To describe the proposed method, we first introduce some notations. We denoted the 89 tissues as \( t_1, ..., t_{89} \) and the 19 miRNAs as \( m_1, ..., m_{19} \). The expression value of an miRNA \( m \) and an mRNA \( y \) across the 89 tissues is denoted as \((m_1, ..., m_{89})\) and \((y_1, ..., y_{89})\). For an miRNA \( m \), let \( s(m) \) denote the target interaction (mRNA) number that corresponds to this miRNA from the miRTarBase database.

Let \( A = \{t_{k_1}, ..., t_{k_h}\} \), \( k_1 < ... < k_h \), be a set of \( h \) tissues of the 89 tissues, where \( h = |A| \). The correlation coefficient of an miRNA \( m \) and an mRNA \( y \) across a sample set \( A \) is defined as

\[
\rho_m(A) = \frac{\sum_{i=1}^{h} (m_{k_i} - \mu_m)(y_{k_i} - \mu_y)}{\sqrt{\sum_{i=1}^{h} (m_{k_i} - \mu_m)^2 \sum_{i=1}^{h} (y_{k_i} - \mu_y)^2}}
\]

where \( \mu_m \) and \( \mu_y \) denote the means of \( m \) and \( y \) across the tissues in the set \( A \).

For an miRNA \( m \), let \( r_{[m,1]}(A), ..., r_{[m,s(m)]}(A) \) denote the correlation coefficients of this miRNA and its target interactions across the tissues in set \( A \), and let \( \bar{r}_m(A) = \sum_{i=1}^{s(m)} r_{[m,i]}(A) / s(m) \) denote the average of these correlation coefficients across the tissue set \( A \). In addition, let \( w_{\text{neg}} \) be the number of negative value of the \( s(m) \) correlation coefficients \( r_{[m,1]}(A), ..., r_{[m,s(m)]}(A) \). Then, we define the negative correlation coefficient proportion as

\[
w_{[m,\text{neg}]} = \frac{w_{\text{neg}}}{s(m)}.
\]

For an miRNA \( m \), the goal of this study is to find a tissue set \( O \) such that \( \bar{r}_m(O) \) is strongly negative. In addition, because there are \( s(m) \) correlation coefficients for the mRNA, we must require that the proportion of negative correlation coefficients among these \( s(m) \) correlation coefficients is greater than a
threshold. That is, we intend to find a tissue set such that \( 1 - w_{[m, neg]} \) is small. Thus, we propose using the loss function

\[
L(O,m) = a \tilde{r}_m(O) + (1 - a)(1 - w_{[m, neg]}) ,
\]  

(1)