 'k-', alpha=0.75, zorder=0)
plt.xlabel("Ground truth - test IC50 (nM)", fontsize = 18)
plt.ylabel("IC50 predictions (nM)", fontsize = 18)
plt.ylim(1, 2.4)
plt.xlim(1, 2.4)
plt.yticks(fontsize = 14)
plt.xticks(fontsize = 14)
plt.title("CV Ridge model predictions vs actual", fontsize = 22)
plt.show()
```



In [61]:
```
# try out same model with bayesian ridge:
# (cross validated models are build on the complete dataset)

b_ridge = linear_model.BayesianRidge(n_iter = 500)

y_pred = cross_val_predict(b_ridge, features_rfs100, labels, cv=5)
score = cross_val_score(b_ridge, features_rfs100, labels, cv=5).mean()

print(score)
print(mean_absolute_error(labels, y_pred))
```

```
0.889482870204386
0.11180523368658295
```

In [62]:
```
x = np.linspace(0,4,10)
plt.figure(figsize = (7, 7))
plt.scatter(labels, y_pred)
plt.plot(x, x, 'k-', alpha=0.75, zorder=0)
plt.xlabel("Ground truth - test IC50 (nM)", fontsize = 18)
plt.ylabel("IC50 predictions (nM)", fontsize = 18)
plt.ylim(1, 2.4)
plt.xlim(1, 2.4)
plt.yticks(fontsize = 14)
plt.xticks(fontsize = 14)
plt.title("CV Bayesian Ridge model predictions vs actual", fontsize = 22)
plt.show()
```



In [63]:
```
## L2 regression cross-validated model (Ridge):
## build L2 model on train set to test on test set; this also generates a good mod
el

ll2 = RidgeCV(alphas=(0.1, 1.0, 10.0)).fit(x_train_rfs100, y_train_rfs100)

y_pred = ll2.predict(x_test_rfs100)
ll2.score(x_test_rfs100, y_test_rfs100) ## this returns an r2 score

# Ridge(alpha=1.0, copy_X=True, fit_intercept=True, max_iter=None,
#       normalize=False, random_state=None, solver='auto', tol=0.001)
```

Out[63]:
```
0.8808706099200574
```

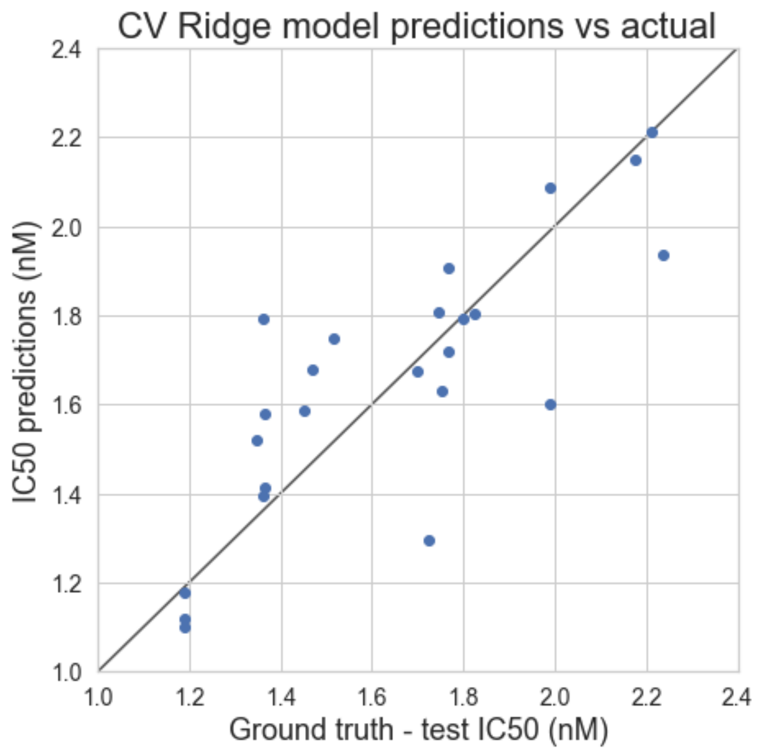
In [64]:
```
ll2.alpha_
```

Out[64]:
```
0.1
```

In [65]:
```
mean_absolute_error(y_test_rfs100, y_pred)
```

Out[65]:
```
0.1477708202673636
```

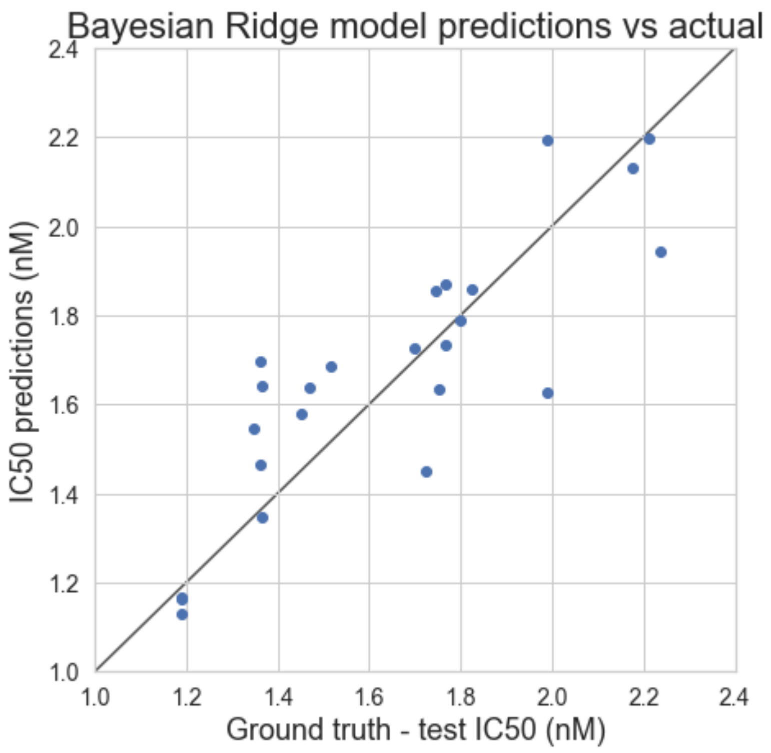
In [66]:
```
x = np.linspace(0,4,10)
plt.figure(figsize = (7, 7))
plt.scatter(y_test_rfs100, y_pred)
plt.plot(x, x, 'k-', alpha=0.75, zorder=0)
plt.xlabel("Ground truth - test IC50 (nM)", fontsize = 18)
plt.ylabel("IC50 predictions (nM)", fontsize = 18)
plt.ylim(1, 2.4)
plt.xlim(1, 2.4)
plt.yticks(fontsize = 14)
plt.xticks(fontsize = 14)
plt.title("CV Ridge model predictions vs actual", fontsize = 22)
plt.show()
```



In [67]:
```
## Bayesian ridge:
b_ridge = linear_model.BayesianRidge(n_iter = 500).fit(x_train_rfs100, y_train_rfs
100)

y_pred = b_ridge.predict(x_test_rfs100)
b_ridge.score(x_test_rfs100, y_test_rfs100)
```

Out[67]:
```
0.9095425827219517
```

In [68]:
```
x = np.linspace(0,4,10)
plt.figure(figsize = (7, 7))
plt.scatter(y_test_rfs100, y_pred)
plt.plot(x, x, 'k-', alpha=0.75, zorder=0)
plt.xlabel("Ground truth - test IC50 (nM)", fontsize = 18)
plt.ylabel("IC50 predictions (nM)", fontsize = 18)
plt.ylim(1, 2.4)
plt.xlim(1, 2.4)
plt.yticks(fontsize = 14)
plt.xticks(fontsize = 14)
plt.title("Bayesian Ridge model predictions vs actual", fontsize = 22)
plt.show()
```



In [69]:
```
mean_absolute_error(y_test_rfs100, y_pred)
```

Out[69]:
```
0.13461928645221477
```

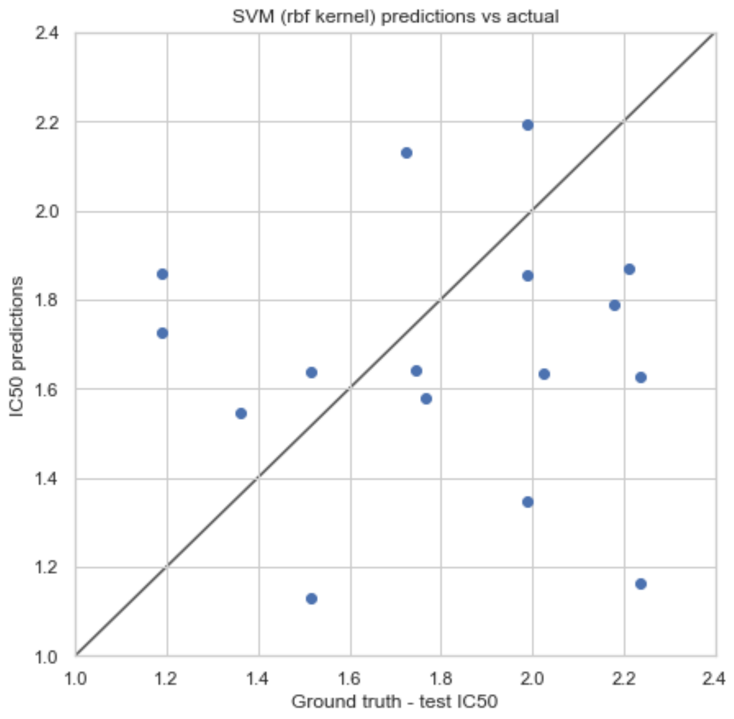
In [70]:
```
# try out SVR tuning here:
svr_model(x_train_rfs100, y_train)
```

Out[70]:
```
(-0.07554827873599722, {'C': 0.5, 'gamma': 'scale', 'kernel': 'rbf'})
```

In [72]:
```
## SVM model:

svr = SVR(kernel = "linear", gamma='auto', C=0.5).fit(x_train_rfs100, y_train)
print(svr.score(x_test_rfs100, y_test) ) ## this returns an r2 score
```

```
-1.356216688940925
```

In [73]:
```
x = np.linspace(0,4,10)
plt.figure(figsize = (7, 7))
plt.scatter(y_test, y_pred)
plt.plot(x, x, 'k-', alpha=0.75, zorder=0)
plt.xlabel("Ground truth - test IC50")
plt.ylabel("IC50 predictions")
plt.ylim(1, 2.4)
plt.xlim(1, 2.4)
plt.title("SVM (rbf kernel) predictions vs actual")
plt.show()
```



In [74]:
```
## KNN model tuning:
knr_model(x_train_rfs100, y_train)
```

Out[74]:
```
(-0.2949873052292718, {'n_neighbors': 6, 'weights': 'distance'})
```

In [75]:
```
## KNN model:

knr = KNeighborsRegressor(n_neighbors=11, weights = "distance").fit(x_train_rfs10
0, y_train)
print(knr.score(x_test_rfs100, y_test) ) ## this returns an r2 score
```

```
-0.029494155320093137
```

In [76]:
```
# try RFE with just the top 50 features to see how it compares:
b_ridge = linear_model.BayesianRidge(n_iter = 500)

rfs50 = RFE(estimator=b_ridge, step=20, n_features_to_select = 50).fit(features, l
abels)

rfs50.n_features_
```

Out[76]:
```
50
```

In [77]:
```
x_train_rfs50 = x_train[:,rfs50.support_]
x_test_rfs50 = x_test[:,rfs50.support_]

print(x_train_rfs50.shape)
print(x_test_rfs50.shape)
```

```
(90, 50)
(30, 50)
```

In [78]:
```
## L1 regression (Lasso):
from sklearn import linear_model
lasso = linear_model.Lasso(alpha=0.5, max_iter = 500).fit(x_train_rfs50, y_train)
lasso.score(x_test_rfs50, y_test)
```

Out[78]:
```
-0.001428799782112744
```

In [79]:
```
## L2 regression cross-validated model (Ridge):
from sklearn.linear_model import RidgeCV

ll2 = RidgeCV(alphas=(0.1, 1.0, 10.0)).fit(x_train_rfs50, y_train)

y_pred = ll2.predict(x_test_rfs50)
ll2.score(x_test_rfs50, y_test) ## this returns an r2 score

# Ridge(alpha=1.0, copy_X=True, fit_intercept=True, max_iter=None,
#       normalize=False, random_state=None, solver='auto', tol=0.001)
```

Out[79]:
```
0.7349019228382516
```

In [80]:
```
mean_absolute_error(y_test, y_pred)
```

Out[80]:
```
0.23522063543663252
```

In [81]:
```
## Bayesian ridge:
b_ridge = linear_model.BayesianRidge(n_iter = 500).fit(x_train_rfs50, y_train)

y_pred = b_ridge.predict(x_test_rfs50)
b_ridge.score(x_test_rfs50, y_test)
```

Out[81]:
```
0.7617479869181036
```

In [82]:
```
mean_absolute_error(y_test, y_pred)
```

Out[82]:
```
0.2238048999381535
```

In [83]:
```
## SVR model tuning:

svr_model(x_train_rfs50, y_train)
```

Out[83]:
```
(0.34873639403343093, {'C': 0.5, 'gamma': 'scale', 'kernel': 'linear'})
```

In [84]:
```
## SVM model:

svr = SVR(kernel = "linear", gamma='auto', C=0.5).fit(x_train_rfs50, y_train)
print(svr.score(x_test_rfs50, y_test) ) ## this returns an r2 score
```

```
0.7240795695981179
```

```
Best performance generated by Ridge regression model trained on top 100 features selec
ted with RFE
```

In [ ]:

```
DATASET 2 DATA EXPLORATION:
```

In [85]:

```
df2 = pd.read_csv('../data/dream_data/SubCh2_TrainingData.csv')
df2.head()
```

Out[85]:

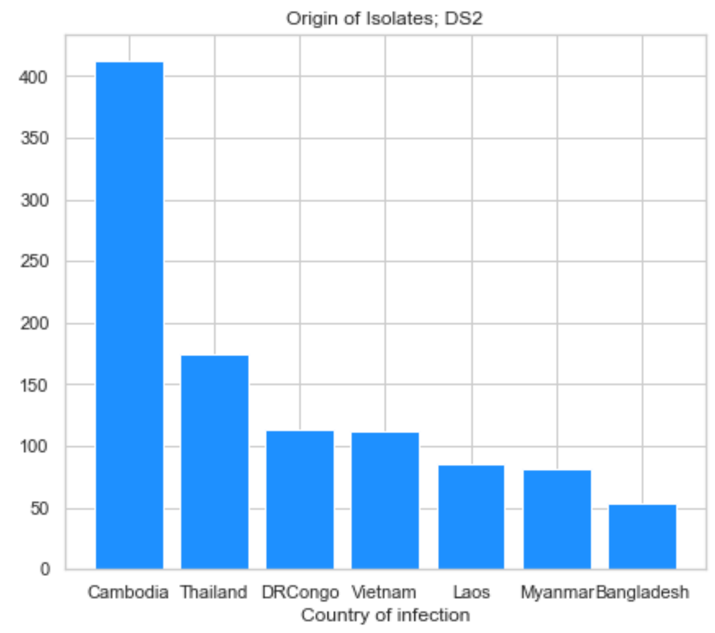
	Sample_Names	Country	Asexual.stage..hpi.	Kmeans.Grp	PF3D7_0100100	PF3D7_0100200	PF3D7_01003
0	GSM1427365	Bangladesh	20	B	0.226311	-0.396829	-1.8045
1	GSM1427366	Bangladesh	18	B	0.554427	0.542001	-1.5615
2	GSM1427367	Bangladesh	16	B	0.587048	0.707557	-1.6045
3	GSM1427368	Bangladesh	8	A	0.680655	-0.744063	-1.4411
4	GSM1427369	Bangladesh	16	B	1.089408	-0.002673	-0.8774

5 rows × 4957 columns

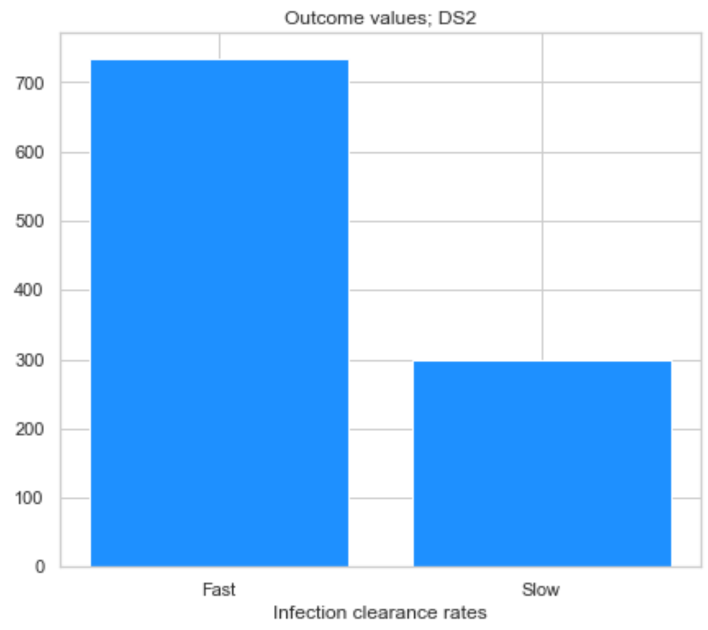
In [86]:

```
## drop any entries that don't have outcome data

output_mask = df2["ClearanceRate"].isna()
df2 = df2[~output_mask]
```

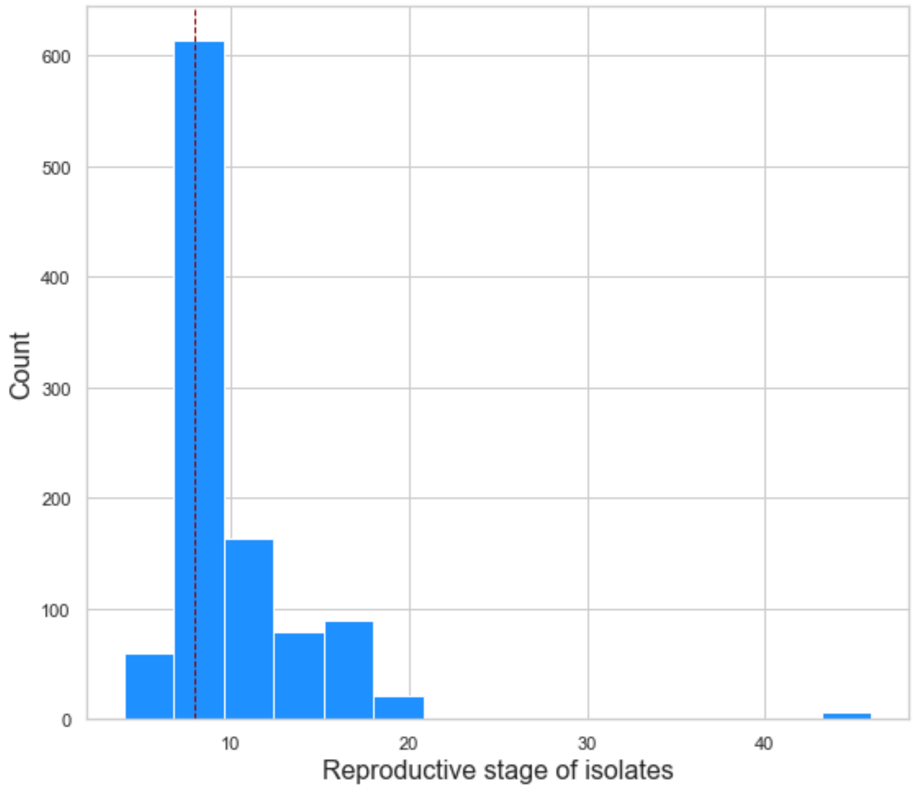
In [87]:
```
## take a look at the nation distribution of ds2 samples

country_freq = df2['Country'].value_counts()
country_freq.index

plt.figure(figsize = (7,6))
plt.bar(country_freq.index, country_freq, color = "dodgerblue")
plt.xlabel('Country of infection')
plt.title("Origin of Isolates; DS2")
plt.show()
```



```
In [88]: clearance_freq = df2['ClearanceRate'].value_counts()
         clearance_freq.index

         plt.figure(figsize = (7,6))
         plt.bar(clearance_freq.index, clearance_freq, color = "dodgerblue")
         plt.xlabel('Infection clearance rates')
         plt.title("Outcome values; DS2")
         plt.show()
```



In [89]:
```
plt.figure(figsize = (9,8))
plt.hist(df2['Asexual.stage..hpi.'], bins = 15, color="dodgerblue")
plt.axvline(df2['Asexual.stage..hpi.'].median(), color='darkred', linestyle='dashe
d', linewidth=1)
plt.xlabel('Reproductive stage of isolates', fontsize = 16)
plt.ylabel('Count', fontsize = 16)
plt.show()
```



In [90]:
```
## look at interesection across microarrays from dataset 1 to dataset 2
ch1 = df.columns
ch2 = df2.columns
len(set(ch1).intersection(ch2))
```

Out[90]:
```
4952
```

In [91]:
```
## encode catagorical variables

df_code = df2.copy()
df_code["Country"] = df_code["Country"].astype("category").cat.codes
df_code["Kmeans.Grp"] = df_code["Kmeans.Grp"].astype("category").cat.codes
df_code["ClearanceRate"] = df_code["ClearanceRate"].replace('Fast', 1)
df_code["ClearanceRate"] = df_code["ClearanceRate"].replace('Slow', 0)
df_code.head()
```

Out[91]:

	Sample_Names	Country	Asexual.stage..hpi.	Kmeans.Grp	PF3D7_0100100	PF3D7_0100200	PF3D7_0100300
0	GSM1427365	0	20	1	0.226311	-0.396829	-1.804581
1	GSM1427366	0	18	1	0.554427	0.542001	-1.561573
2	GSM1427367	0	16	1	0.587048	0.707557	-1.604587
3	GSM1427368	0	8	0	0.680655	-0.744063	-1.441137
4	GSM1427369	0	16	1	1.089408	-0.002673	-0.877413

5 rows × 4957 columns

In [92]:
```
## impute missing data

from sklearn.impute import KNNImputer

imputer = KNNImputer(n_neighbors=3, weights = 'distance')
df_impute = imputer.fit_transform(df_code.iloc[:,1:-1].to_numpy())
```

In [93]:
```
## put imputed data back into a labeled pd dataframe

pd_impute = pd.DataFrame(df_impute)
pd_impute.columns = df_code.drop(["Sample_Names", "ClearanceRate"], axis = 1).colu
mns
pd_impute = pd.concat([df_code["ClearanceRate"], pd_impute], axis = 1, join = "inn
er")
```

In [94]:
```
#pd_impute.to_csv('imputed_ch2_data.csv')
```

In [95]:
```
pd_impute.shape
```

Out[95]:
```
(1025, 4956)
```

In [96]:
```
# Normalize expresssion data across each gene:
norm_plot = pd.concat([pd_impute["ClearanceRate"], pd_impute.drop(["Country", "Ase
xual.stage..hpi.", "Kmeans.Grp", "ClearanceRate"],
                                                                         axis = 1).apply
(lambda x: (x - np.mean(x))/np.std(x))], axis = 1)
```

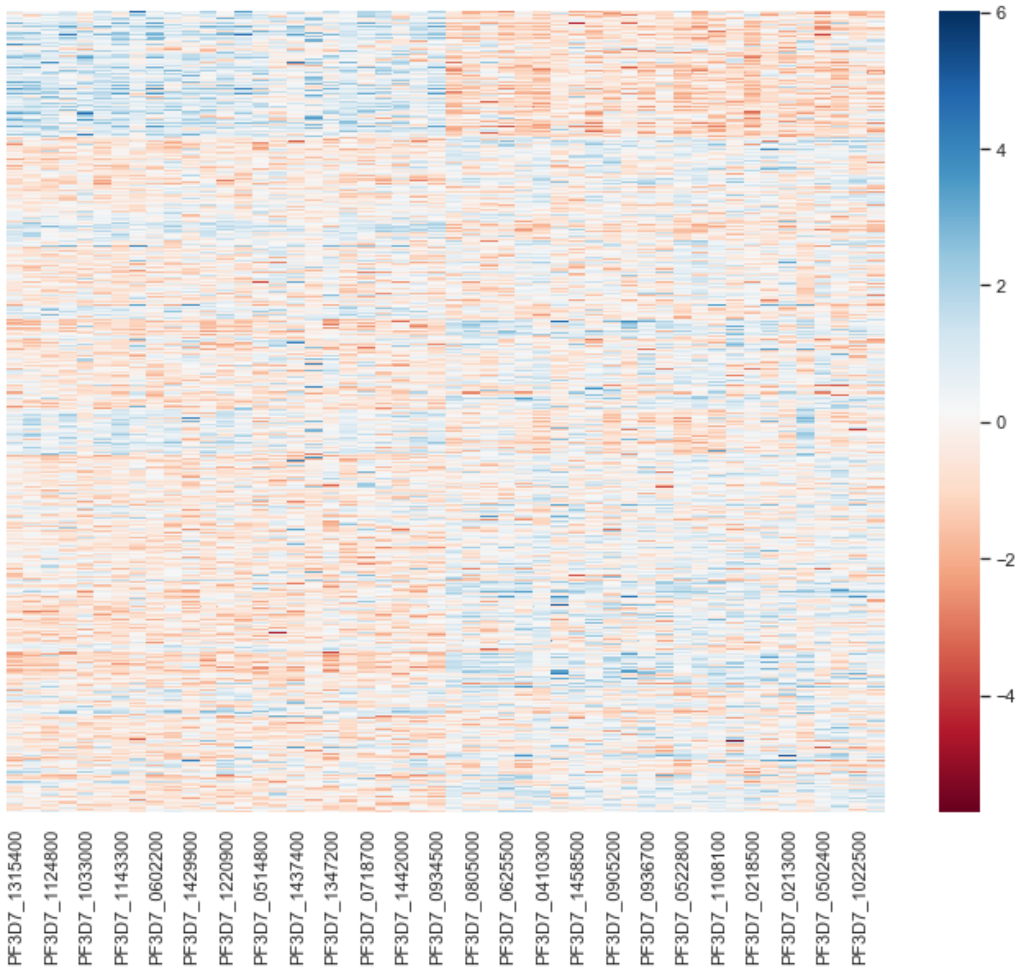
In [97]:
```
# run a welchs t-test to evaluate the difference in expression levels between trea
ted and untreated for each gene
# (function runs across each column in the dataframe)

def welch_t_test(col):
    return (
        (col.loc['fast_mean'] - col.loc['slow_mean']) /
        np.sqrt(
            col.loc['fast_std']**2/fast_mask.sum() + col.loc['slow_std']**2/slow_m
ask.sum()
        )
    )
```

In [98]:
```
## Clearance Rate masks:
fast_mask = norm_plot["ClearanceRate"] == 1
slow_mask = norm_plot["ClearanceRate"] == 0

## calculate mean and st.dev expression for each gene for DHA and UT samples seper
ately -- append to end of each column

idx_rename = {'mean':'fast_mean','std':'fast_std'}
compare_fast = norm_plot[fast_mask].agg(['mean', 'std'])
compare_fast.rename(index = idx_rename, inplace = True)

idx_rename = {'mean':'slow_mean','std':'slow_std'}
compare_slow = norm_plot[slow_mask].agg(['mean','std'])
compare_slow.rename(index = idx_rename, inplace = True)

compare = pd.concat([compare_fast, compare_slow], sort = False).drop("ClearanceRat
e", axis = 1)


idx_rename = {0:'fast_mean', 1:'fast_std', 2:'slow_mean', 3:'slow_std', 4:'ttest'}
compare = compare.append(compare.apply(welch_t_test), ignore_index = True, sort =
False)
compare.rename(index = idx_rename, inplace = True)
```

In [99]:
```
## generate df of top 50 differentially expressed genes between fast and slow clea
rance samples
top50 = pd.concat([compare.loc['ttest'].nlargest(n = 25, keep = 'all'),
                   compare.loc['ttest'].nsmallest(n = 25, keep = 'all')], axis =
0)

df50 = pd.concat([norm_plot["ClearanceRate"], norm_plot[top50.index]], axis = 1)
```

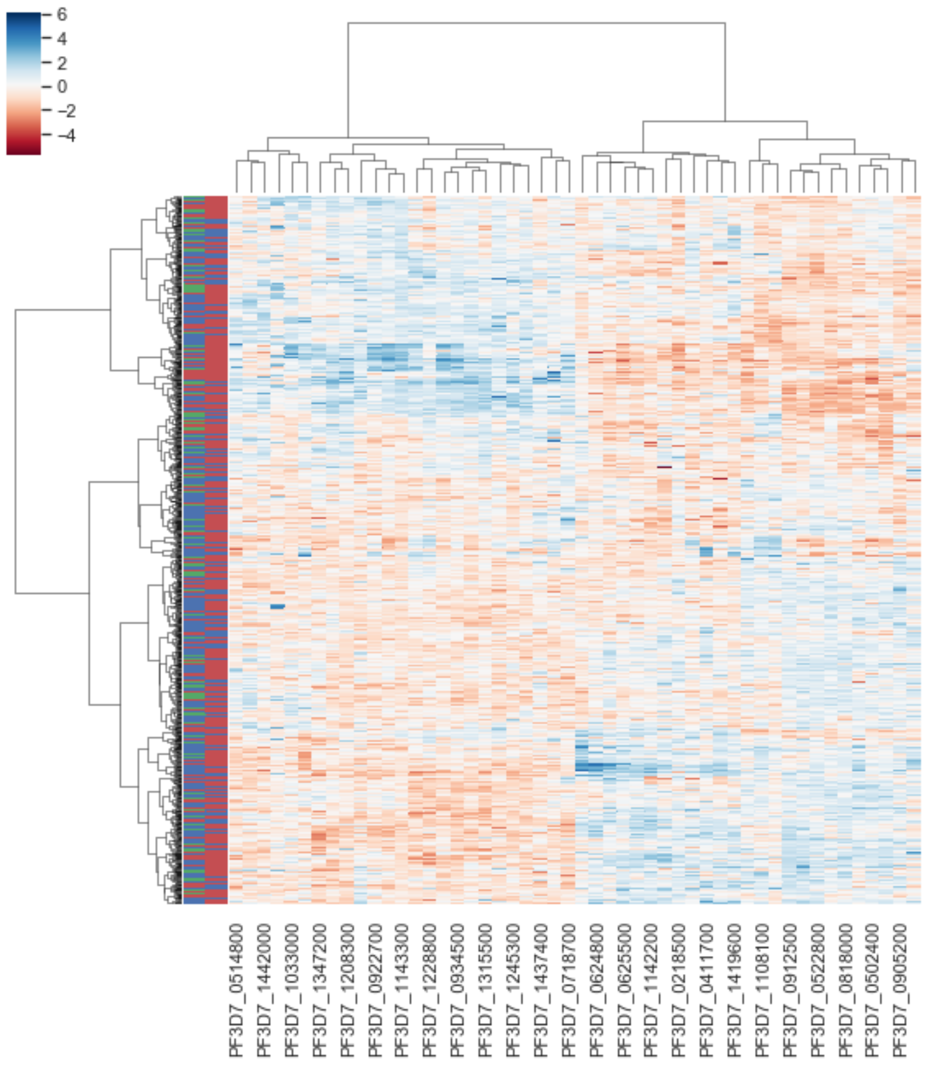
In [100]:
```
ds2_top50 = top50.index
```

In [101]:
```
## generate heat map of top 50 differentially expressed genes, seperated by fast/s
low clearance rates

sns.set(rc={'figure.figsize':(12,9)})
sns.heatmap(pd.concat([df50[df50["ClearanceRate"] == 1].drop("ClearanceRate", axis
= 1),
                        df50[df50["ClearanceRate"] == 0].drop("ClearanceRate", axis
= 1)]),
            yticklabels=False, cmap = 'RdBu')
plt.show()
```



In [102]:
```
## look at a quick clustermap of the samples (second annotation bar)
## with the kmeans cluster data given in ds2 (first annotation bar)

cluster_map_clearance = dict(zip(pd_impute["ClearanceRate"].unique(), "rbg"))
cluster_map_cluster = dict(zip(pd_impute["Kmeans.Grp"].unique(), "rbg"))
row_colors_clearance = pd_impute["ClearanceRate"].map(cluster_map_clearance)
row_colors_cluster = pd_impute["Kmeans.Grp"].map(cluster_map_cluster)

sns.clustermap(pd.concat([df50[df50["ClearanceRate"] == 1].drop("ClearanceRate", a
xis = 1),
                          df50[df50["ClearanceRate"] == 0].drop("ClearanceRate", a
xis = 1)]),
               cmap = 'RdBu', row_colors=[row_colors_cluster, row_colors_clearanc
e], method = "ward", yticklabels = False)
```

Out[102]:
```
<seaborn.matrix.ClusterGrid at 0x11e1ccc88>
```



DATASET 2 MODELS:

In [103]:
```
## generate numpy objects for train/test split

features = df_impute
outputs = df_code.iloc[:,-1].to_numpy()


print('Features DF size: ', features.shape)
print('Outputs DF size: ', outputs.shape)
```

```
Features DF size:  (1034, 4955)
Outputs DF size:  (1034,)
```

In [104]:
```
## train/test split 70/30

x_train, x_test, y_train, y_test = train_test_split(features, outputs, test_size=
0.3, random_state=1)

print(x_train.shape)
print(x_test.shape)
print(y_train.shape)
print(y_test.shape)
```

```
(723, 4955)
(311, 4955)
(723,)
(311,)
```

In [105]:
```
## code for generating ROC plots and confusion matricies:

from sklearn.metrics import confusion_matrix
from sklearn.utils.multiclass import unique_labels

def generate_roc_plot(fpr, tpr, title='Reciever operating plot'):
    roc_auc = auc(fpr, tpr)

    # generate ROC plot:
    plt.figure(figsize = (10, 8))
    lw = 2
    plt.plot(fpr, tpr, color='darkorange',
             lw=lw, label='ROC curve (area = %0.2f)' % roc_auc)
    plt.plot([0, 1], [0, 1], color='navy', lw=lw, linestyle='--')
    plt.xlim([0.0, 1.0])
    plt.ylim([0.0, 1.05])
    plt.xlabel('False Positive Rate', fontsize = 16)
    plt.ylabel('True Positive Rate', fontsize = 16)
    plt.title(title, fontsize = 20)
    plt.legend(loc="lower right", fontsize = 14)
    plt.xticks(fontsize = 14)
    plt.yticks(fontsize = 14)
    plt.show()



def plot_confusion_matrix(y_true, y_pred, classes,
                          normalize=False,
                          title=None,
                          cmap=plt.cm.Blues):
    """
    This function prints and plots the confusion matrix.
    Normalization can be applied by setting `normalize=True`.

    Code from scikit-learn.org
    """
    if not title:
        if normalize:
            title = 'Normalized confusion matrix'
        else:
            title = 'Confusion matrix, without normalization'

    # Compute confusion matrix
    cm = confusion_matrix(y_true, y_pred)
    # Only use the labels that appear in the data
    classes = classes[unique_labels(y_true, y_pred)]
    if normalize:
        cm = cm.astype('float') / cm.sum(axis=1)[:, np.newaxis]
        print("Normalized confusion matrix")
    else:
        print('Confusion matrix, without normalization')

    print(cm)
    print(cm.shape)

    fig, ax = plt.subplots()
    im = ax.imshow(cm, interpolation='nearest', cmap=cmap)
    ax.figure.colorbar(im, ax=ax)
    # We want to show all ticks...
    ax.set(xticks=np.arange(cm.shape[1]),
           yticks=np.arange(-0.5, cm.shape[0]))
    ax.set_xticklabels(["Slow", "Fast"], fontsize = 14)
    ax.set_yticklabels(["Slow", "Fast"], fontsize = 14)
    ax.set_title(title, fontsize = 20)
    ax.set_ylabel("True label", fontsize = 16)
    ax.set_xlabel("Predicted label", fontsize = 16)
```

In [108]:
```
## Write Random forest classification model tuning script:
from sklearn.ensemble import RandomForestClassifier
from sklearn.model_selection import GridSearchCV

def rfc_model(X, y):
    # Perform Grid-Search
    gsc = GridSearchCV(
        estimator=RandomForestClassifier(),
        param_grid={
            'max_depth': range(4,9),
            'n_estimators': (50, 100, 1000),
            'min_samples_split': range(2,5)
        },
        cv=5, verbose=0, n_jobs=-1)

    grid_result = gsc.fit(X, y)
    best_params = grid_result.best_params_

    rfc = RandomForestClassifier(max_depth=best_params["max_depth"],
                                 n_estimators=best_params["n_estimators"],
                                 min_samples_split = best_params["min_samples_spli
t"],
                                 random_state=False,
                                 verbose=False) # Perform K-Fold CV
    scores = cross_val_score(rfc, X, y, cv=5)
    return scores, best_params

rfc_model(features, outputs)
```

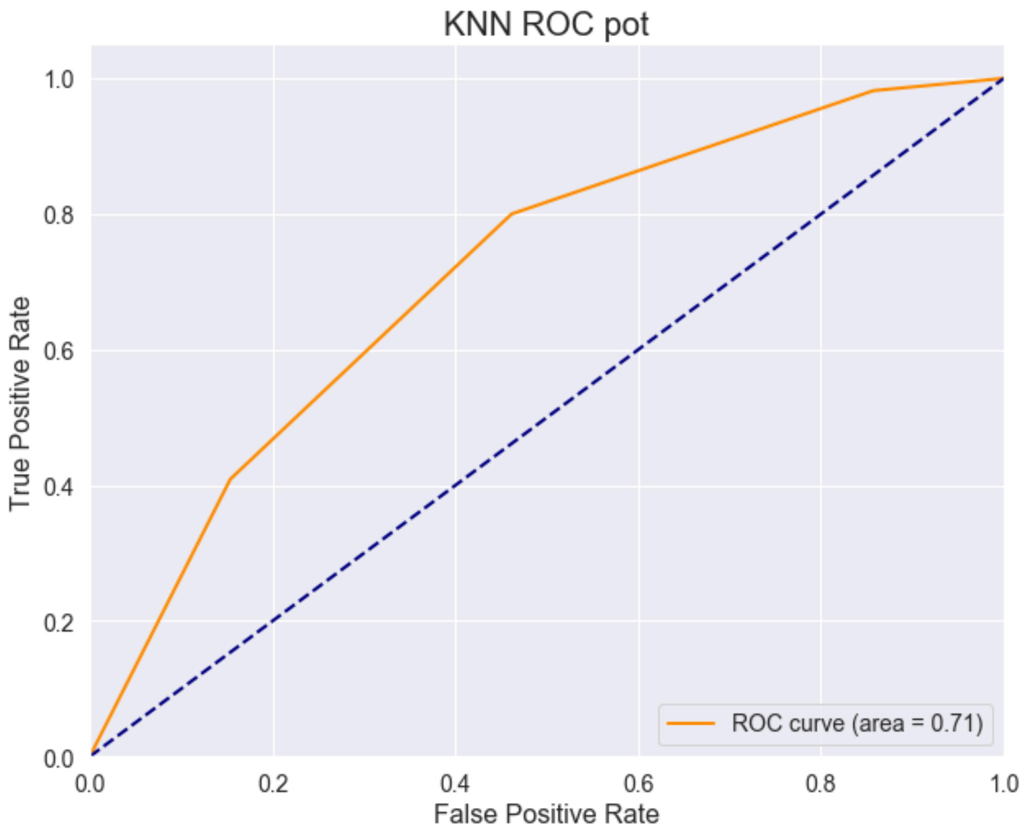
Out[108]:
```
(array([0.71497585, 0.73429952, 0.73429952, 0.70531401, 0.69902913]),
 {'max_depth': 5, 'min_samples_split': 4, 'n_estimators': 100})
```

In [113]:
```
# random forest classifier:

sns.set(rc={'figure.figsize':(8,6)})

rfc = RandomForestClassifier(n_estimators = 100, bootstrap = True, max_depth = 5,
                             min_samples_split = 4,
                             max_features = 'sqrt').fit(x_train, y_train)

y_pred = rfc.predict(x_test)
y_probs = rfc.predict_proba(x_test)

false_positive_rate, true_positive_rate, thresholds = roc_curve(y_test, y_probs[:,
1])
roc_auc = auc(false_positive_rate, true_positive_rate)
print("Random Forest classifier AUC: ", roc_auc)
print("Accuracy: ", accuracy_score(y_test, y_pred))
```

```
Random Forest classifier AUC:  0.747002997002997
Accuracy:  0.729903536977492
```

In [114]:
```python
# and KNN classifier:
sns.set(rc={'figure.figsize':(8,6)})

from sklearn.neighbors import KNeighborsClassifier
from sklearn.model_selection import cross_val_score

knn = KNeighborsClassifier(n_neighbors=3).fit(x_train, y_train)

y_pred = knn.predict(x_test)
y_probs = knn.predict_proba(x_test)

false_positive_rate, true_positive_rate, thresholds = roc_curve(y_test, y_probs[:,
1])
roc_auc = auc(false_positive_rate, true_positive_rate)
print("KNN classifier AUC: ", roc_auc)
print("Accuracy: ", accuracy_score(y_test, y_pred))
generate_roc_plot(false_positive_rate, true_positive_rate, title = "KNN ROC pot")
```

```
KNN classifier AUC:  0.7114885114885114
Accuracy:  0.7234726688102894
```



In [115]:
```
## SVM classifier tuning function:

from sklearn.svm import SVC

def svm_model(X, y):
    # Perform Grid-Search
    gsc = GridSearchCV(
        estimator=SVC(),
        param_grid={
            'C': (0.5, 1, 10),
            'gamma': ("scale", "auto")
        },
        cv=5, verbose=0, n_jobs=-1)

    grid_result = gsc.fit(X, y)
    best_params = grid_result.best_params_

    svc = SVC(C=best_params["C"],
              gamma=best_params["gamma"],
              verbose=False) # Perform K-Fold CV
    scores = cross_val_score(svc, X, y, cv=10)

    return scores, best_params

svm_model(features, outputs)
```

Out[115]:
```
(array([0.71153846, 0.71153846, 0.70192308, 0.71153846, 0.73786408,
        0.66019417, 0.70873786, 0.70873786, 0.65048544, 0.72815534]),
 {'C': 0.5, 'gamma': 'scale'})
```

In [116]:
```
# SVM Linear kernel next:
from sklearn.svm import SVC

svm = SVC(C = 0.5, kernel = "linear", gamma='scale').fit(x_train, y_train)

y_scores = svm.decision_function(x_test)
y_pred = svm.predict(x_test)

false_positive_rate, true_positive_rate, thresholds = roc_curve(y_test, y_scores)
roc_auc = auc(false_positive_rate, true_positive_rate)
print("SVM linar kernel classifier AUC: ", roc_auc)
print("Accuracy: ", accuracy_score(y_test, y_pred))
```

```
SVM linar kernel classifier AUC:  0.8546453546453546
Accuracy:  0.8102893890675241
```

In [117]:
```
# SVM rbf kernel next: (poly kernal did worse)

from sklearn.svm import SVC

svm = SVC(C = 0.5, kernel = "rbf", degree = 3, gamma='scale').fit(x_train, y_trai
n)

y_scores = svm.decision_function(x_test)
y_pred = svm.predict(x_test)

false_positive_rate, true_positive_rate, thresholds = roc_curve(y_test, y_scores)
roc_auc = auc(false_positive_rate, true_positive_rate)
print("SVM poly kernel classifier AUC: ", roc_auc)
```

```
SVM poly kernel classifier AUC:  0.8211288711288711
```

In [118]:

```
from sklearn.linear_model import LogisticRegression

def lr_model(X, y):
    # Perform Grid-Search
    gsc = GridSearchCV(
        estimator=LogisticRegression(),
        param_grid={
            'C': (0.5, 1, 10),
            'solver': ("lbfgs", "newtong-cg", "saga")
        },
        cv=5, verbose=0, n_jobs=-1)

    grid_result = gsc.fit(X, y)
    best_params = grid_result.best_params_

    lr = LogisticRegression(C=best_params["C"], max_iter = 1000,
                            solver=best_params["solver"],
                            verbose=False) # Perform K-Fold CV
    scores = cross_val_score(lr, X, y, cv=10)

    return scores, best_params

lr_model(features, outputs)
```

```
/Users/Natalie/miniconda3/envs/new_sk/lib/python3.6/site-packages/sklearn/linear
_model/_sag.py:330: ConvergenceWarning: The max_iter was reached which means the
coef_ did not converge
  "the coef_ did not converge", ConvergenceWarning)
/Users/Natalie/miniconda3/envs/new_sk/lib/python3.6/site-packages/sklearn/linear
_model/_sag.py:330: ConvergenceWarning: The max_iter was reached which means the
coef_ did not converge
  "the coef_ did not converge", ConvergenceWarning)
/Users/Natalie/miniconda3/envs/new_sk/lib/python3.6/site-packages/sklearn/linear
_model/_sag.py:330: ConvergenceWarning: The max_iter was reached which means the
coef_ did not converge
  "the coef_ did not converge", ConvergenceWarning)
/Users/Natalie/miniconda3/envs/new_sk/lib/python3.6/site-packages/sklearn/linear
_model/_sag.py:330: ConvergenceWarning: The max_iter was reached which means the
coef_ did not converge
  "the coef_ did not converge", ConvergenceWarning)
/Users/Natalie/miniconda3/envs/new_sk/lib/python3.6/site-packages/sklearn/linear
_model/_sag.py:330: ConvergenceWarning: The max_iter was reached which means the
coef_ did not converge
  "the coef_ did not converge", ConvergenceWarning)
/Users/Natalie/miniconda3/envs/new_sk/lib/python3.6/site-packages/sklearn/linear
_model/_sag.py:330: ConvergenceWarning: The max_iter was reached which means the
coef_ did not converge
  "the coef_ did not converge", ConvergenceWarning)
/Users/Natalie/miniconda3/envs/new_sk/lib/python3.6/site-packages/sklearn/linear
_model/_sag.py:330: ConvergenceWarning: The max_iter was reached which means the
coef_ did not converge
  "the coef_ did not converge", ConvergenceWarning)
/Users/Natalie/miniconda3/envs/new_sk/lib/python3.6/site-packages/sklearn/linear
_model/_sag.py:330: ConvergenceWarning: The max_iter was reached which means the
coef_ did not converge
  "the coef_ did not converge", ConvergenceWarning)
/Users/Natalie/miniconda3/envs/new_sk/lib/python3.6/site-packages/sklearn/linear
_model/_sag.py:330: ConvergenceWarning: The max_iter was reached which means the
coef_ did not converge
  "the coef_ did not converge", ConvergenceWarning)
/Users/Natalie/miniconda3/envs/new_sk/lib/python3.6/site-packages/sklearn/linear
_model/_sag.py:330: ConvergenceWarning: The max_iter was reached which means the
coef_ did not converge
  "the coef_ did not converge", ConvergenceWarning)
/Users/Natalie/miniconda3/envs/new_sk/lib/python3.6/site-packages/sklearn/linear
_model/_sag.py:330: ConvergenceWarning: The max_iter was reached which means the
coef_ did not converge
  "the coef_ did not converge", ConvergenceWarning)
```

```
Out[118]: (array([0.85576923, 0.75      , 0.55769231, 0.76923077, 0.86407767,
                  0.65048544, 0.73786408, 0.67961165, 0.48543689, 0.88349515]),
           {'C': 1, 'solver': 'saga'})
```

```
In [119]: # logistic regression -- lbgfs solver:

lrm = LogisticRegression(max_iter = 1000, C = 0.5).fit(x_train, y_train)

y_scores = lrm.decision_function(x_test)
y_pred = lrm.predict(x_test)

false_positive_rate, true_positive_rate, thresholds = roc_curve(y_test, y_scores)
roc_auc = auc(false_positive_rate, true_positive_rate)
print("Logistic Regression classifier AUC: ", roc_auc)
print("Accuracy: ", accuracy_score(y_test, y_pred))
# generate_roc_plot(false_positive_rate, true_positive_rate, title = "Logistic Reg
ression ROC pot")
```

```
Logistic Regression classifier AUC:  0.8683316683316683
Accuracy:  0.819935691318328
```

```
In [120]: # logistic regression -- saga solver:
          from sklearn.linear_model import LogisticRegression

          lrm = LogisticRegression(max_iter = 1000, solver = "saga", C = 0.5).fit(x_train, y
          _train)

          y_scores = lrm.decision_function(x_test)
          y_pred = lrm.predict(x_test)

          false_positive_rate, true_positive_rate, thresholds = roc_curve(y_test, y_scores)
          roc_auc = auc(false_positive_rate, true_positive_rate)
          print("Logistic Regression classifier AUC: ", roc_auc)
          # generate_roc_plot(false_positive_rate, true_positive_rate, title = "Logistic Reg
          ression ROC pot")
```

```
Logistic Regression classifier AUC:  0.8683816183816184
```

Trying feature selection by SVM next:

```
In [121]: svm = SVC(C = 0.5, kernel = "linear", gamma='scale').fit(x_train, y_train)
          svm.n_support_
```

```
Out[121]: array([183, 276], dtype=int32)
```

```
In [122]: ## svm selected features:

          x_train_svm = x_train[:,svm.support_]
          x_test_svm = x_test[:,svm.support_]

          print(x_train_svm.shape)
          print(x_test_svm.shape)
```

```
(723, 459)
(311, 459)
```

```
In [123]:     ## run best models on SVM selected features only
```

```
In [124]: # Random Forest:

          rfc = RandomForestClassifier(n_estimators = 1000, bootstrap = True, max_depth = 8,
                                       max_features = 'sqrt').fit(x_train_svm, y_train)

          y_pred = rfc.predict(x_test_svm)
          y_probs = rfc.predict_proba(x_test_svm)

          false_positive_rate, true_positive_rate, thresholds = roc_curve(y_test, y_probs[:,
          1])
          roc_auc = auc(false_positive_rate, true_positive_rate)
          print("Random Forest classifier AUC: ", roc_auc)
          print("Accuracy: ", accuracy_score(y_test, y_pred))
```

```
Random Forest classifier AUC:  0.7354145854145854
Accuracy:  0.729903536977492
```

In [125]:
```
# SVM Linear kernel:

svm = SVC(C = 0.5, kernel = "linear", gamma='scale').fit(x_train_svm, y_train)

y_scores = svm.decision_function(x_test_svm)
y_pred = svm.predict(x_test_svm)

false_positive_rate, true_positive_rate, thresholds = roc_curve(y_test, y_scores)
roc_auc = auc(false_positive_rate, true_positive_rate)
print("SVM linar kernel classifier AUC: ", roc_auc)
print("Accuracy: ", accuracy_score(y_test, y_pred))
```

```
SVM linar kernel classifier AUC:  0.705944055944056
Accuracy:  0.707395498392283
```

In [126]:
```
# logistic regression -- lbgfs solver:

lrm = LogisticRegression(max_iter = 1000, C = 0.5).fit(x_train_svm, y_train)

y_scores = lrm.decision_function(x_test_svm)
y_pred = lrm.predict(x_test_svm)

false_positive_rate, true_positive_rate, thresholds = roc_curve(y_test, y_scores)
roc_auc = auc(false_positive_rate, true_positive_rate)
print("Logistic Regression classifier AUC: ", roc_auc)
print("Accuracy: ", accuracy_score(y_test, y_pred))
```

```
Logistic Regression classifier AUC:  0.750949050949051
Accuracy:  0.7459807073954984
```

```
Alrighty; those did not improve!
Next look RFE feature selection:
```

In [127]:
```
# narrow to 100 features:
svm = SVC(C = 0.5, kernel = "linear", gamma='scale').fit(x_train, y_train)
#lr = LogisticRegression(max_iter = 1000)

rfs100 = RFE(estimator=svm, n_features_to_select=100 ,step=50).fit(features, outpu
ts)

rfs100.n_features_
```

Out[127]:
```
100
```

In [165]:
```
# save names of top 100 features selected by RFE

m2_rfe_features = pd_impute.iloc[:,1:].columns[rfs100.support_]
```

In [128]:
```
# make selected feature sets:

x_train_rfs100 = x_train[:,rfs100.support_]
x_test_rfs100 = x_test[:,rfs100.support_]

print(x_train_rfs100.shape)
print(x_test_rfs100.shape)
```

```
(723, 100)
(311, 100)
```

In [129]:
```
    ## run random forest, SVM, and logistic regression on the selected features:
```

In [130]:
```
# Random Forest:

rfc = RandomForestClassifier(n_estimators = 1000, bootstrap = True, max_depth = 8,
                             max_features = 'sqrt').fit(x_train_rfs100, y_train)

y_pred = rfc.predict(x_test_rfs100)
y_probs = rfc.predict_proba(x_test_rfs100)

false_positive_rate, true_positive_rate, thresholds = roc_curve(y_test, y_probs[:,
1])
roc_auc = auc(false_positive_rate, true_positive_rate)
print("Random Forest classifier AUC: ", roc_auc)
print("Accuracy: ", accuracy_score(y_test, y_pred))
```

```
Random Forest classifier AUC:  0.7983016983016984
Accuracy:  0.7427652733118971
```

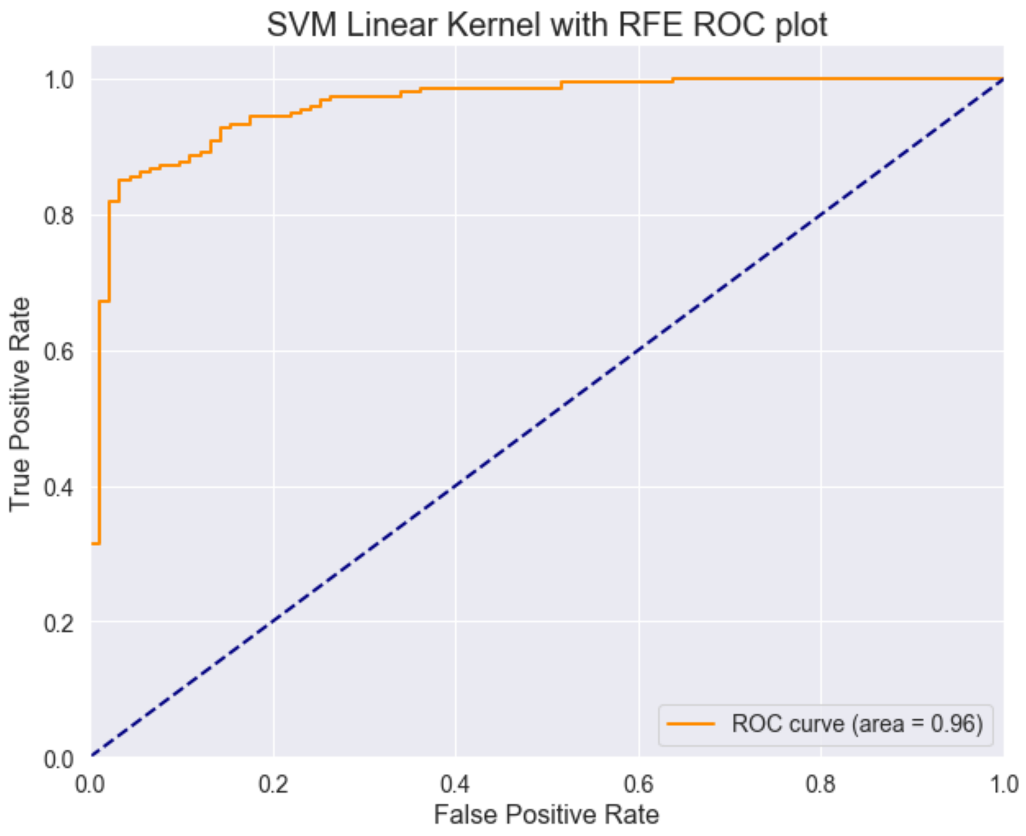
In [132]:
```
## SVM Tuning:

def svm_model(X, y):
    # Perform Grid-Search
    gsc = GridSearchCV(
        estimator=SVC(),
        param_grid={
            'kernel': ("rbf", "linear"),
            'C': (0.5, 1, 10),
            'gamma': ("scale", "auto")
        },
        cv=5, verbose=0, n_jobs=-1)

    grid_result = gsc.fit(X, y)
    best_params = grid_result.best_params_

    svc = SVC(C=best_params["C"],
              kernel=best_params["kernel"],
              gamma=best_params["gamma"],
              verbose=False) # Perform K-Fold CV
    scores = cross_val_score(svc, X, y, cv=10)
    return scores, best_params

svm_model(features[:,rfs100.support_], outputs)
```

Out[132]:
```
(array([0.90384615, 0.90384615, 0.86538462, 0.875     , 0.96116505,
        0.89320388, 0.91262136, 0.90291262, 0.80582524, 0.9223301 ]),
 {'C': 10, 'gamma': 'scale', 'kernel': 'linear'})
```

In [134]:
```
# SVM Linear kernel:

svm_best = SVC(C = 0.5, kernel = "linear", gamma='scale').fit(x_train_rfs100, y_tr
ain)

y_scores = svm_best.decision_function(x_test_rfs100)
y_pred = svm_best.predict(x_test_rfs100)

false_positive_rate, true_positive_rate, thresholds = roc_curve(y_test, y_scores)
roc_auc = auc(false_positive_rate, true_positive_rate)
print("SVM linar kernel classifier AUC: ", roc_auc)
print("Accuracy: ", accuracy_score(y_test, y_pred))
```

```
SVM linar kernel classifier AUC:  0.9613886113886114
Accuracy:  0.9067524115755627
```

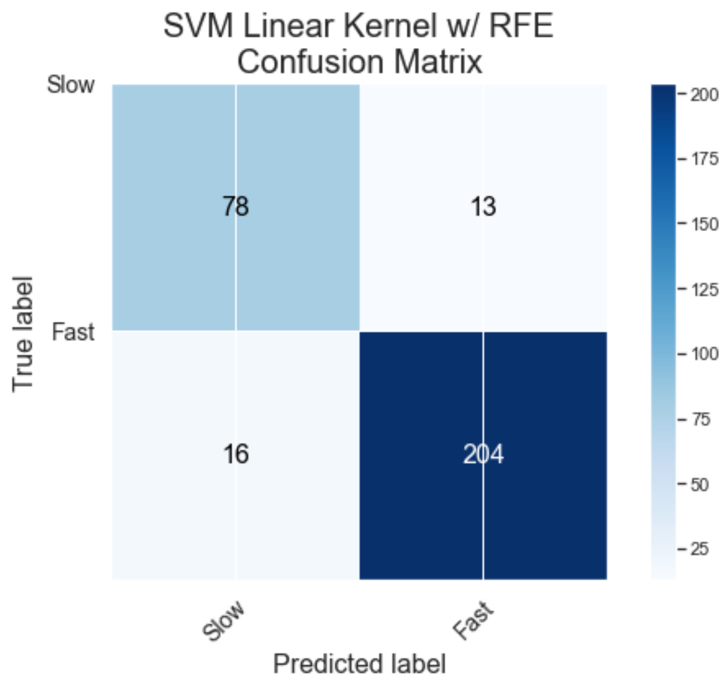
In [135]:
```
generate_roc_plot(false_positive_rate, true_positive_rate, title = "SVM Linear Ker
nel with RFE ROC plot")
```



In [138]:
```
plot_confusion_matrix(y_true = y_test, y_pred = y_pred, classes = df2["ClearanceRa
te"], title = "SVM Linear Kernel w/ RFE\nConfusion Matrix")
```

```
Confusion matrix, without normalization
[[ 78  13]
 [ 16 204]]
(2, 2)
```

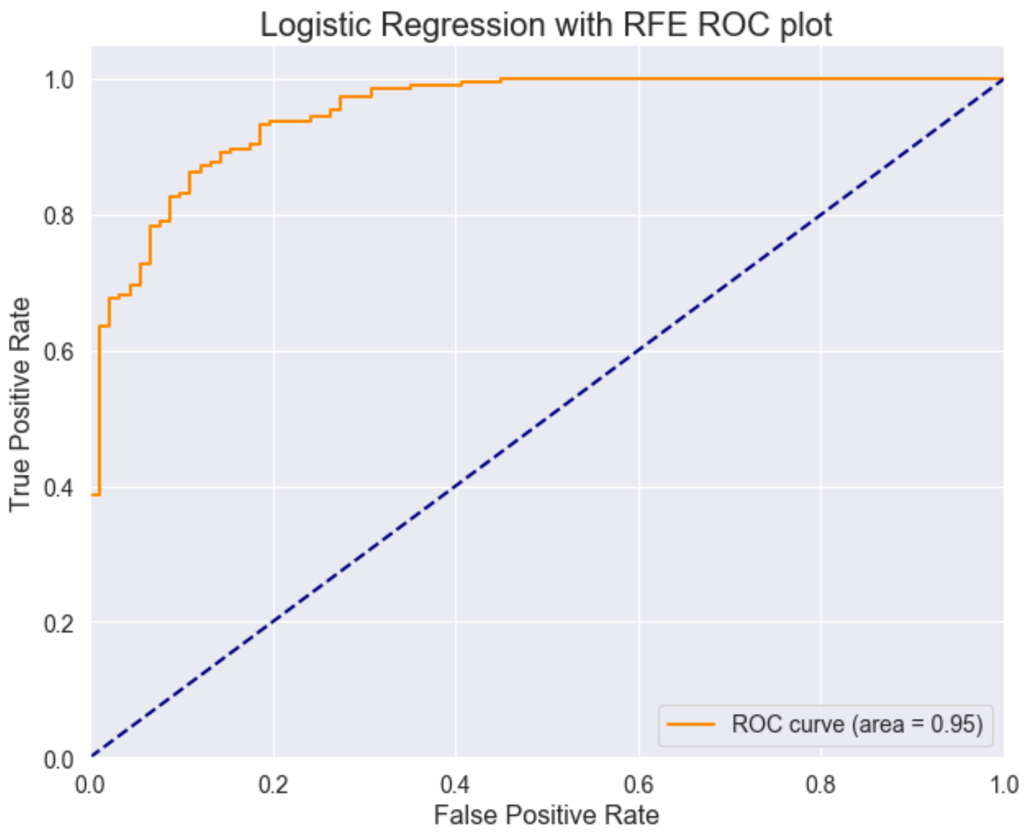
Out[138]:
```
<matplotlib.axes._subplots.AxesSubplot at 0x11e036940>
```



In [139]:
```
# logistic regression -- lbgfs solver:

lrm = LogisticRegression(max_iter = 1000, C = 0.5).fit(x_train_rfs100, y_train)

y_scores = lrm.decision_function(x_test_rfs100)
y_pred = lrm.predict(x_test_rfs100)

false_positive_rate, true_positive_rate, thresholds = roc_curve(y_test, y_scores)
roc_auc = auc(false_positive_rate, true_positive_rate)
print("Logistic Regression classifier AUC: ", roc_auc)
print("Accuracy: ", accuracy_score(y_test, y_pred))
```

```
Logistic Regression classifier AUC:  0.9511988011988013
Accuracy:  0.8938906752411575
```

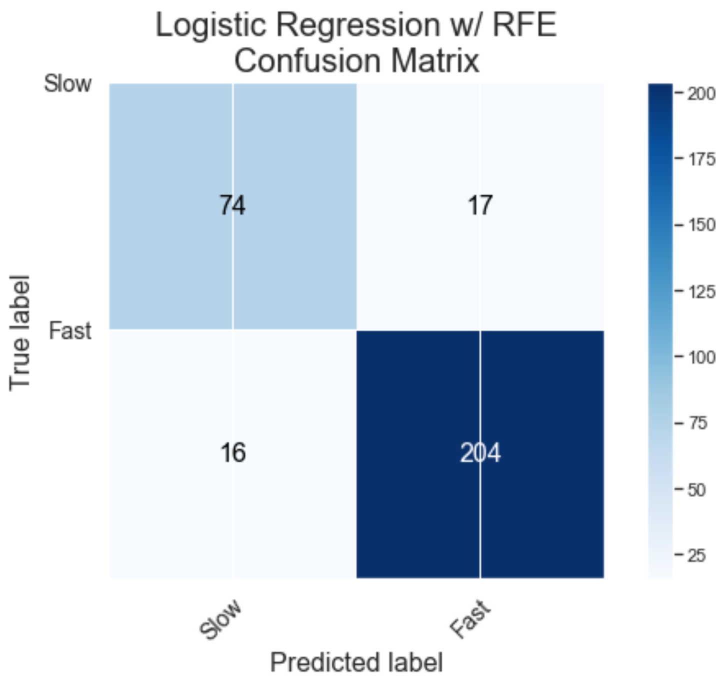
In [140]:
```
generate_roc_plot(false_positive_rate, true_positive_rate, title = "Logistic Regre
ssion with RFE ROC plot")
```



In [141]:
```
plot_confusion_matrix(y_true = y_test, y_pred = y_pred, classes = df2["ClearanceRa
te"], title = "Logistic Regression w/ RFE\nConfusion Matrix")
# cmap=plt.cm.Blues
```

```
Confusion matrix, without normalization
[[ 74  17]
 [ 16 204]]
(2, 2)
```

Out[141]:
```
<matplotlib.axes._subplots.AxesSubplot at 0x11fa90a90>
```



In [142]:
```
from sklearn.discriminant_analysis import LinearDiscriminantAnalysis

lda = LinearDiscriminantAnalysis(solver = "svd").fit(x_train_rfs100, y_train)

y_scores = lda.decision_function(x_test_rfs100)
y_pred = lda.predict(x_test_rfs100)

false_positive_rate, true_positive_rate, thresholds = roc_curve(y_test, y_scores)
roc_auc = auc(false_positive_rate, true_positive_rate)
print("LDA classifier AUC: ", roc_auc)
print("Accuracy: ", accuracy_score(y_test, y_pred))
```

```
LDA classifier AUC:  0.9434065934065934
Accuracy:  0.8681672025723473
```

In [143]:
```
## Next try selecting top 50 features with RFE:

# Create the RFE object and rank each feature
svm = SVC(C = 0.5, kernel = "linear", gamma='scale').fit(x_train, y_train)
#lr = LogisticRegression(max_iter = 1000)

rfs50 = RFE(estimator=svm, n_features_to_select=50 ,step=25).fit(features, output
s)

rfs50.n_features_
```

Out[143]:
```
50
```

In [144]:
```
x_train_rfs50 = x_train[:,rfs50.support_]
x_test_rfs50 = x_test[:,rfs50.support_]

print(x_train_rfs50.shape)
print(x_test_rfs50.shape)
```

```
(723, 50)
(311, 50)
```

In [146]:
```
# Random Forest:

rfc = RandomForestClassifier(n_estimators = 1000, bootstrap = True, max_depth = 8,
                             max_features = 'sqrt').fit(x_train_rfs50, y_train)

y_pred = rfc.predict(x_test_rfs50)
y_probs = rfc.predict_proba(x_test_rfs50)

false_positive_rate, true_positive_rate, thresholds = roc_curve(y_test, y_probs[:,
1])
roc_auc = auc(false_positive_rate, true_positive_rate)
print("Random Forest classifier AUC: ", roc_auc)
```

```
Random Forest classifier AUC:  0.8153346653346654
```

In [147]:
```
# SVM Linear kernel:

svm = SVC(C = 0.5, kernel = "linear", gamma='scale').fit(x_train_rfs50, y_train)

y_scores = svm.decision_function(x_test_rfs50)
y_pred = svm.predict(x_test_rfs50)

false_positive_rate, true_positive_rate, thresholds = roc_curve(y_test, y_scores)
roc_auc = auc(false_positive_rate, true_positive_rate)
print("SVM linar kernel classifier AUC: ", roc_auc)
```

```
SVM linar kernel classifier AUC:  0.9378121878121878
```

In [148]:
```
# logistic regression -- lbgfs solver:

lrm = LogisticRegression(max_iter = 1000, C = 0.5).fit(x_train_rfs50, y_train)

y_scores = lrm.decision_function(x_test_rfs50)
y_pred = lrm.predict(x_test_rfs50)

false_positive_rate, true_positive_rate, thresholds = roc_curve(y_test, y_scores)
roc_auc = auc(false_positive_rate, true_positive_rate)
print("Logistic Regression classifier AUC: ", roc_auc)
```

```
Logistic Regression classifier AUC:  0.9362637362637363
```

In [ ]:

```
```

MODEL FEATURE INTERSECTION:

In [170]:
```
# Look at the interesection between the features for the best models for each data
set:
#m1_rfe_features = dfmean.iloc[:,1:-1].columns[rfs100.support_]
#m2_rfe_features = pd_impute.iloc[:,1:].columns[rfs100.support_]

np.intersect1d(m1_rfe_features, m2_rfe_features)
```

Out[170]:
```
array(['PF3D7_0502400', 'PF3D7_0902600', 'PF3D7_1001000', 'PF3D7_1240400'],
      dtype=object)
```

```
CROSS APPLYING CLASSIFICATION MODEL:
```

Try applying Model 2 (the classifier) to the in vitro (dataset 1) micro array data:

In [156]:
```
unperturbed_mask = df["Treatment"] == "UT"
df_xapply = df[unperturbed_mask]
```

In [157]:
```
df_xapply["Timepoint"] = df_xapply["Timepoint"].apply(time_convert)
df_xapply.shape
```

```
/Users/Natalie/miniconda3/envs/new_sk/lib/python3.6/site-packages/ipykernel_laun
cher.py:1: SettingWithCopyWarning:
A value is trying to be set on a copy of a slice from a DataFrame.
Try using .loc[row_indexer,col_indexer] = value instead

See the caveats in the documentation: http://pandas.pydata.org/pandas-docs/stabl
e/user_guide/indexing.html#returning-a-view-versus-a-copy
  """Entry point for launching an IPython kernel.
```

Out[157]:
```
(136, 5546)
```

In [158]:
```
xapply_features = df_xapply[m2_rfe_features].to_numpy()
xapply_labels = df_xapply["DHA_IC50"].to_numpy()

print(xapply_features.shape)
print(xapply_labels.shape)
```

```
(136, 100)
(136,)
```

In [159]:
```
# apply best SVM Linear model to this data!

xapply_pred = svm_best.predict(xapply_features)
```

In [160]:
```
xapply_out = pd.DataFrame([xapply_labels, xapply_pred]).transpose()
xapply_out.columns = ["IC_50", "Predicted_Clearance"]
xapply_out["Predicted_Clearance"] = xapply_out["Predicted_Clearance"].replace(0, "
Slow")
xapply_out["Predicted_Clearance"] = xapply_out["Predicted_Clearance"].replace(1, "
Fast")
```

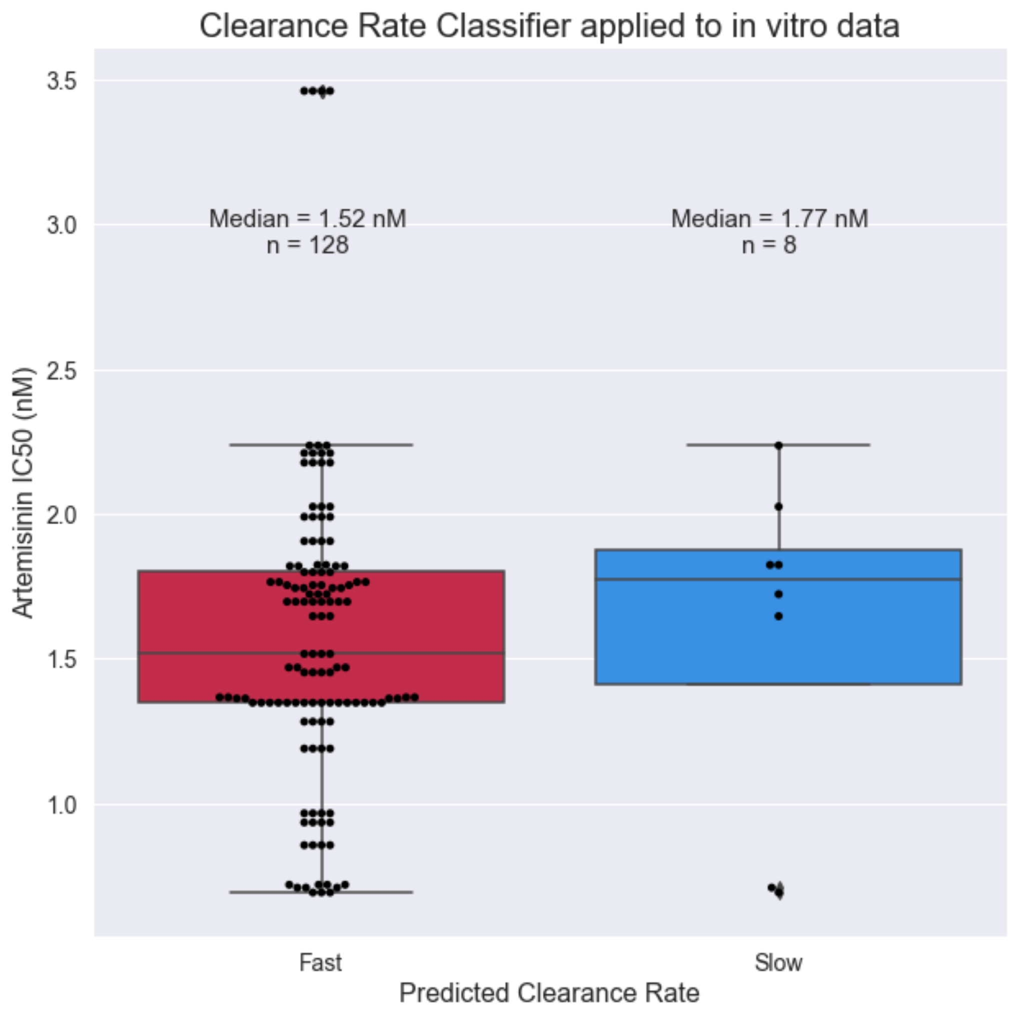
In [161]:
```
xapply_out["Predicted_Clearance"].value_counts()
```

Out[161]:
```
Fast    128
Slow      8
Name: Predicted_Clearance, dtype: int64
```

```
In [163]: xapply_out.groupby("Predicted_Clearance").median()
Out[163]:
```

Predicted_Clearance	IC_50
Fast	1.5170
Slow	1.7735

```
In [164]: plt.figure(figsize = (10, 10))
          my_palette = {"Fast": "crimson", "Slow": "dodgerblue"}
          sns.boxplot(y = "IC_50", x = "Predicted_Clearance", data = xapply_out, palette = m
          y_palette)
          sns.swarmplot(y = "IC_50", x = "Predicted_Clearance", data = xapply_out, color = "
          black")
          plt.xlabel('Predicted Clearance Rate', fontsize = 16)
          plt.ylabel('Artemisinin IC50 (nM)', fontsize = 16)
          plt.title("Clearance Rate Classifier applied to in vitro data", fontsize = 20)
          plt.xticks(fontsize=14)
          plt.yticks(fontsize=14)
          plt.text(x = -0.03, y = 2.9, s = "Median = 1.52 nM\nn = 128", fontsize=15, ha = "c
          enter")
          plt.text(x = 0.98, y = 2.9, s = "Median = 1.77 nM\nn = 8", fontsize=15, ha = "cent
          er")
          plt.show()
```



```
In [ ]:
```