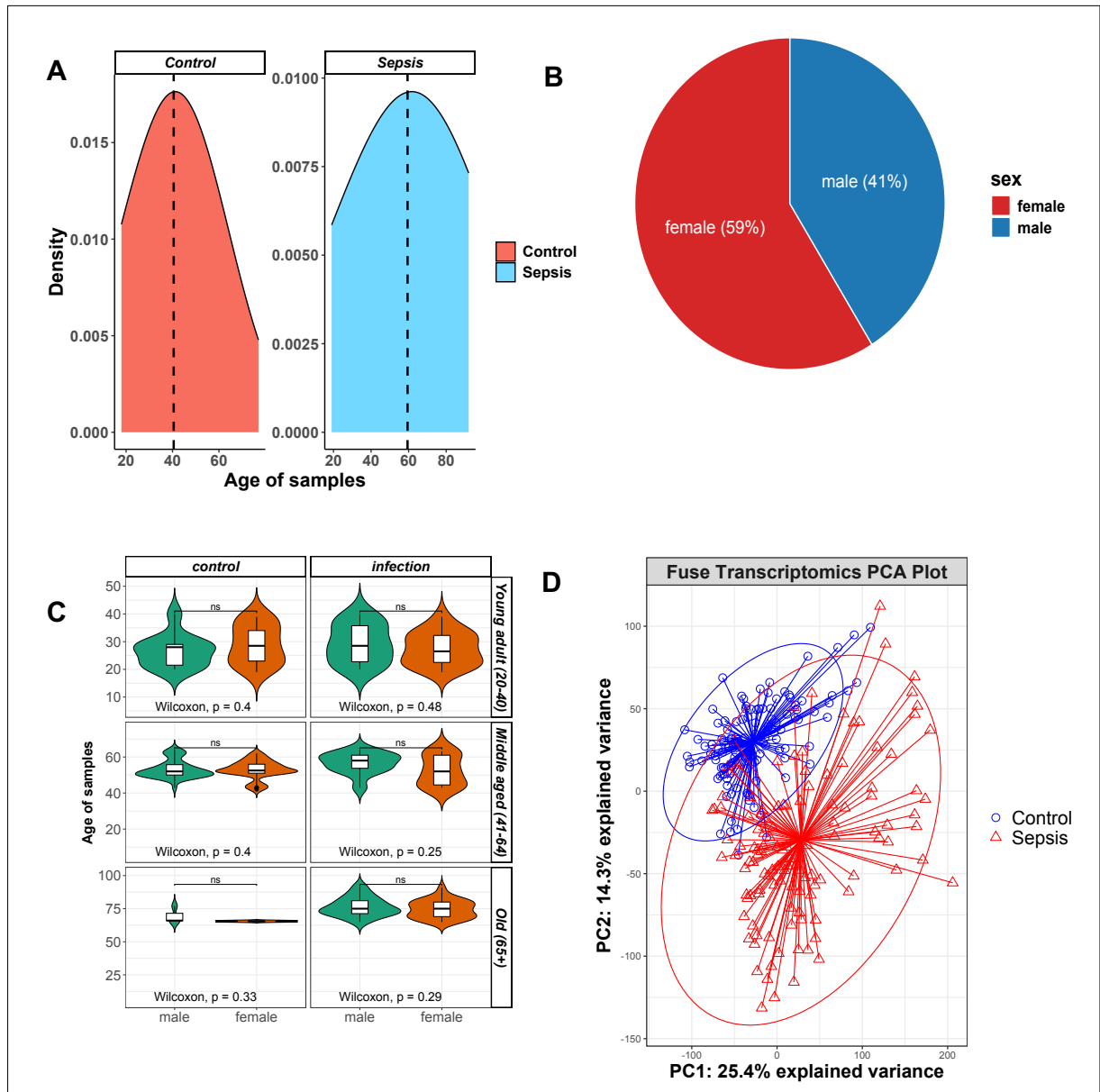
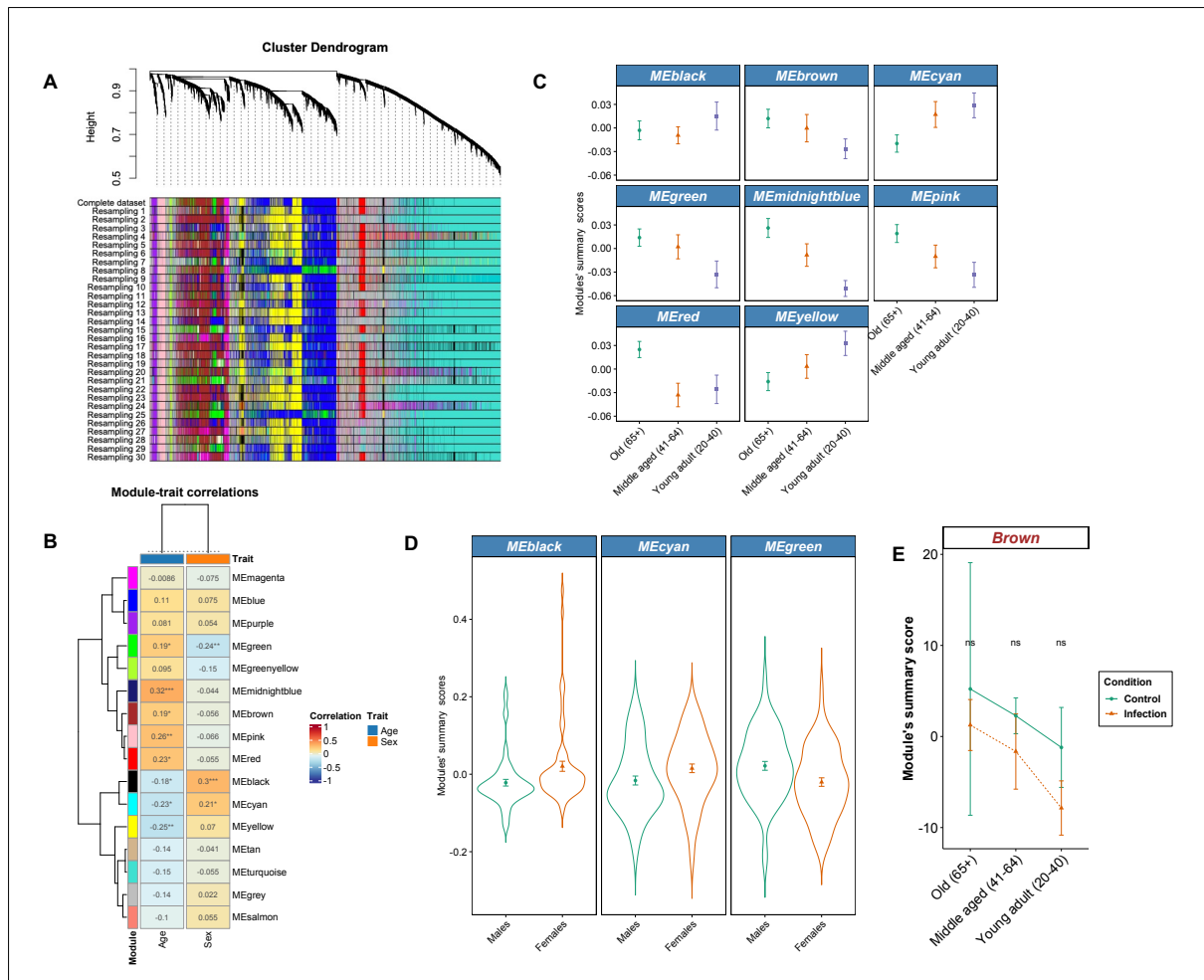


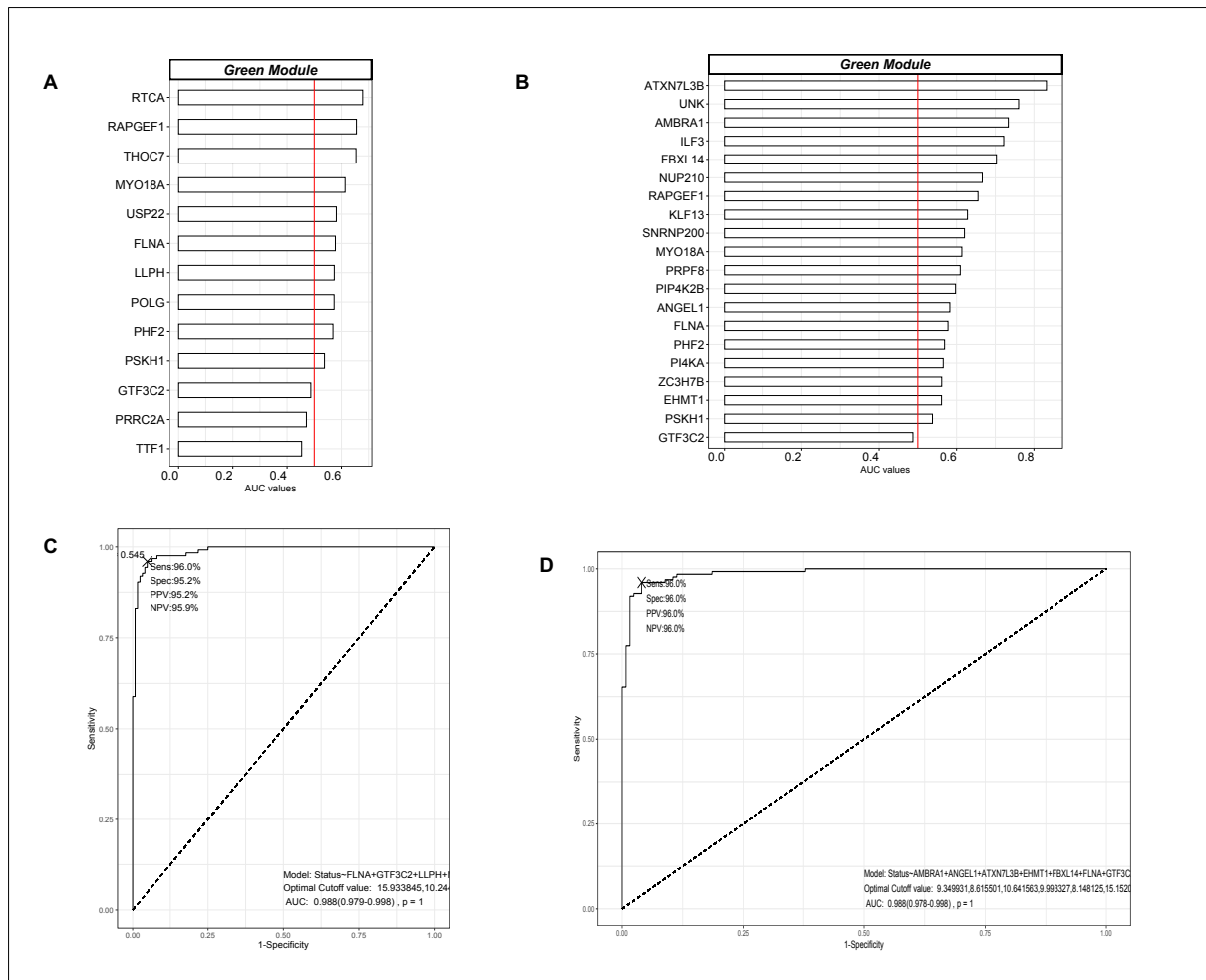


**Figure S1: Demographic and transcriptomic characteristics of the FUSE cohort** (A) Age distribution plot of FUSE cohort samples stratified by control and sepsis groups. Black dotted vertical lines indicate the mean age for each group. (B) Pie chart illustrating the sex distribution of FUSE cohort samples. (C) Violin plots comparing age between control and infection groups across males and females, stratified by different age categories using age- and sex-matched samples. Wilcoxon tests revealed no sex-related differences across age groups. (D) Principal component analysis plot providing an overview of transcriptomic profiles, with control samples (blue ellipse) and infection/sepsis samples (red ellipse).



**Figure S2. Network stability and associations with demographic variables**

(A) Hierarchical clustering dendrogram of module stability analysis. Branches represent modules identified in the control group, with module assignments from resampled datasets indicated after the first row. (B) Heatmap showing correlations between module eigengenes and demographic variables (age and sex). Significant Spearman correlations are denoted with asterisks. (C) Age-stratified comparison of eigengene values for modules significantly associated with age. (D) Violin plots of sex-associated module eigengene values in males versus females. (E) Brown module eigengene values across control and Sepsis/Infection groups, stratified by age groups.



**Figure S3: Receiver Operating Characteristic (ROC) analysis of hub genes**

(A) Bar plot showing AUC values of each age-associated hub genes. (B) Bar plot showing AUC values of each sex-associated hub genes. The red vertical line indicates an AUC of 0.5, corresponding to random classification. (C) ROC curve from multivariate analysis of all age-associated hub genes combined, indicating improved classification performance compared to individual genes. (D) ROC curve from multivariate analysis of all sex-associated hub genes combined, showing enhanced predictive accuracy relative to single-gene models. PPV and NPV values are provided to indicate the reliability of the model in correctly identifying true positives and true negatives.

### Supplementary Data:

Supplementary Data 1A: Transcription factor motif enrichment results for analyzed gene sets associated with age

Supplementary Data 1B: Transcription factor motif enrichment results for analyzed gene sets associated with sex

Supplementary Data 2: Functional enrichment results for genes in the green module

