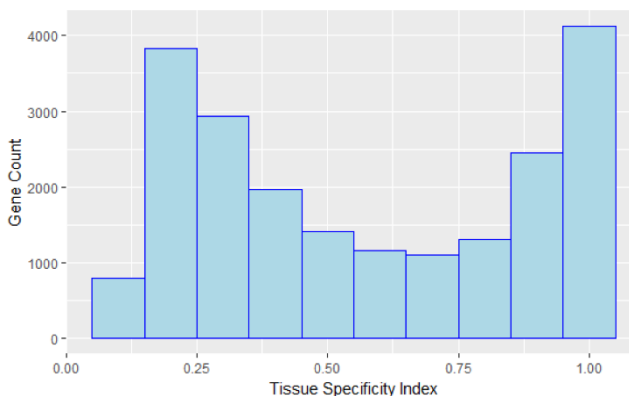


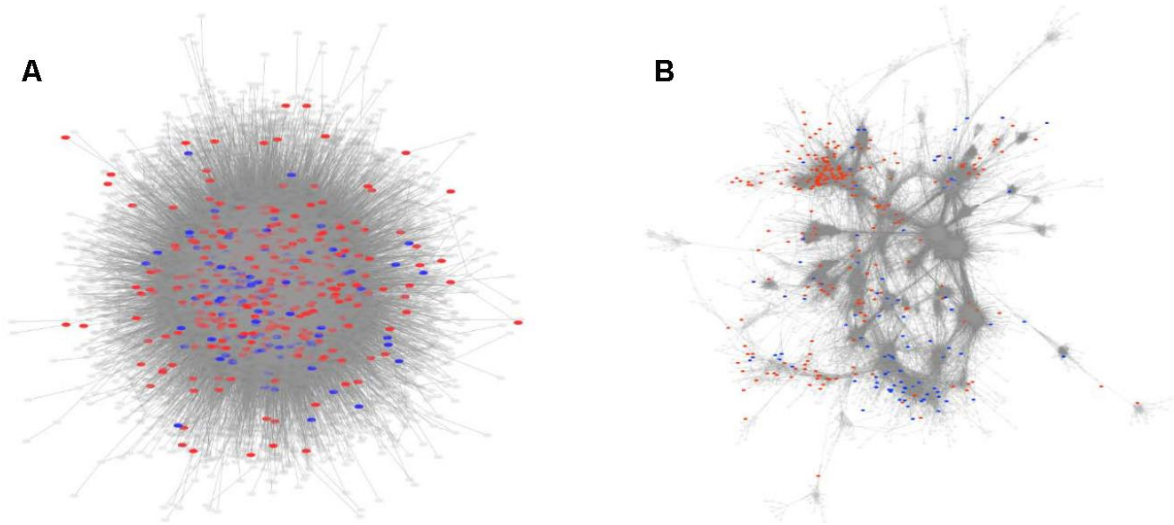
## SUPPLEMENTARY FIGURES

| Data Collection   |
|---|
| <ul style="list-style-type: none"><li>127 healthy ageing RNA-Seq and microarray datasets (mouse, rat and human) were downloaded from GEO and AgeMap</li></ul>   |
| Expression Analysis   |
| <ul style="list-style-type: none"><li>A linear regression was carried out on each dataset and tested with an F-test to identify genes differentially expressed with age.</li><li>The probability of any given gene being over- or underexpressed was then calculated for each dataset, and an average taken across all datasets, for use in the next step</li></ul>   |
| Value Counting  |
| <ul style="list-style-type: none"><li>Protein coding one-2-one human homologues were identified, and for each gene the number of times it was differentially expressed across all datasets was counted.</li><li>This value was then used with a binomial test, to test if each gene tended to be significantly over- or underexpressed across all the datasets it appeared in, using the probability of over- or underexpression calculated previously.</li></ul> |
| FDR Correction  |
| <ul style="list-style-type: none"><li>To correct for FDR, the whole analysis was repeated 10,000 times on random permutations of the datasets (i.e. gene names were shuffled in each dataset and the binomial tests were repeated).</li><li>The results of these simulations were then collated, and a regression was carried out to estimate the p-value at which <math>FDR &lt; 0.05</math> for each tissue and direction of expression individually.</li></ul> |

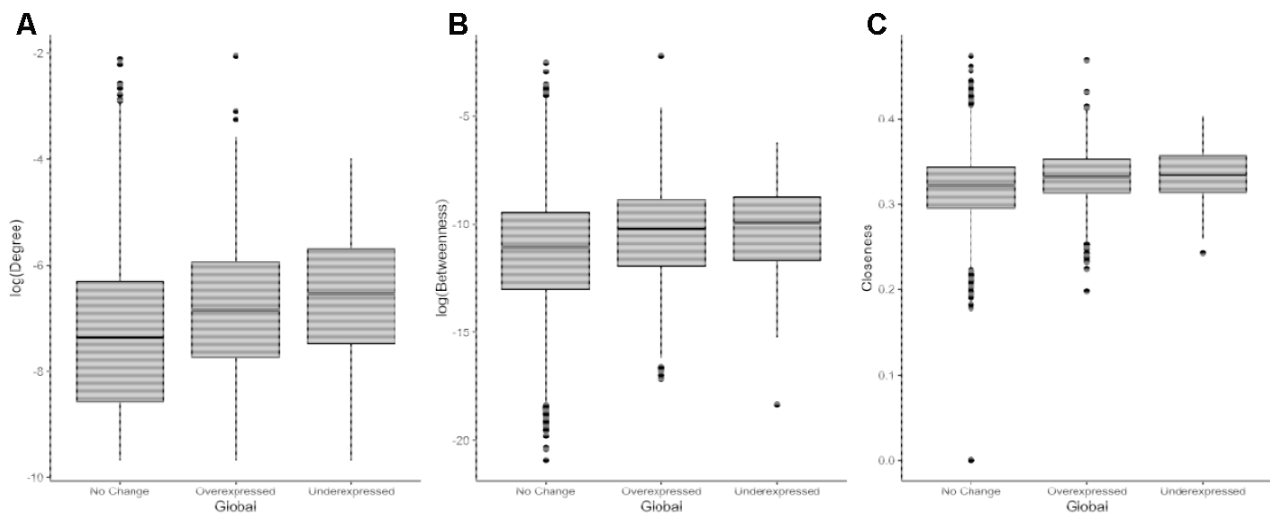
Supplementary Figure 1. Summary of the meta-analysis method.



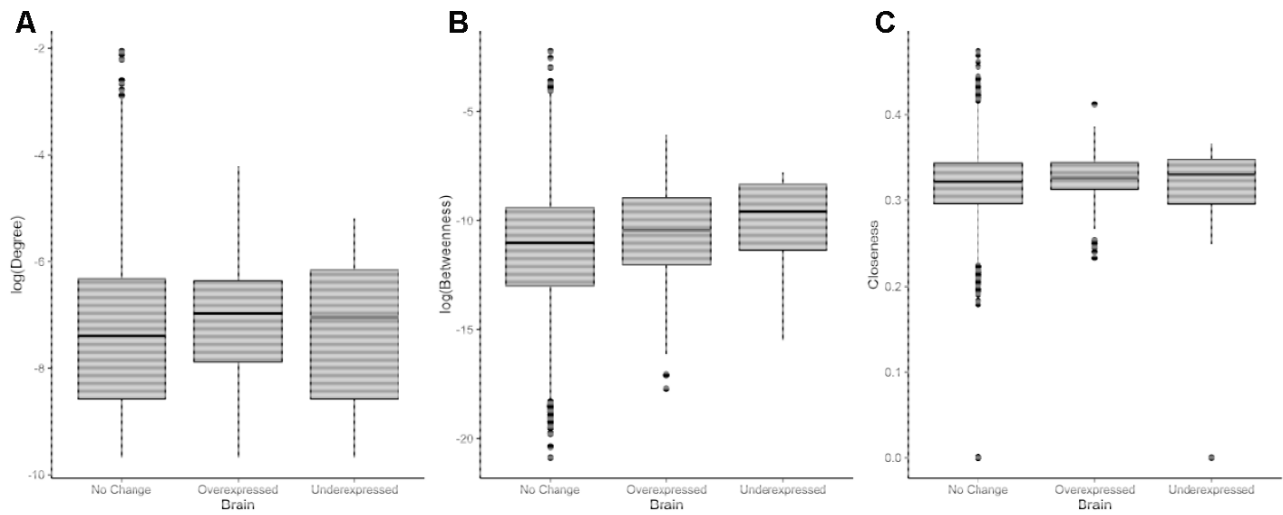
Supplementary Figure 2. Distribution of  $\tau$  tissue specificity scores in the whole GTEx expression dataset. A  $\tau$  specificity index of 0 indicates complete nonspecific expression while an index of 1 indicates completely specific expression.



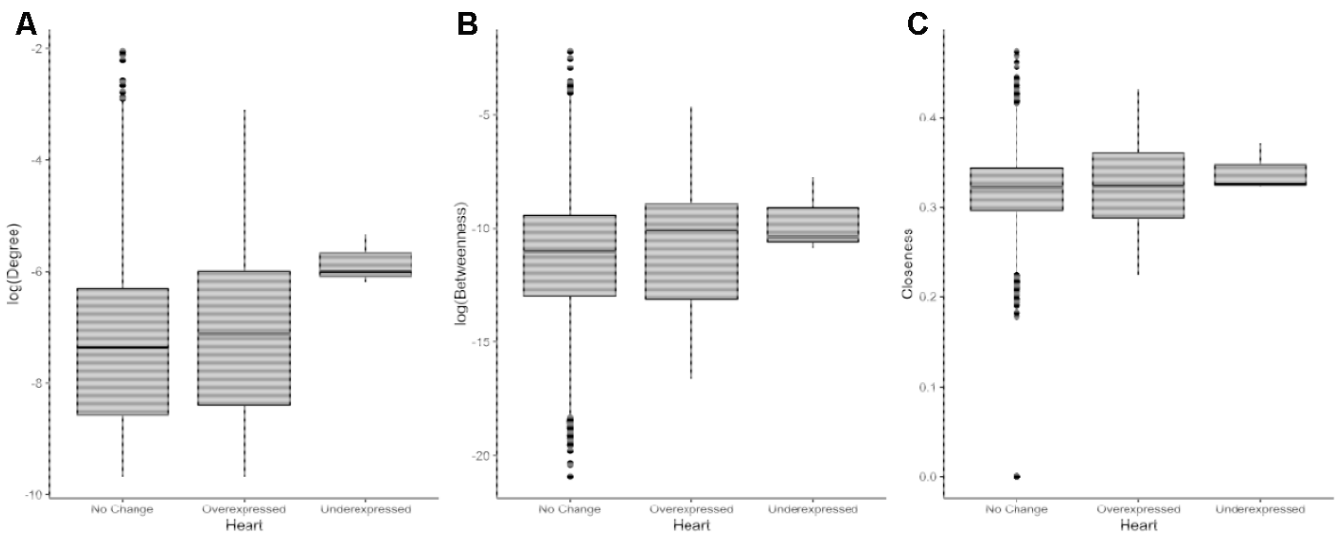
**Supplementary Figure 3.** Interaction networks showing the locations of the overexpressed (red) and underexpressed (blue) genes in the (A) BioGRID PPI network and the (B) GeneFriends coexpression network.



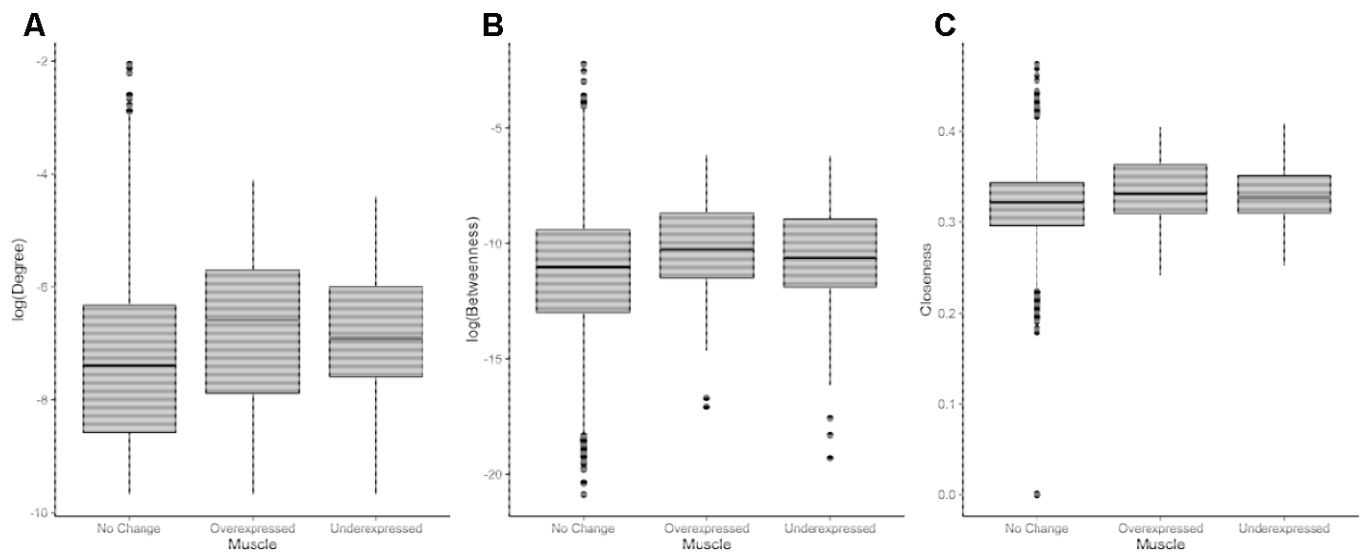
**Supplementary Figure 4.** Distributions of degree (normalised by dividing by the maximum degree of a graph  $n-1$ , where  $n$  is the number of nodes in graph  $G$ ) (A), betweenness (B) and closeness (C) centrality measures in a genome-wide PPI network for overexpressed, underexpressed and unchanged genes from the global analysis



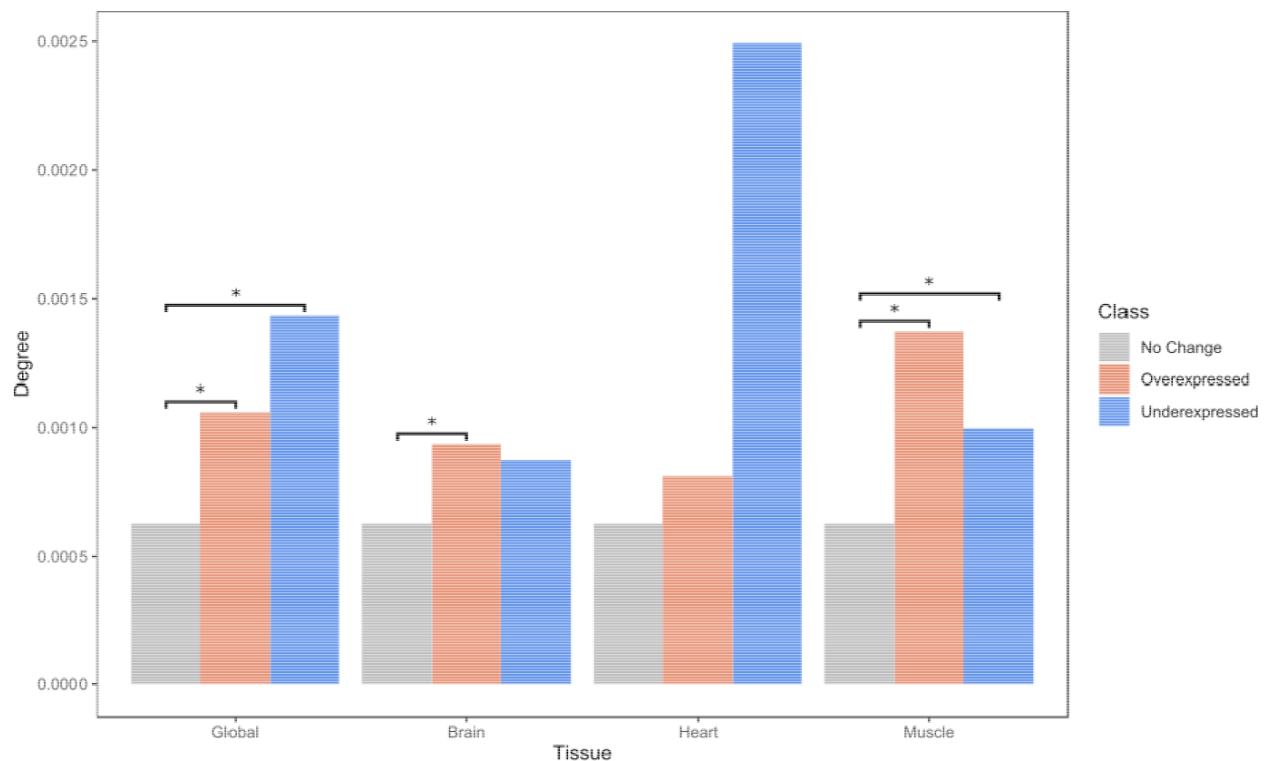
**Supplementary Figure 5.** Distributions of degree (normalised by dividing by the maximum degree of a graph  $n-1$ , where  $n$  is the number of nodes in graph  $G$ ) (A), betweenness (B) and closeness (C) centrality measures in a genome-wide PPI network for overexpressed, underexpressed and unchanged genes from the brain analysis.



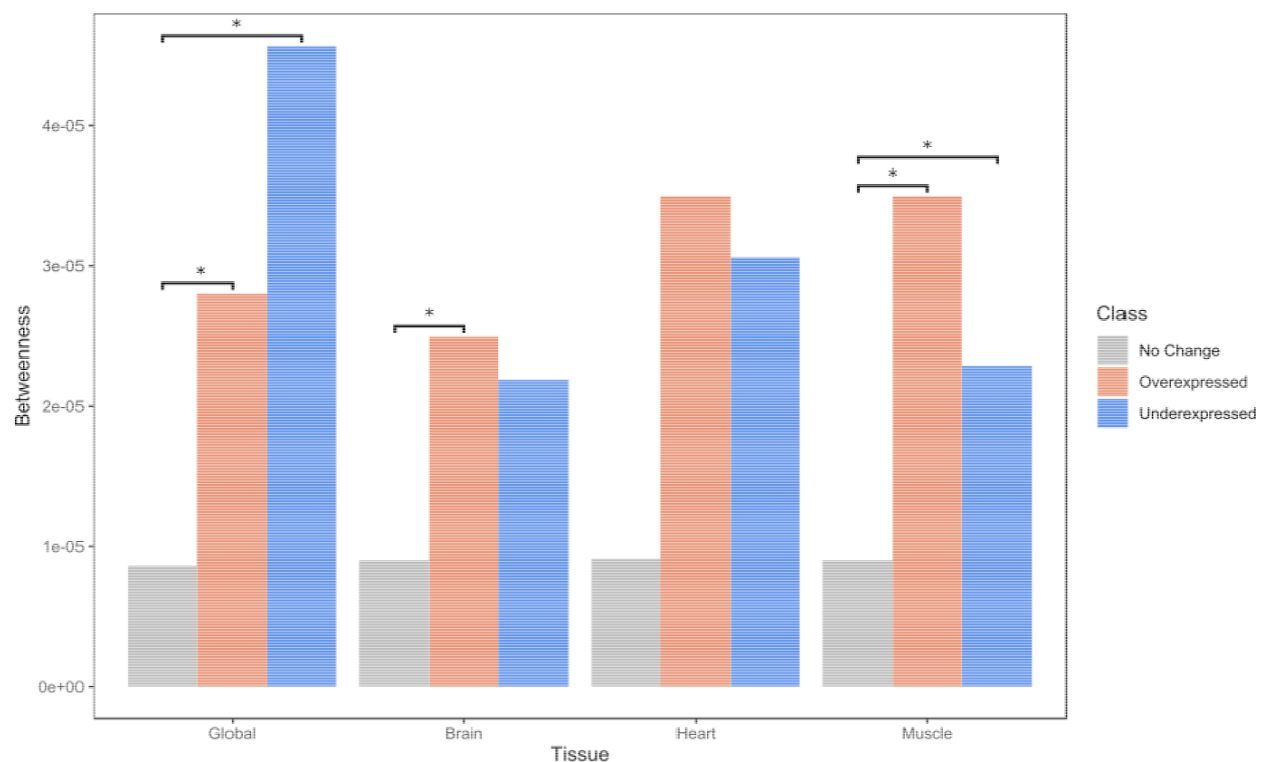
**Supplementary Figure 6.** Distributions of degree (normalised by dividing by the maximum degree of a graph  $n-1$ , where  $n$  is the number of nodes in graph  $G$ ) (A), betweenness (B) and closeness (C) centrality measures in a genome-wide PPI network for overexpressed, underexpressed and unchanged genes from the heart analysis.



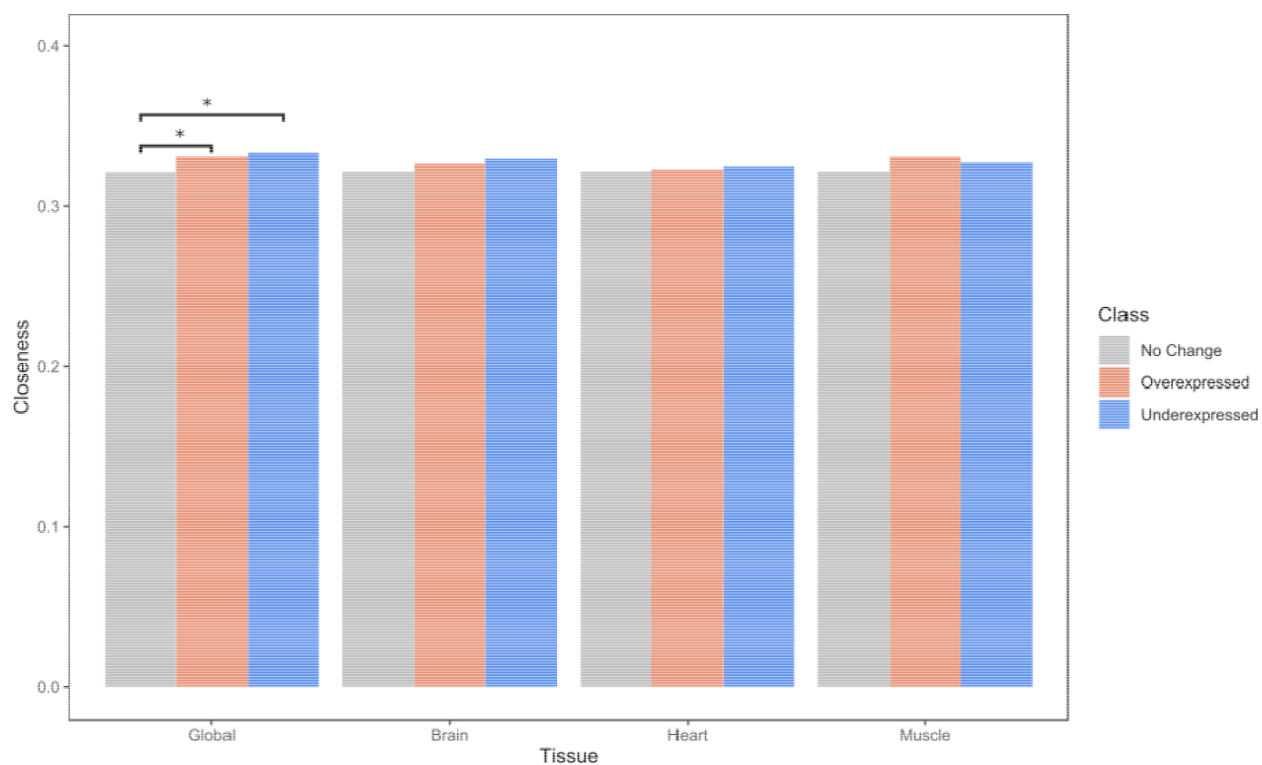
**Supplementary Figure 7.** Distributions of degree (normalised by dividing by the maximum degree of a graph  $n-1$ , where  $n$  is the number of nodes in graph  $G$ ) (A), betweenness (B) and closeness (C) centrality measures in a genome-wide PPI network for overexpressed, underexpressed and unchanged genes from the muscle analysis.



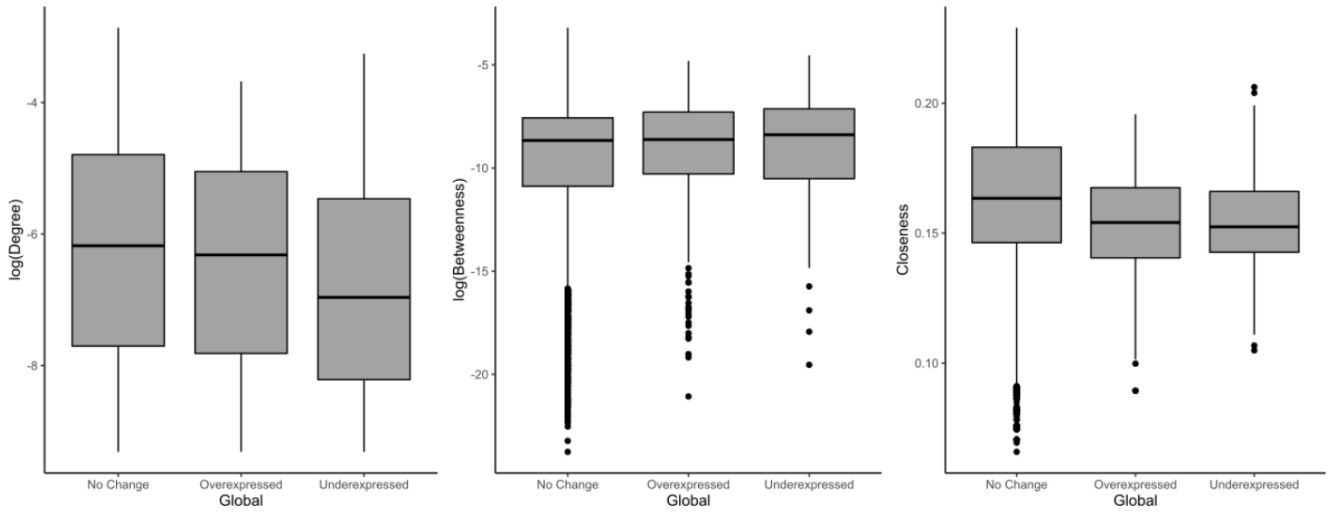
**Supplementary Figure 8.** Median degree (normalised by dividing by the maximum degree of a graph  $n-1$ , where  $n$  is the number of nodes in graph  $G$ ) values in a genome-wide PPI network for overexpressed, underexpressed and unchanged genes from each analysis. \* indicates significance tested by a Mann-Whitney U test (Bonferroni corrected).



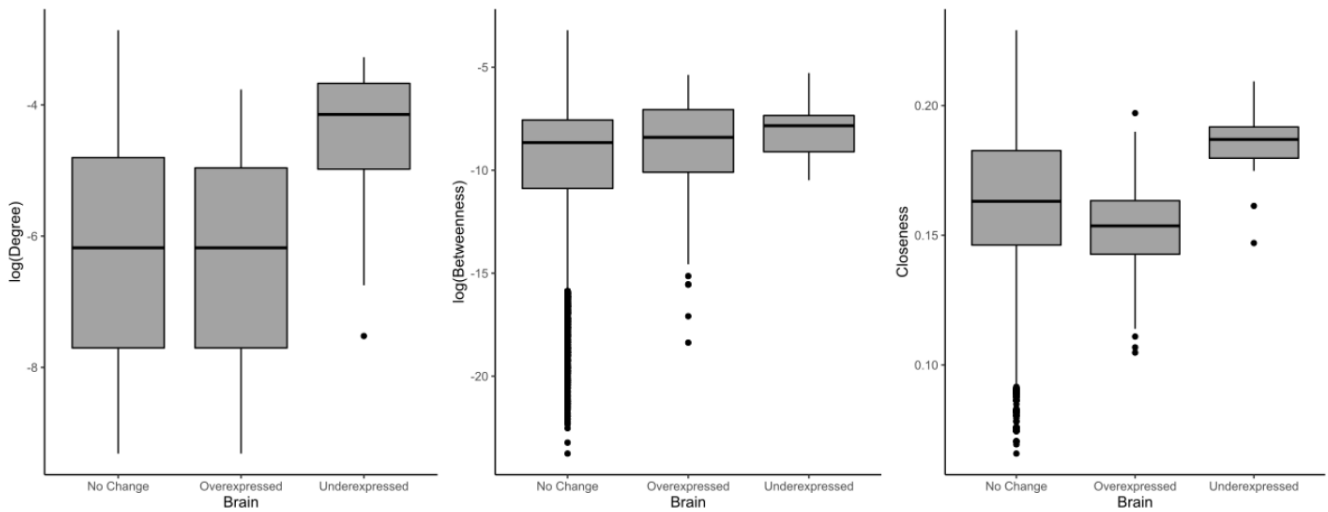
**Supplementary Figure 9. Median betweenness values in a genome-wide PPI network for overexpressed, underexpressed and unchanged genes from each analysis. \*** indicates significance tested by a Mann-Whitney U test (Bonferroni corrected).



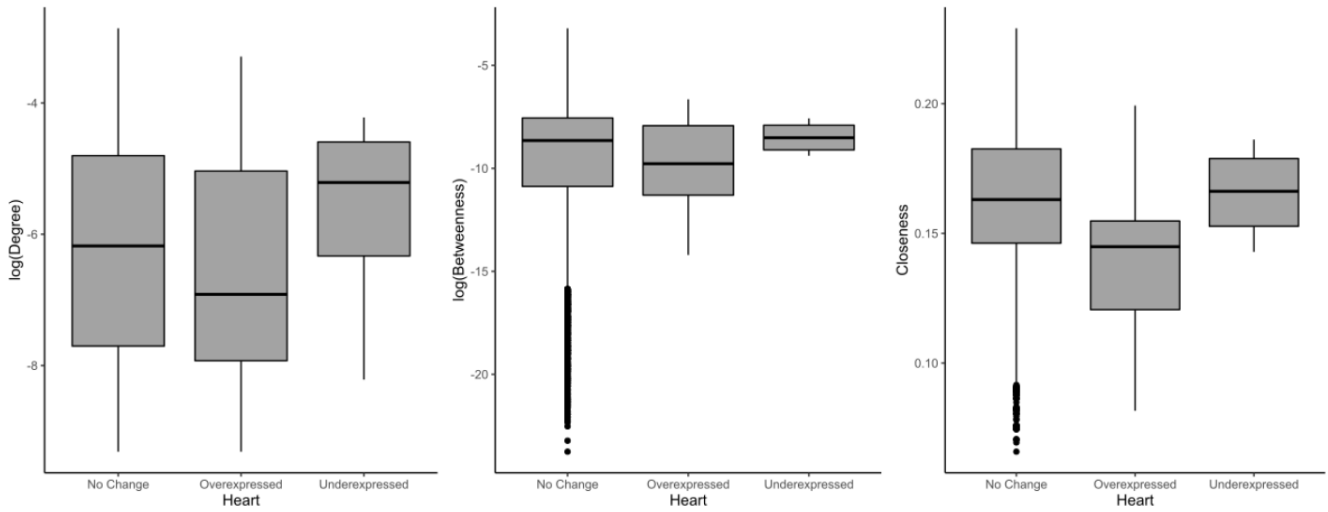
**Supplementary Figure 10. Median closeness values in a genome-wide PPI network for overexpressed, underexpressed and unchanged genes from each analysis. \*** indicates significance tested by a Mann-Whitney U test (Bonferroni corrected).



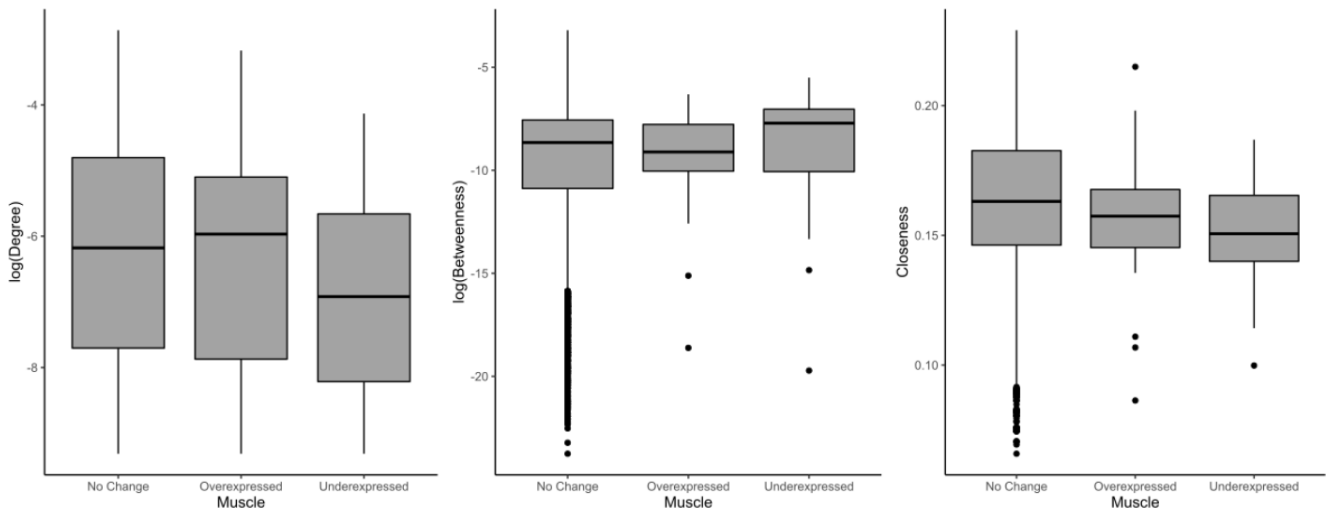
**Supplementary Figure 11.** Distributions of degree (normalised by dividing by the maximum degree of a graph  $n-1$ , where  $n$  is the number of nodes in graph  $G$ ) (A), betweenness (B) and closeness (C) centrality measures in an unweighted co-expression network extracted from GeneFriends for overexpressed, underexpressed and unchanged genes from the global analysis.



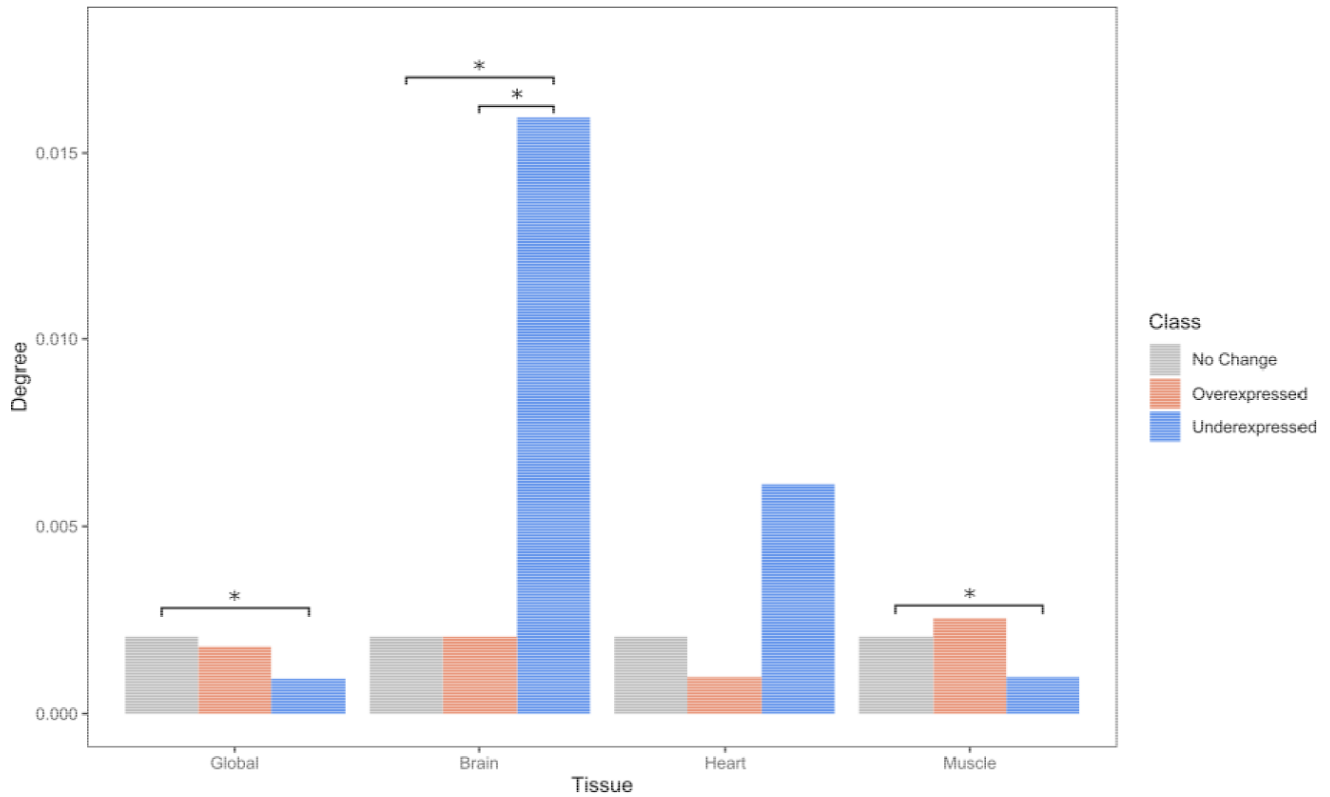
**Supplementary Figure 12.** Distributions of degree (normalised by dividing by the maximum degree of a graph  $n-1$ , where  $n$  is the number of nodes in graph  $G$ ) (A), betweenness (B) and closeness (C) centrality measures in an unweighted co-expression network extracted from GeneFriends for overexpressed, underexpressed and unchanged genes from the brain analysis.



**Supplementary Figure 13.** Distributions of degree (normalised by dividing by the maximum degree of a graph  $n-1$ , where  $n$  is the number of nodes in graph  $G$ ) (A), betweenness (B) and closeness (C) centrality measures in an unweighted co-expression network extracted from GeneFriends for overexpressed, underexpressed and unchanged genes from the heart analysis.

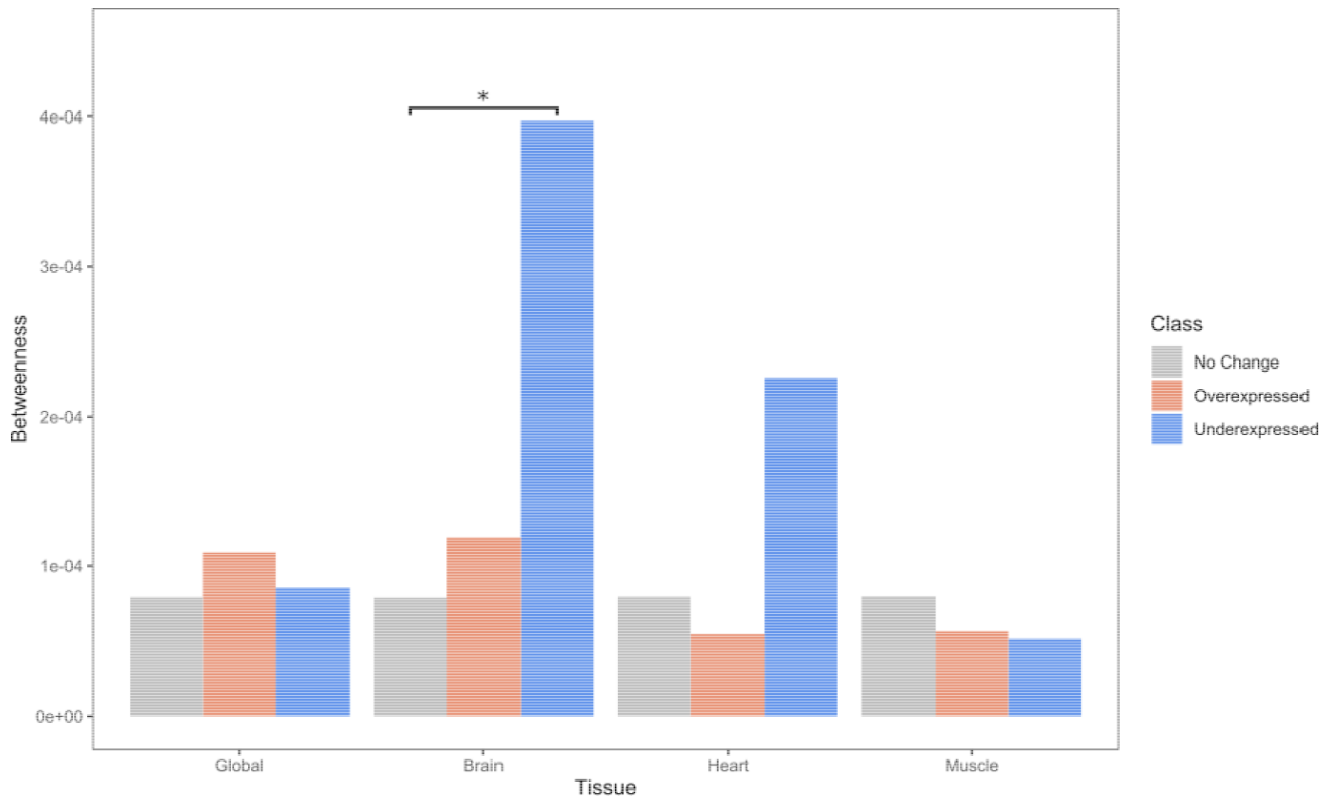


**Supplementary Figure 14.** Distributions of degree (normalised by dividing by the maximum degree of a graph  $n-1$ , where  $n$  is the number of nodes in graph  $G$ ) (A), betweenness (B) and closeness (C) centrality measures in an unweighted co-expression network extracted from GeneFriends for overexpressed, underexpressed and unchanged genes from the muscle analysis.

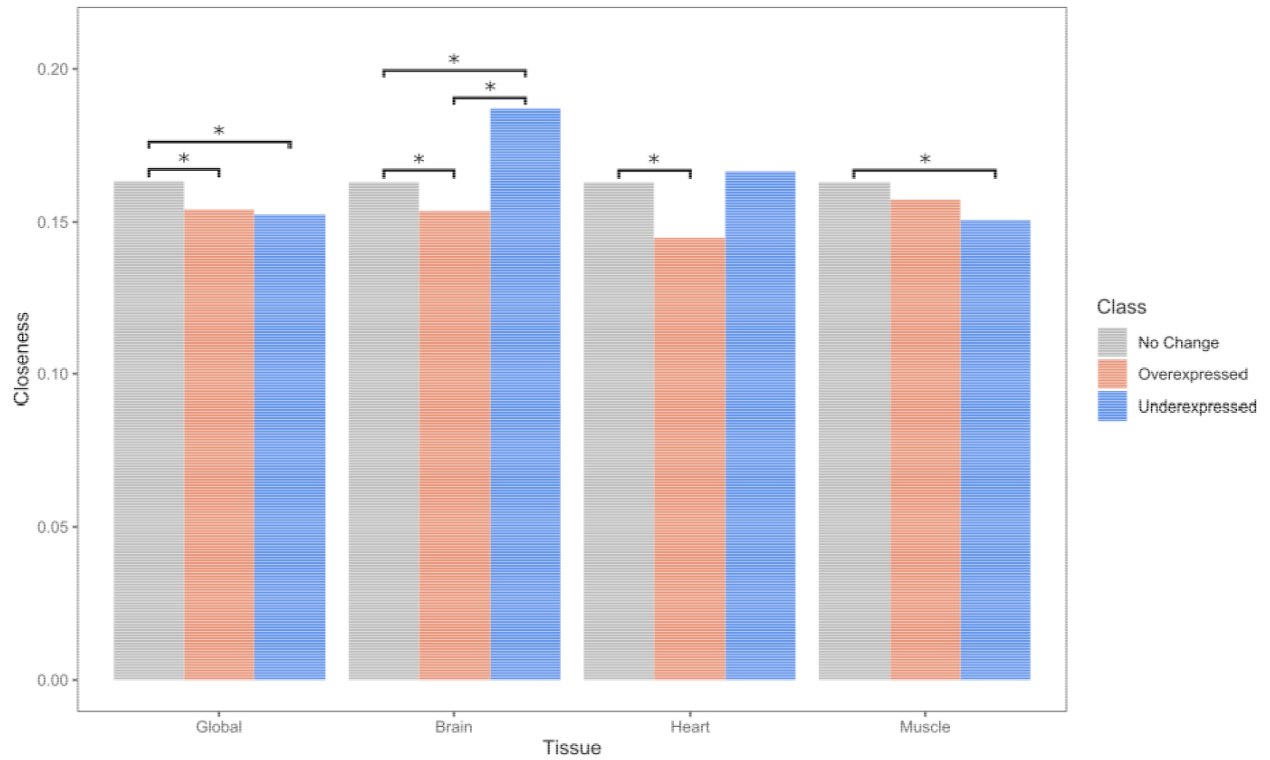


**Supplementary Figure 15. Median degree (normalised by dividing by the maximum degree of a graph  $n-1$ , where  $n$  is the number of nodes in graph  $G$ ) values in an unweighted co-expression network extracted from GeneFriends for overexpressed, underexpressed and unchanged genes from each analysis. \* indicates significance tested by a Mann-Whitney U test (Bonferroni corrected).**

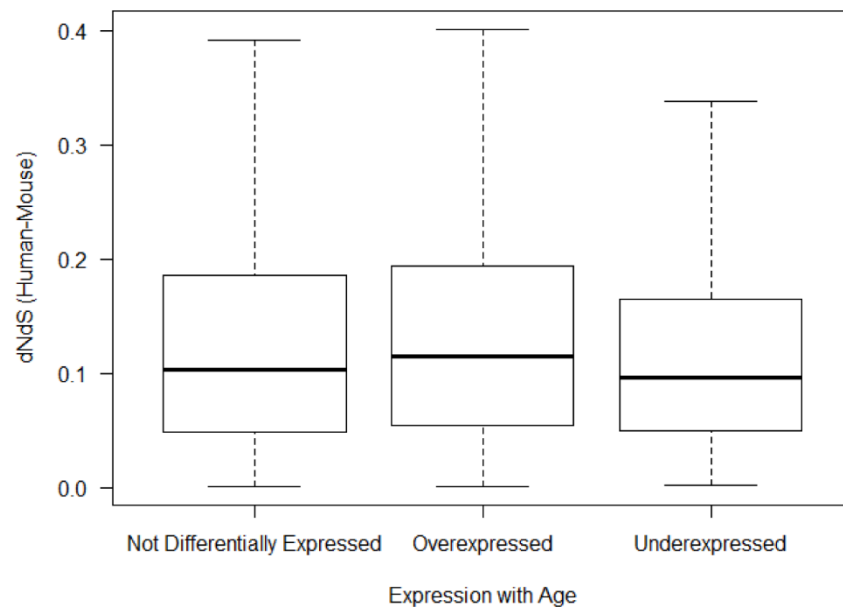




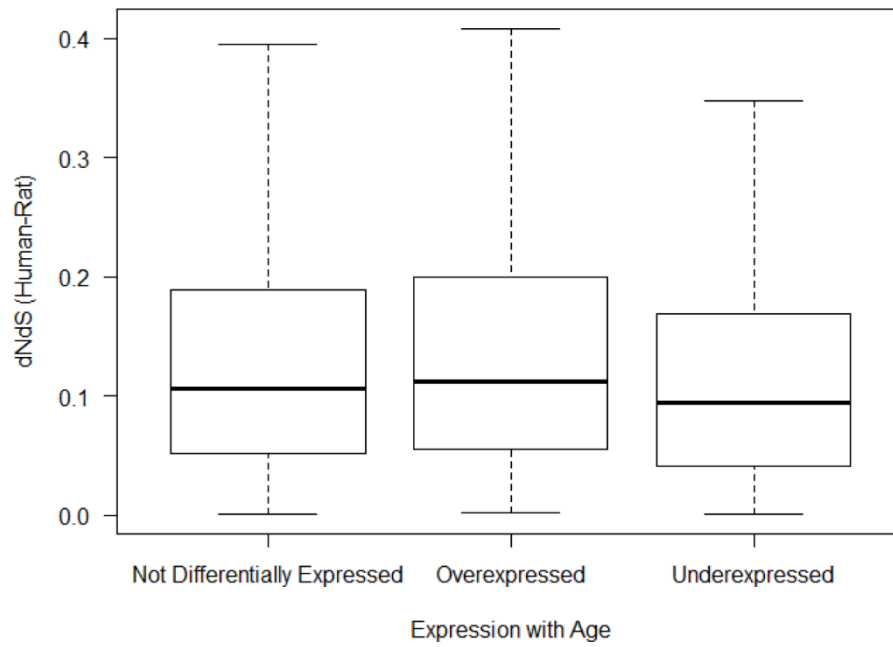
**Supplementary Figure 16. Median betweenness values in an unweighted co-expression network extracted from GeneFriends for overexpressed, underexpressed and unchanged genes from each analysis.** \* indicates significance tested by a Mann-Whitney U test (Bonferroni corrected).



**Supplementary Figure 17. Median closeness values in an unweighted co-expression network extracted from GeneFriends for overexpressed, underexpressed and unchanged genes from each analysis. \*** indicates significance tested by a Mann-Whitney U test (Bonferroni corrected).



**Supplementary Figure 18. Distribution of human-mouse dNds scores for the different gene classifications (not differentially expressed, overexpressed and underexpressed).**



**Supplementary Figure 19. Distribution of human-rat dNdS scores for the different gene classifications (not differentially expressed, overexpressed and underexpressed).**