Univariate Cox regression to identify the **conventional** mortality predictors

Multivariate Cox regression to identify the independent conventional predictors: BMI, frailty index and cf-DNA level

Dimension reduction (feature selection) using penalized Ridge regression model containing the conventional markers and the transcriptomic data

**Cox multivariate model to identify the final mortality-predicting signature**

Network analysis for the final **signature transcripts** to elucidate the underlying biology

Univariate Cox regression to identify the mortality-predicting **transcripts** (n=478)

Identification of the independent transcriptomic predictors by adjusting for BMI, frailty index and cf-DNA level (n=331)

Pathway and network analyses for the 331 transcripts

Evaluation of the Lasso and Ridge penalized models and the C-index boosting algorithm containing the different variable combinations
a) conventional markers
b) transcriptomic data
c) conventional markers and transcriptomic data together

Assessment of model performance:
- discriminative power
- accuracy of predictive modeling
- relative goodness of fit