SUPPLEMENTARY METHODS

The Supplementary Methods below were adopted from Murano et al. (2019) under the terms of Creative Commons Attribution 4.0 International License (CC BY)(1).

Computing overlap *P-values* of gene expression patterns in different datasets

BaseSpace (Illumina, San Diego, CA) was used to compare the signatures in publicly available microarray datasets with a signature provided by the user using a "Running Fisher" algorithm, as previously described (2–6). In brief, the overlap *P-value*, i.e., the direction of the correlation between two given gene expression datasets (*b1, b2*), and the *P-values* of the similarities between two subsets of gene expression datasets were calculated as follows:

Each gene signature set was rank-ordered according to the absolute fold-change value. Upregulated and downregulated genes were denoted by positive and negative signs, respectively, to indicate directionality. A directional subset was generated for each direction, such as *b1+, b1-, b2+,* and *b2-*.

Next, all subset pairs were identified as *b1Di*, *b2Dj*, where *Di* and *Dj* were the available directions (+ or −) in *b1* and *b2*, respectively. We applied the Running Fisher algorithm to each subset pair. The top-ranking genes in the first subset *b1Di* were collected as a group, *G*. The second subset *b2Dj* was scanned from top to bottom in rank order to identify each rank with a gene matching a member in group *G*. At each matching rank, *K*, the scanned portion of the second subset *b2Dj*, consisted of *N* genes. The overlap between group *G* and the *N* genes was defined as *M*. Fisher's exact test that was performed at rank *K* to evaluate the statistical significance of observing *M* overlaps between a set of size *G* and a set of size *N*, where the set of size *G* comes from platform *P1*. The set of size *N* comes from platform *P2*, given the sizes of *P1* and *P2* and the overlap between *P1* and *P2*. At the end of the scan, we retained the best *P-value* and applied multiple-hypothesis-testing correction factor. The negative log of the multiple-testing-corrected best *P-value* ($P_{b1Di \rightarrow b2Dj}$) was a score ($S_{b1Di \rightarrow b2Dj}$) for the subset pair. Here, the subscript *b1Di* → *b2Dj* indicates that *b1Di* was the first subset used to define the top genes *G,* and *b2Dj* was the second subset used for the scan.

$$S_{b1Di \rightarrow b2Dj} = -\ln P_{\mathrm{b1Di} \rightarrow \mathrm{b2Dj}} \quad (1)$$

Next, we performed the Running Fisher algorithm in the reverse direction. The same procedure in this reverse direction produced another score $S_{b2Di \rightarrow b1Dj}$) for the same subset pair. The two scores were averaged to represent the magnitude of the similarity between the two subsets.

$$S_{b1Dib2Dj} = \frac{S_{b1Di \rightarrow b2Dj} + S_{b2Dj \rightarrow b1Di}}{2} \quad (2)$$

The *P-value* ($P_{b1Dib2Dj}$) between *b1Di* and *b2Dj* was calculated using the following equation:

$$P_{b1Dib2Dj} = exp\ (-S_{b1Dib2Dj}) \quad (3)$$

A positive sign was assigned to pairwise correlation scores (S_{b1+b2+} and S_{b1-b2-}) for a subset pair of the same direction (*b1+b2+*, *b1-b2-*), and a negative sign was assigned to pairwise correlation scores (S_{b1+b2-} and S_{b1-b2+}) for a subset pair of opposite directions (*b1+b2-*, *b1-b2+*). Then, we calculated the overall score (*Sb1b2*) between b1 and b2 from the correlation scores (S_{b1+b2+}, S_{b1-b2-}, S_{b1+b2-}, and S_{b1-b2+}) of subset pairs using the following equation:

$$S_{b1b2} = \frac{S_{b1+b1+} + S_{b1-b2-}}{2} - \frac{S_{b1+b1-} + S_{b1-b2+}}{2} \quad (4)$$

The sign of Sb1b2 reflected whether the two signatures were positively or negatively correlated. The overall *P-value* (P_{b1b2}) between *b1* and *b2* was calculated using the following equation:

$$P_{b1b2} = exp\ (-|S_{b1b2}|) \quad (5)$$

This overall *P-value* is referred to as the "overlap *P-value*" between two gene expression patterns in this paper.

REFERENCES IN SUPPLEMENTARY METHODS

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