APPENDIX C

Functional enrichment analysis was performed on Blue module genes and genes in sectors 2, 3, 5, 6 and 8 of Fig. 4a from the differential network analysis using the DAVID database (Dennis et al. 2003). Suppl. Tables 3-8 depict enriched functions and processes with uncorrected p-values < 0.05. Also shown are p-values after Bonferroni and Hochberg correction. Blue module genes were significant after Bonferroni correction for oxidoreductase activity and monooxygenase activity (Suppl. Table 3). Functional analysis on all genes from sector 3 - not only the Yellow/Grey module genes - is shown in Suppl. Table 5. Sector 3 genes were significantly enriched for extracellular space and extracellular matrix after Bonferroni calculation; these findings are similar to the results for the Yellow module Sector 3 genes presented in Table 3. Sector 6 genes were significant for oxidoreductase activity (p = 0.0123) and monooxygenase activity (p = 0.0490) (Suppl. Table 7). Results for sectors 2 and 8 were not significant after Bonferroni correction (Suppl. Tables 4 and 8).

WGCNA facilitates a biologically motivated gene screening method but it is not a strict hypothesis testing procedure. While significance levels (p-values) and permutation tests provide some guidance regarding the statistical significance of the findings, the results of network analysis require careful validation in independent data sets. Network methods are no antidote to errors in the experimental design (e.g. batch effects) or errors in the measurements. In brief, "garbage in" will result in "garbage out".