Early diagnosis and triage of pediatric sepsis using metabolic and inflammatory mediator biomarkers.

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Additional File 2: Results of the metabolomic and protein-mediator biomarker phenotyping in the two age subgroups.

Fig. E1 Principal Component Analysis results for the 2-5 year old cohorts, using metabolomics (a), protein-mediators (b), and combined metabolomics and protein-mediator (c) data. Red circles: PICU-sepsis cohort; Blue circles: ED-sepsis cohort; Green circles: ED-control cohort.

Fig. E2 Partial Least Squares Discriminant Analysis for the 2-5 year old cohorts, using metabolomics (a), protein-mediators (b), and combined metabolomics and protein-mediator (c) data. Red circles: PICU-sepsis cohort; Blue circles: ED-sepsis cohort; Green circles: ED-control cohort.

Fig. E3 Orthogonal Partial Least Squares Discriminant Analysis for the 2-5 year old cohorts, using metabolomics (a), protein-mediator (b), and combined metabolomics and protein-mediator (c) data. Red circles: PICU-sepsis cohort; Blue circles: ED-sepsis cohort; Green circles: ED-control cohort.

Fig. E4 Principal Component Analysis results for the 6-17 year old cohorts, using metabolomics (a), protein-mediators (b), and combined metabolomics and protein-mediator (c) data. Red circles: PICU-sepsis cohort; Blue circles: ED-sepsis cohort; Green circles: ED-control cohort.

Fig. E5 Partial Least Squares Discriminant Analysis for the 6-17 year old cohorts, using metabolomics (a), protein-mediator (b), and combined metabolomics and protein-mediator (c) data. Red circles: PICU-sepsis cohort; Blue circles: ED-sepsis cohort; Green circles: ED-control cohort.

Fig. E6 Orthogonal Partial Least Squares Discriminant Analysis for the 6-17 year old cohorts, using metabolomics (a), protein-mediator (b), and combined metabolomics and protein-mediator (c) data. Red circles: PICU-sepsis cohort; Blue circles: ED-sepsis cohort; Green circles: ED-control cohort.

Fig. E7 The loading plots for each principal component (PC1, PC2 and PC3) for PCA models calculated for the 2-17 year old cohorts using metabolic profiling (a), inflammatory protein-mediator profiling (b), and combined biomarker profiling (c) data. The loadings plots demonstrate which metabolites/inflammatory protein-mediators most contribute to each component in the PCA models (the bigger bar, the more influential the variable) and how these variables are correlated.
Figure E1. PCA Results for 2-5 year old cohorts.

a. Metabolomics results

\[
R^2_{X\text{cum}} = 0.426; \\
Q^2_{X\text{cum}} = 0.261
\]

PC1 = 19.7\% \\
PC2 = 14.5\% \\
PC3 = 8.4\%

b. Protein-mediator results

\[
R^2_{X\text{cum}} = 0.44; \\
Q^2_{X\text{cum}} = 0.257
\]

PC1 = 19.9\% \\
PC2 = 15.9\% \\
PC3 = 8.26\%
c. Combined results.

\[ R_{X_{\text{cum}}} = 0.383; \]
\[ Q_{2_{\text{cum}}} = 0.261 \]

PC1 = 21.7%
PC2 = 9.72%
PC3 = 6.87%
Figure E2. PLS-DA results for 2-5 year old cohort.

a. Metabolomics results

![Metabolomics Results](image)

\[ R^2_{Y_{\text{cum}}} = 0.61; \quad Q^2_{\text{cum}} = 0.43 \]

b. Protein-mediator results

![Protein-mediator Results](image)

\[ R^2_{Y_{\text{cum}}} = 0.55 \]
\[ Q^2_{\text{cum}} = 0.36 \]
c. Combined results

\[ R_{2Y_{\text{cum}}} = 0.69; \]
\[ Q_{2_{\text{cum}}} = 0.57 \]
Figure E3. OPLS-DA results for the 2-5 year old cohorts.

a. Metabolomics
PICU-sepsis vs. ED-sepsis

b. Protein-mediators
c. Combined results

R2Y = 0.78; Q2 = 0.65
R2Y = 0.86; Q2 = 0.82
R2Y = 0.88; Q2 = 0.84
Figure E4. PCA Results for 6-17 year old cohorts.

a. Metabolomics results

b. Protein-mediator results
c. Combined results.

\[ R_{X_{\text{cum}}}^2 = 0.398; \]
\[ Q_{2_{\text{cum}}}^2 = 0.309 \]

PC1 = 23.9%  
PC2 = 10.2%  
PC3 = 5.72%
Figure E5. PLS-DA results for 6-17 year old cohort.

a. Metabolomics results

![Metabolomics results graph]

R²cum = 0.62; Q²cum = 0.42

b. Protein-mediator results

![Protein-mediator results graph]

R²cum = 0.54; Q²cum = 0.45
c. Combined results

\[ R_2Y_{\text{cum}} = 0.70; \]
\[ Q_2_{\text{cum}} = 0.61 \]
Figure E6. OPLS-DA results for the 6-17 year old cohorts.

a. Metabolomics
   PICU-sepsis vs. ED-sepsis
   ED-sepsis vs. ED-controls
   PICU-sepsis vs. ED-controls

R2Y = 0.79; Q2 = 0.68
R2Y = 0.66; Q2 = 0.45
R2Y = 0.89; Q2 = 0.83

b. Protein-mediators

R2Y = 0.67; Q2 = 0.45
R2Y = 0.70; Q2 = 0.64
R2Y = 0.86; Q2 = 0.79
c. Combined results

\[ R^2_Y = 0.82; Q^2 = 0.76 \]
\[ R^2_Y = 0.77; Q^2 = 0.70 \]
\[ R^2_Y = 0.88; Q^2 = 0.86 \]
Fig. E7 The loading plots for each principal component (PC1, PC2 and PC3) for PCA models in 2-17y cohort.

a. Metabolic profiling data
b. Inflammatory protein-mediator profiling results
c. Combined Results