Quantify deregulation of pathways in cancer

Yotam Drier

April 24, 2017

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1 Introduction

The pathifier is an algorithm that infers pathway deregulation scores for each tumor sample on the basis of expression data. This score is determined, in a context-specific manner, for every particular dataset and type of cancer that is being investigated. The algorithm transforms gene-level information into pathway-level information, generating a compact and biologically relevant representation of each sample [1]. As the algorithm learns the pathway normal flow from normal samples, expression of relevant normal samples must be supplied, however, the structure of the pathway need not be given, just the identity of genes taking part in each pathway.

2 Analyzing data set using pathifier library

2.1 Load the library

Load the pathifier library:

> library(pathifier)
2.2 Load the data set
Load the data set ‘Sheffer’ (built in Pathifier package) [2].

> data(Sheffer)

2.3 Load pathway database
Load the two pathways (MISMATCH REPAIR and REGULATION OF AUTOPHAGY) by KEGG [3] (supplied with the package)

> data(KEGG)

2.4 Quantify deregulation of pathways
Calculate the deregulation score by running pathifier

> PDS<-quantify_pathways_deregulation(sheffer$data, sheffer$allgenes, +   kegg$gs, kegg$pathwaynames, sheffer$normals, attempts = 100, +   min_exp=sheffer$minexp, min_std=sheffer$minstd)

robust_score_bydist. min_exp= 4 , min_std= 0.2254005
pathway 1 > sig: 0.08223931
pathway 2 > sig: 0.09600581
2 pathways processed with start= by ranks

The deregulation scores are now in PDS$scores, ready for further analysis.

2.5 Brief analysis
Show scores for normals samples are generally lower

> x<-NULL
> x$normals<-PDS$scores$MISMATCH_REPAIR[sheffer$normals]
> x$tumors<-PDS$scores$MISMATCH_REPAIR[!sheffer$normals]
> boxplot(x)
> boxplot(x, ylab="score")
List samples whose regulation of autophagy is highly deregulated

```r
> as.character(sheffer$samples[PDS$scores$REGULATION_OF_AUTOPHAGY>0.8])
```

1. "00485_U_13/02/2004_63_F_WN_2_1_0_4_DOD_80 _Y_19 _S_B_W_M_TT_M_O_8_L_4.8 _XX_2_2 _8
2. "00888_B_2/7/2003 _69_M_WN_3_0_0_0_DUN_46 _X_46 _S_?_W_W_TT_M_O_9_L_4 _XX_X_0 _21
3. "00947_U_2/7/2003 _62_M_WN_3_1_1_4_DOD_39 _Y_5 _O_B_W_M_TT_O_0_7_L_X _XX_2_1 _17
4. "03752_A_3/7/2003 _54_M_WN_2_0_0_1_NED_136_X_136_S_G_W_M_TT_M_Y_8_L_6 _S3_2_0 _11
5. "03820_V_22/07/2003_72_F_WN_1_0_0_4_NED_200_Y_83 _O_?_W_W_0 _M_0_7_L_X _XX_2_0 _X

References
