Assignment 4

Problem 1

In this problem, you will predict tumor type from gene expression data. Since there are many more gene features than observations of patients, we will use ridge and LASSO regularization for logistic regression to reduce overfitting and help select the most relevant features out of a large group of features. This dataset has a multi-class outcome variable. The possible tumor types are BRCA, COAD, KIRC, LUAD, or PRAD. You will analyze this dataset by building a multinomial regression model with 1 and 2 regularization. The recommended approach is the glmnet package in R, which is covered in the code in class. You can check the "Multinomial Regression" section found at this link for specific information about multinomial regression in glmnet.

(a) Load the labels and data with read.csv. Remove any columns with missing entries. Remove any columns with variance less than 0.001. Standardize each gene predictor column to have mean 0 and standard deviation 1 (this is important when doing regularized regression). Split the dataset randomly into a training and validation set.

In [1]:
```
#%% Step 1 - Load Data & Prep Data
import pandas as pd;

x = pd.read_table('C:/Users/danma/Downloads/gene_data.csv', sep=",",)
y = pd.read_table('C:/Users/danma/Downloads/gene_labels.csv', sep=",",)

#possibly remove sample name column
x = x.iloc[: , 1:]
y = y.iloc[: , 1:]

from sklearn.preprocessing import OrdinalEncoder
enc = OrdinalEncoder()
y = enc.fit_transform(y)
y = pd.DataFrame(y, columns = ["Class"])

print(x.head())
print(y.head())
#%% Step 2 - Remove Variance < 0.001
from sklearn.feature_selection import VarianceThreshold

selector = VarianceThreshold(threshold = 0.001)
selector.fit(x)

concol = [column for column in x.columns
          if column not in x.columns[selector.get_support()]]

#print("Columns with Variance < 0.001")
#for features in concol:
#    print(features)

x_reduced = x.drop(concol,axis=1)

del concol, selector
#%% Step 3 - Standardize the Data
from sklearn.preprocessing import StandardScaler
```

```
scaler = StandardScaler()
x_scaled = scaler.fit_transform(x_reduced)

x_scaled = pd.DataFrame(x_scaled, columns = x_reduced.columns)#return to dataframe with column n

del x_reduced, scaler, x
#%% Step 4 - Split Data
from sklearn.model_selection import train_test_split

x_train, x_test, y_train, y_test = train_test_split(x_scaled, y)
print(x_train.dtypes)
del y
```

```
   gene_0    gene_1    gene_2    gene_3     gene_4  gene_5    gene_6  \
0     0.0  2.017209  3.265527  5.478487  10.431999     0.0  7.175175   
1     0.0  0.592732  1.588421  7.586157   9.623011     0.0  6.816049   
2     0.0  3.511759  4.327199  6.881787   9.870730     0.0  6.972130   
3     0.0  3.663618  4.507649  6.659068  10.196184     0.0  7.843375   
4     0.0  2.655741  2.821547  6.539454   9.738265     0.0  6.566967   

     gene_7  gene_8  gene_9  ...  gene_20521  gene_20522  gene_20523  \
0  0.591871     0.0     0.0  ...    4.926711    8.210257    9.723516   
1  0.000000     0.0     0.0  ...    4.593372    7.323865    9.740931   
2  0.452595     0.0     0.0  ...    5.125213    8.127123   10.908640   
3  0.434882     0.0     0.0  ...    6.076566    8.792959   10.141520   
4  0.360982     0.0     0.0  ...    5.996032    8.891425   10.373790   

   gene_20524  gene_20525  gene_20526  gene_20527  gene_20528  gene_20529  \
0    7.220030    9.119813   12.003135    9.650743    8.921326    5.286759   
1    6.256586    8.381612   12.674552   10.517059    9.397854    2.094168   
2    5.401607    9.911597    9.045255    9.788359   10.090470    1.683023   
3    8.942805    9.601208   11.392682    9.694814    9.684365    3.292001   
4    7.181162    9.846910   11.922439    9.217749    9.461191    5.110372   

   gene_20530  
0         0.0  
1         0.0  
2         0.0  
3         0.0  
4         0.0  

[5 rows x 20531 columns]
   Class
0    4.0
1    3.0
2    4.0
3    4.0
4    0.0
gene_0        float64
gene_1        float64
gene_2        float64
gene_3        float64
gene_4        float64
               ...   
gene_20526    float64
gene_20527    float64
gene_20528    float64
gene_20529    float64
gene_20530    float64
Length: 20221, dtype: object
```

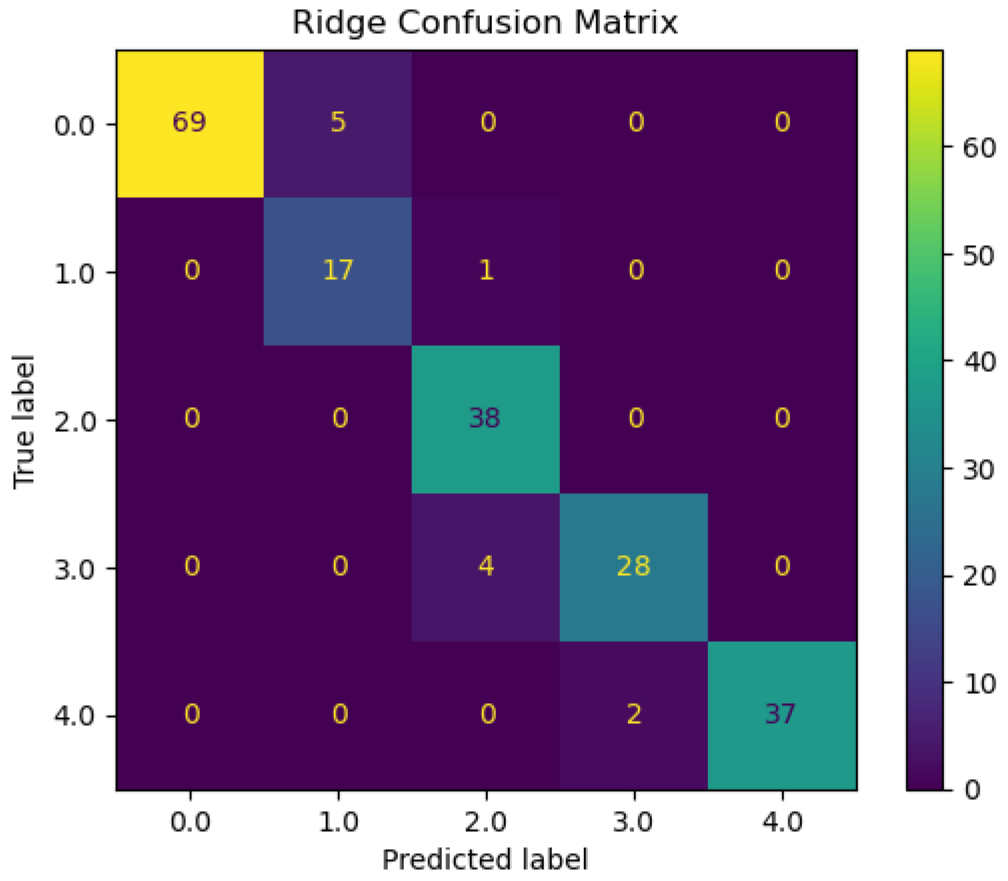
(b) Use ridge logistic regression with 10-fold cross validation to model the response given the gene expression predictors. What is your optimal value of the regularization

parameter λ? Apply your model to give predictions using the optimal value of λ. Make a confusion matrix showing the accuracy of your model on the training and test set.

In [2]:
```
#%% Step 4.5 Testing Logistic Regression and RidgeClassification to ensure that they yield the s
#from sklearn.linear_model import LogisticRegressionCV
import warnings
warnings.filterwarnings('ignore')
#clf = LogisticRegressionCV(cv=10, random_state=0, Cs=list_alphas, penalty="l2", solver="saga", 
#print(clf.Cs)

#y_ridge_pred = clf.predict(x_test)
#from sklearn.linear_model import RidgeClassifierCV
#list_alphas = [1e-15, 1e-10, 1e-8, 1e-5, 1e-4, 1e-3,1e-2, 1e-1, 1, 5, 10, 20]
#clf = RidgeClassifierCV(cv=10, alphas=list_alphas).fit(x_train, y_train.values.ravel())
#print("Ridge optimal λ = ",clf.alpha_)

#y_ridge_pred = clf.predict(x_test)

#from sklearn.metrics import confusion_matrix
#using ravel to create single array and round to create classifier prediction for confusion matr
#print(confusion_matrix(y_test.values.ravel(),y_ridge_pred.round(0)))
#matrix shows exact match

#%% Step 5 - Ridge Regression, 10 Fold, Optimal Lambda, Confusion Matrix Accuracy
from sklearn.linear_model import RidgeCV
import numpy as np
#list_alphas = np.logspace(-15, 1.35, 400) ran large range but defaulted at the 1e-15 after a 5 
list_alphas = [1e-15, 1e-10, 1e-8, 1e-5, 1e-4, 1e-3,1e-2, 1e-1, 1, 5, 10, 20]
clf = RidgeCV(cv=10, alphas=list_alphas).fit(x_train, y_train.values.ravel())
print("Ridge optimal λ = ",clf.alpha_)

y_ridge_pred = clf.predict(x_test)

from sklearn.metrics import confusion_matrix
#using ravel to create single array and round to create classifier prediction for confusion matr
cm = confusion_matrix(y_test.values.ravel(),y_ridge_pred.round(0))
print(cm)

from sklearn.metrics import confusion_matrix, ConfusionMatrixDisplay
disp = ConfusionMatrixDisplay.from_predictions(y_test.values.ravel(),y_ridge_pred.round(0))
disp.ax_.set_title("Ridge Confusion Matrix")
```

```
Ridge optimal λ =  1e-15
[[69  5  0  0  0]
 [ 0 17  1  0  0]
 [ 0  0 38  0  0]
 [ 0  0  4 28  0]
 [ 0  0  0  2 37]]
```

Out[2]:
```
Text(0.5, 1.0, 'Ridge Confusion Matrix')
```

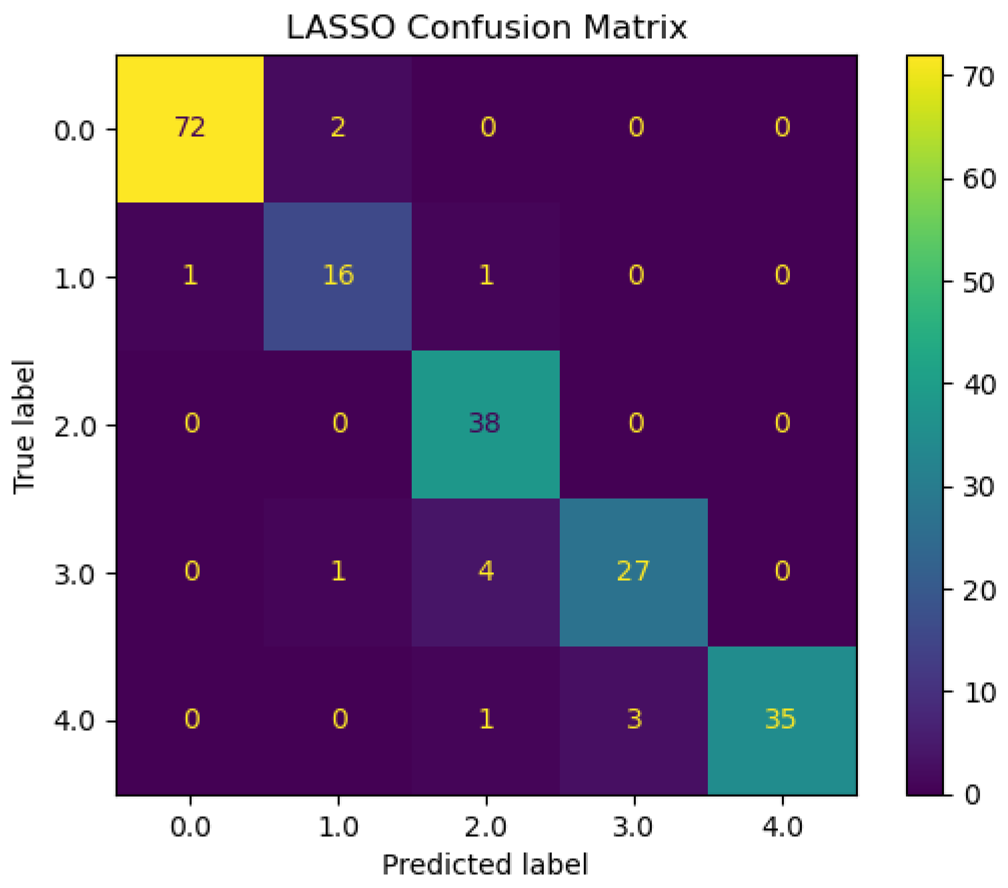


(c) Use LASSO logistic regression with 10-fold cross validation to model the response given the gene expression predictors. What is your optimal value of the regularization parameter λ? Apply your model to give predictions using the optimal value of λ. Make a confusion matrix showing the accuracy of your model on the training and test set.

In [3]:
```
#%% Step 6 - LASSO Regression, 10 Fold, Optimal Lambda, Confusion Matrix Accuracy
from sklearn.linear_model import LassoCV
list_alphas = np.logspace(-15, 1.35, 400)
reg = LassoCV(cv=10, alphas=list_alphas, n_jobs=-1, positive=True).fit(x_train, y_train.values.r
print("LASSO optimal λ = ",reg.alpha_)

y_lasso_pred = reg.predict(x_test)

cm = confusion_matrix(y_test.values.ravel(),y_lasso_pred.round(0))
print(cm)
#matrix shows incorrect guesses and a wider range
from sklearn.metrics import confusion_matrix, ConfusionMatrixDisplay
disp = ConfusionMatrixDisplay.from_predictions(y_test.values.ravel(),y_lasso_pred.round(0))
disp.ax_.set_title("LASSO Confusion Matrix")
```

```
LASSO optimal λ =  0.01720736162119889
[[72  2  0  0  0]
 [ 1 16  1  0  0]
 [ 0  0 38  0  0]
 [ 0  1  4 27  0]
 [ 0  0  1  3 35]]
```

Out[3]:
```
Text(0.5, 1.0, 'LASSO Confusion Matrix')
```



(d) Give a list of the top 20 most relevant genes that are selected by your LASSO model at the optimal value of λ. The coefficients for a multinomial regression model will be a p × C matrix where C is the number of classes and p is the number of feature columns. What relation do your selected genes have to tumor expression? You can determine this by looking at which of the C coefficients associated with a certain gene are non-zero. Positive values in a certain index correspond to a high probability of the tumor associated with that index, while negative values correspond to a lower probability.

In [4]:
```
#%% Step 7 - 20 Most Relevant Predictors from LASSO
#%% Step 7.1 - Fitting Logistic Regression to get Coef for all Tumors
from sklearn.linear_model import LogisticRegression
#fitting Logistic Regression for All Coefficients
lasso = LogisticRegression(C=(1/reg.alpha_), penalty="l1", solver="saga", n_jobs=-1, max_iter=50
lasso.fit(x_train, y_train.values.ravel())

y_pred = lasso.predict(x_test)

from sklearn.metrics import confusion_matrix, ConfusionMatrixDisplay
disp = ConfusionMatrixDisplay.from_predictions(y_test.values.ravel(),y_pred)
disp.ax_.set_title("Logistic(L1) Confusion Matrix")

#%% Step 7.2 - Pull Coefficient Matrix from Logistic Regression
imp = lasso.coef_
imp = imp.transpose()
#%% Step 7.3 - Coefficients from LASSO model
import numpy as np
importance = pd.DataFrame({'gene': reg.feature_names_in_, 'coef': reg.coef_}, columns=['gene', '
importancesorted = importance.sort_values(by=['coef'], ascending=False)
top20 = importancesorted.head(20)
print("Top 20 Most Relevant Genes from LASSO:\n")
from tabulate import tabulate
print(tabulate(top20, headers='keys', tablefmt='fancy_grid', showindex=False))
#%% Step 8 - Relation of Genes to Tumors
#%% Step 8.1 - Top20(LASSO) from LogReg
```

```
cat = enc.categories_[0]
importance[enc.categories_[0]] = imp
importancesorted = importance.sort_values(by=['coef'], ascending=False)
top20 = importancesorted.head(20)
print("Top 20 Most Relevant Genes from LASSO with Coefficients from LogReg(L1):\n")
from tabulate import tabulate
print(tabulate(top20, headers='keys', tablefmt='fancy_grid', showindex=False))
#%% Step 8.2 - Relation
#swap negatives for low, positives for high, zeros for none
values = top20.iloc[: , -5:]
values[values < 0] = -1
values[values > 0] = 1

mapping = {1:'high prob', -1:'low prob', 0:'no relation'}
values = values.astype(int).replace({'BRCA': mapping, 'COAD': mapping, 'KIRC': mapping, 'LUAD':
#drop coef column, and print new dataframe with labels rather than numerical coef
values.insert (0, 'gene', top20['gene'])

from tabulate import tabulate
print(tabulate(values, headers='keys', tablefmt='fancy_grid', showindex=False))
```

Top 20 Most Relevant Genes from LASSO:

gene	coef
gene_7964	0.239987
gene_17801	0.148374
gene_15895	0.139831
gene_9175	0.104834
gene_15896	0.0934613
gene_14798	0.0836215
gene_6748	0.0776556
gene_17354	0.0602209
gene_17947	0.0560126
gene_15897	0.0537163
gene_1985	0.0500587
gene_17770	0.0496268
gene_16372	0.0472182
gene_3448	0.044937
gene_1096	0.0384208
gene_11352	0.0375544
gene_4178	0.0368476
gene_18745	0.0341307
gene_12995	0.03376
gene_89	0.0325858

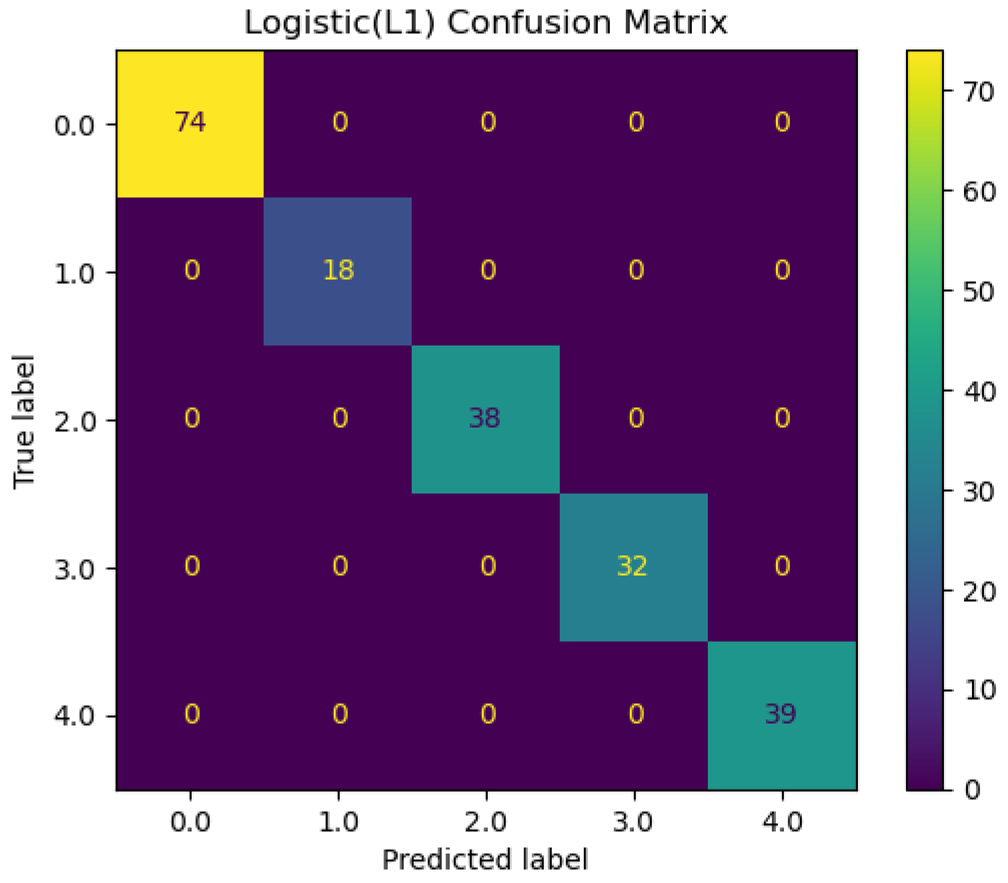
Top 20 Most Relevant Genes from LASSO with Coefficients from LogReg(L1):

gene	coef	BRCA	COAD	KIRC	LUAD	PRAD
gene_7964	0.239987	-0.0119166	0.000293193	0.00247657	0.00302671	0
gene_17801	0.148374	-0.0116178	1.6951e-05	0	0.00256883	0.00365369
gene_15895	0.139831	-0.00437362	-0.00128574	-0.00146497	0.0133789	0

gene_9175	0.104834	-0.00184726	0	-3.14153e-05	-0.000539021	0.00859551
gene_15896	0.0934613	-0.00479577	-0.00244398	-0.00152268	0.014313	0
gene_14798	0.0836215	-0.00349389	0	0	0	0.00726285
gene_6748	0.0776556	-0.00955641	0.00027983	0	0.00183729	0.0023235
gene_17354	0.0602209	-0.00613088	-0.000337495	0	0.000684865	0.00362625
gene_17947	0.0560126	-0.00858408	0	0.000569894	0.00294707	0.00183268
gene_15897	0.0537163	-0.00618079	-0.00141973	-0.00287263	0.0111935	0.00150453
gene_1985	0.0500587	-0.00123909	-0.00135218	0	0.0024306	0
gene_17770	0.0496268	-0.00530287	-0.00151893	-0.0023983	0.0102311	0.00121388
gene_16372	0.0472182	-0.00877967	0	0.00157926	0.000727958	0.00307611
gene_3448	0.044937	-0.00423893	-0.00284569	-0.000559029	0.00439151	0.00547704
gene_1096	0.0384208	-0.00326005	0	0	-0.000927262	0.00754385
gene_11352	0.0375544	-0.00283576	-0.00133562	-0.00132521	0.0115707	0
gene_4178	0.0368476	-0.00304655	-0.000235833	-0.000373665	0	0.00686411
gene_18745	0.0341307	-0.00356398	-0.00157403	0	0	0.00685959
gene_12995	0.03376	-0.00375339	0	0	-0.000112193	0.00736767

gene_89	0.0325858	-0.00743663	0	0	0	0.0051108

gene	BRCA	COAD	KIRC	LUAD	PRAD
gene_7964	low prob	high prob	high prob	high prob	no relation
gene_17801	low prob	high prob	no relation	high prob	high prob
gene_15895	low prob	low prob	low prob	high prob	no relation
gene_9175	low prob	no relation	low prob	low prob	high prob
gene_15896	low prob	low prob	low prob	high prob	no relation
gene_14798	low prob	no relation	no relation	no relation	high prob
gene_6748	low prob	high prob	no relation	high prob	high prob
gene_17354	low prob	low prob	no relation	high prob	high prob
gene_17947	low prob	no relation	high prob	high prob	high prob
gene_15897	low prob	low prob	low prob	high prob	high prob
gene_1985	low prob	low prob	no relation	high prob	no relation
gene_17770	low prob	low prob	low prob	high prob	high prob
gene_16372	low prob	no relation	high prob	high prob	high prob
gene_3448	low prob	low prob	low prob	high prob	high prob
gene_1096	low prob	no relation	no relation	low prob	high prob
gene_11352	low prob	low prob	low prob	high prob	no relation
gene_4178	low prob	low prob	low prob	no relation	high prob
gene_18745	low prob	low prob	no relation	no relation	high prob
gene_12995	low prob	no relation	no relation	low prob	high prob
gene_89	low prob	no relation	no relation	no relation	high prob



Note: If columns are highly correlated, LASSO will often arbitrarily select a single column, so a full report of relevent genes would involve predictors selected by LASSO and genes that are highly correlated. Other techniques like group LASSO can select subsets of related genes, these will not be covered in this class. You could also try to combine the 1 and 2 penalties to get representation of meaningful predictors that are also correlated (see the reference material above).