**Additional Table 1. Coverage of database regulons**. It includes four tables, one per annotation

database and spreadsheet, that show the percentage of terms that are covered by the TFs

provided by TRRUST v2 and DoRothEA as well as the different databases of regulons.

**Additional Table 2. Results of GSAusing TFs directly**. It includes four tables, one per annotation

database and spreadsheet, that show the proportion of times that each term results significant (*p*

< 0.05) and the median ranking after applying the Fisher’s exact test to 1000 random lists of TFs.

**Additional Table 3. Different distribution of TFs regulons**. It includes four tables, one per

annotation database and spreadsheet, that show the number of TFs that regulate each gene in

DoRothEA C.

**Additional Table 4. Annotations representation of the most TF targeted genes.** It includes four

tables, one per annotation database and spreadsheet, that show the top 10 terms which have

more genes within the 20 genes with more TFs.

**Additional Table 5. Results of TFs regulons GSA simulations comparing Fisher's exact and**

**Wallenius’ tests.**. It includes eight tables, one per test, annotation database and spreadsheet, that

shows the proportion of times that each term results significant (*p* < 0.05) and the median ranking

after applying each test to 1000 random lists of TFs.

**Additional Table 6. Results of a TFs regulons GSA using TFs related to SLE comparing Fisher's**

**exact and Wallenius tests**. It includes eight tables, one per test, annotation database and

spreadsheet, that shows the terms *p* values and its significance rank obtained after applying each

test to the TFs related to SLE.

**Additional Table 7. Results of TFs regulons GSA using TFs related to Cancer comparing**

**Fisher's exact and Wallenius tests**. It includes eight tables, one per test, annotation database and

spreadsheet, that shows the terms *p* values and its significance rank obtained after applying each

test using the TFs related to Cancer.