Supplementary Material S1. Overall workflow of TSCytoPred from data collection to time-series cytokine expression inference.

Data collection and Preprocessing Collect longitudinal cytokine and gene expression profiles from CODA Select patients having both multi-omics data available for three time points within a 15-day period Extract common features in all samples and remove those with more than 50% missing values Perform random forest imputation for remaining missing values, library size normalization and log transformation Total of 16,116 genes and 185 cytokines

Selecting genes associated with cytokines

Select genes known to be related to cytokines as transcription factors based on CytReg database

Identify genes associated with selected genes based on protein-protein interaction from the STRING database

Calculate Spearman correlation between each gene and its corresponding cytokine

Select top 50 genes most highly correlated with each cytokine

Total of 3,429 genes

Inferring time-series cytokine expression

MLP Block

$$egin{aligned} h_{\ell,1} &= ext{leakyReLU}(W_{\ell,1}x^g + b_{\ell,1}), \ h_{\ell,2} &= ext{leakyReLU}(W_{\ell,2}h_{\ell,1} + b_{\ell,2}), \ heta_\ell &= ext{leakyReLU}(W_{\ell,3}h_{\ell,2} + b_{\ell,3}), \end{aligned}$$

Interpolation Block

Use extracted features from MLP block

$$\hat{x}_i^c = heta_{\ell,1} + rac{\delta_i}{t_k - t_i} \cdot (heta_{\ell,k} - heta_{\ell,1})$$

Select the predicted timepoints matched to the actual timepoints and calculate the mean absolute error loss

Predicted cytokine profiles