**Table S5: GO enrichment of tissue hubs versus the global interactome.** Analysis was performed using the DAVID functional annotation chart with GO term Level of 5. Only terms with a corrected p-value  $< 10^{-5}$  with at least 50 genes in the query set are reported. DAVID identified 386 genes out of the 451 tissue hubs. The analysis was performed against a background list of 7,909 genes identified by DAVID out of 11,225 genes in the global interactome.

| GO Term  | Count | FDR<br>corrected<br>p-value |
|--|-------|-----------------------------|
| GO:0043067 regulation of programmed cell death   | 107   | 1.09E-24                    |
| GO:0042981 regulation of apoptosis   | 106   | 1.01E-24                    |
| GO:0006464 protein modification process  | 136   | 4.37E-23                    |
| GO:0051246 regulation of protein metabolic process   | 84    | 4.15E-23                    |
| GO:0010604 positive regulation of macromolecule metabolic process                              | 104   | 4.87E-21                    |
| GO:0031325 positive regulation of cellular metabolic process                                   | 104   | 2.36E-20                    |
| GO:0010605 negative regulation of macromolecule metabolic process                              | 91    | 6.82E-19                    |
| GO:0031324 negative regulation of cellular metabolic process                                   | 89    | 1.54E-18                    |
| GO:0044267 cellular protein metabolic process  | 170   | 3.76E-18                    |
| GO:0031326 regulation of cellular biosynthetic process   | 183   | 8.48E-18                    |
| GO:0043068 positive regulation of programmed cell death  | 66    | 9.56E-18                    |
| GO:0010556 regulation of macromolecule biosynthetic process                                    | 178   | 9.68E-18                    |
| GO:0010942 positive regulation of cell death   | 66    | 1.08E-17                    |
| GO:0043065 positive regulation of apoptosis  | 65    | 2.27E-17                    |
| GO:0010468 regulation of gene expression   | 178   | 3.36E-17                    |
| GO:0019219 regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 172   | 7.07E-16                    |
| GO:0045449 regulation of transcription   | 162   | 7.31E-16                    |
| GO:0032268 regulation of cellular protein metabolic process                                    | 65    | 3.84E-15                    |
| GO:0009891 positive regulation of biosynthetic process   | 80    | 4.54E-15                    |
| GO:0031328 positive regulation of cellular biosynthetic process                                | 79    | 9.44E-15                    |
| GO:0043066 negative regulation of apoptosis  | 55    | 8.99E-15                    |
| GO:0043069 negative regulation of programmed cell death  | 55    | 2.58E-14                    |
| GO:0051173 positive regulation of nitrogen compound metabolic process                          | 76    | 2.45E-14                    |
| GO:0060548 negative regulation of cell death   | 55    | 2.35E-14                    |
| GO:0051252 regulation of RNA metabolic process   | 122   | 6.03E-14                    |
| GO:0010557 positive regulation of macromolecule biosynthetic process                           | 75    | 1.01E-13                    |
| GO:0010629 negative regulation of gene expression  | 64    | 1.54E-13                    |
| GO:0009966 regulation of signal transduction   | 83    | 1.68E-13                    |
| GO:0051253 negative regulation of RNA metabolic process  | 52    | 4.16E-13                    |
| GO:0006355 regulation of transcription, DNA-dependent  | 117   | 7.42E-13                    |
| GO:0045941 positive regulation of transcription  | 67    | 1.04E-12                    |
| GO:0051172 negative regulation of nitrogen compound metabolic process                          | 63    | 1.14E-12                    |
| GO:0010628 positive regulation of gene expression  | 68    | 1.23E-12                    |

| GO:0045935 positive regulation of nucleobase, nucleoside, nucleotide and | 71  | 1 455 10 |
|--|-----|----------|
| CO:0045934 negative regulation of nucleobase, nucleoside, nucleotide and | / 1 | 1.45E-12 |
| nucleic acid metabolic process   | 62  | 2.20E-12 |
| GO:0016481 negative regulation of transcription                          | 58  | 2.37E-12 |
| GO:0045892 negative regulation of transcription, DNA-dependent           | 50  | 3.05E-12 |
| GO:0010558 negative regulation of macromolecule biosynthetic process     | 64  | 3.19E-12 |
| GO:0009890 negative regulation of biosynthetic process                   | 65  | 7.44E-12 |
| GO:0031327 negative regulation of cellular biosynthetic process          | 64  | 9.33E-12 |
| GO:0012502 induction of programmed cell death                            | 46  | 3.06E-11 |
| GO:0045893 positive regulation of transcription, DNA-dependent           | 57  | 8.66E-11 |
| GO:0051254 positive regulation of RNA metabolic process                  | 57  | 1.14E-10 |
| GO:0030163 protein catabolic process                                     | 65  | 1.44E-10 |
| GO:0044257 cellular protein catabolic process                            | 64  | 1.42E-10 |
| GO:0007242 intracellular signaling cascade                               | 99  | 2.81E-10 |
| GO:0043632 modification-dependent macromolecule catabolic process        | 59  | 4.08E-09 |
| GO:0007243 protein kinase cascade  | 46  | 5.11E-09 |
| GO:0006916 anti-apoptosis  | 33  | 8.67E-09 |
| GO:0016310 phosphorylation   | 71  | 9.11E-09 |
| GO:0051174 regulation of phosphorus metabolic process                    | 53  | 9.95E-09 |
| GO:0019220 regulation of phosphate metabolic process                     | 53  | 9.95E-09 |
| GO:0006259 DNA metabolic process   | 53  | 1.47E-08 |