Transcriptome profiling reveals Silibinin dose-dependent response network in non-small lung cancer cells
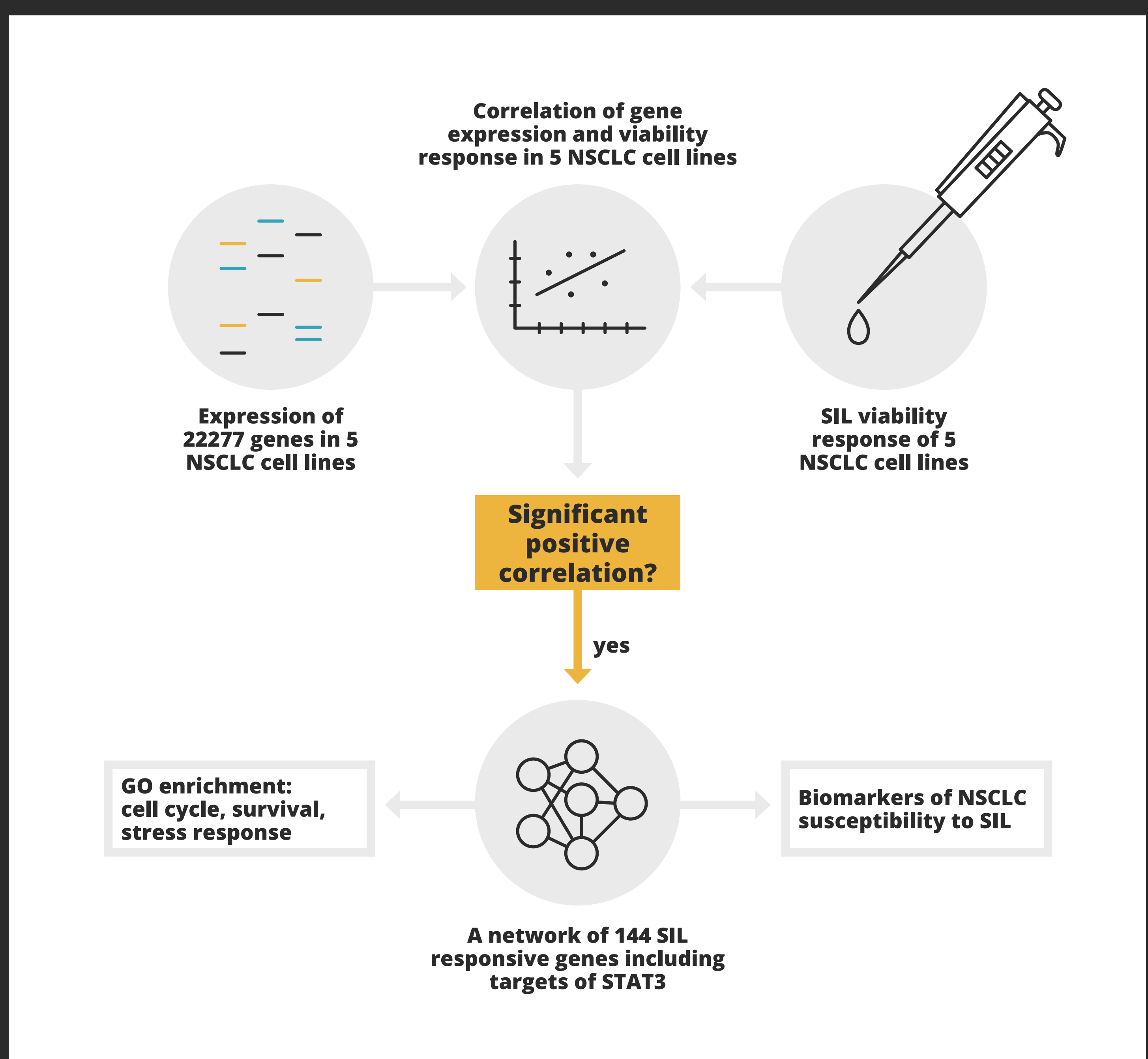
BACKGROUND

Silibinin (SIL), a natural flavonolignan from the milk thistle (*Silybum marianum*), is known to exhibit remarkable hepatoprotective, antineoplastic and EMT **inhibiting effects in different cancer cells** by targeting multiple molecular targets and pathways. However, the majority of **previous studies** investigated the effects of this phytocompound in only **one particular cell line**.

Here, we conduct a systematic analysis of dose-dependent viability response to SIL in five non-small cell lung cancer (NSCLC) lines that gradually differ with respect to their intrinsic EMT stage.

Epithelial ⟶ Mesenchymal

| H1650 | H1975 | A549 | H838 | H2030 |

RESULTS

By correlating gene expression profiles of NSCLC cell lines with the pattern of their SIL IC50 response, a **group of cell cycle, survival and stress responsive genes, including some prominent targets of STAT3 (BIRC5, FOXM1, BRCA1), was identified**. The relevance of these computationally-selected genes to the SIL viability response of NSCLC cells was confirmed by the transient knockdown test. In contrast to other EMT-inhibiting compounds, no correlation between the SIL IC50 and the intrinsic EMT stage of NSCLC cells was observed.

Correlation of gene expression and viability response in 5 NSCLC cell lines

Expression of 22277 genes in 5 NSCLC cell lines

SIL viability response of 5 NSCLC cell lines

Significant positive correlation?

yes

GO enrichment: cell cycle, survival, stress response

A network of 144 SIL responsive genes including targets of STAT3

Biomarkers of NSCLC susceptibility to SIL

CONCLUSIONS

Our experimental results show that the **SIL viability response of differently constituted NSCLC cells is linked to a subnetwork of tightly interconnected genes** whose transcriptomic pattern can be used as a benchmark for assessing individual SIL sensitivity instead of the conventional EMT signature.

Insights gained in this study pave the way for the **optimization of customized adjuvant therapy of malignancies using Silibinin**.