

## Exploring the Anticancer Mechanism of Isolated Compounds from Endophytic Fungi of the Meliaceae Family by a Network Pharmacological Analysis

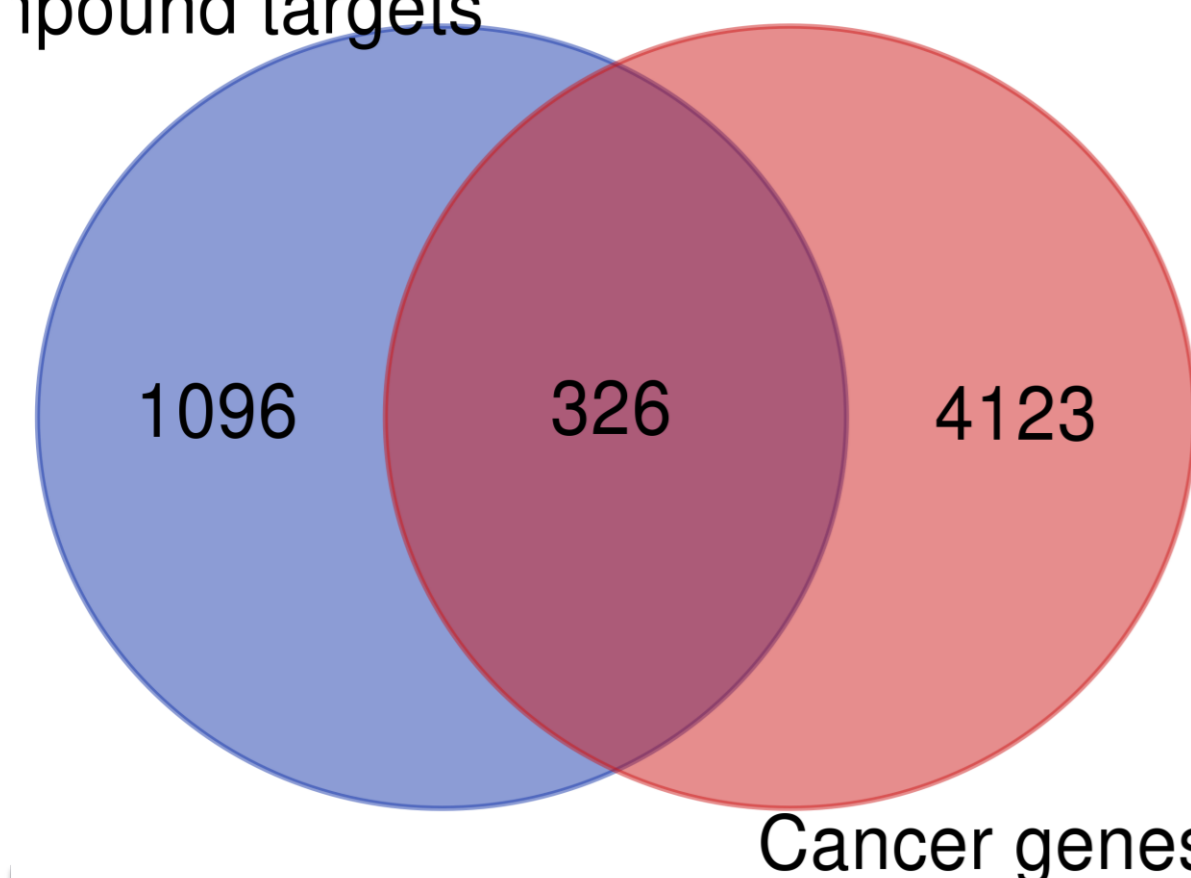
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### BACKGROUND

Traditional single-target drug discovery misses the multi-target complexity of cancer and underexplores fungal endophytes as sources of bioactive compounds. Endophytic fungi from the Meliaceae family produce diverse secondary metabolites, but their molecular targets and systemic mechanisms in cancer remain poorly understood. This study applied a network-pharmacology approach to understand the mechanisms of anticancer activity of fungal metabolites from Meliaceae endophytes.

Compound targets

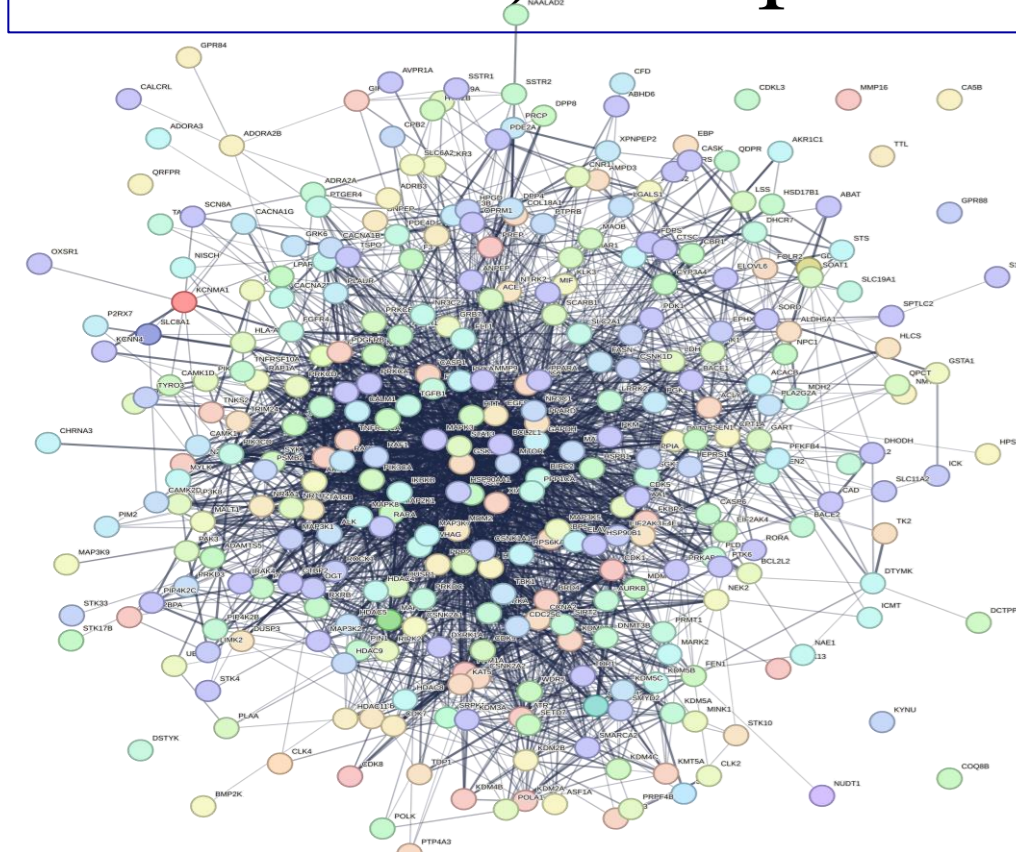


**Fig 1**  
Venn diagram showing DEGs

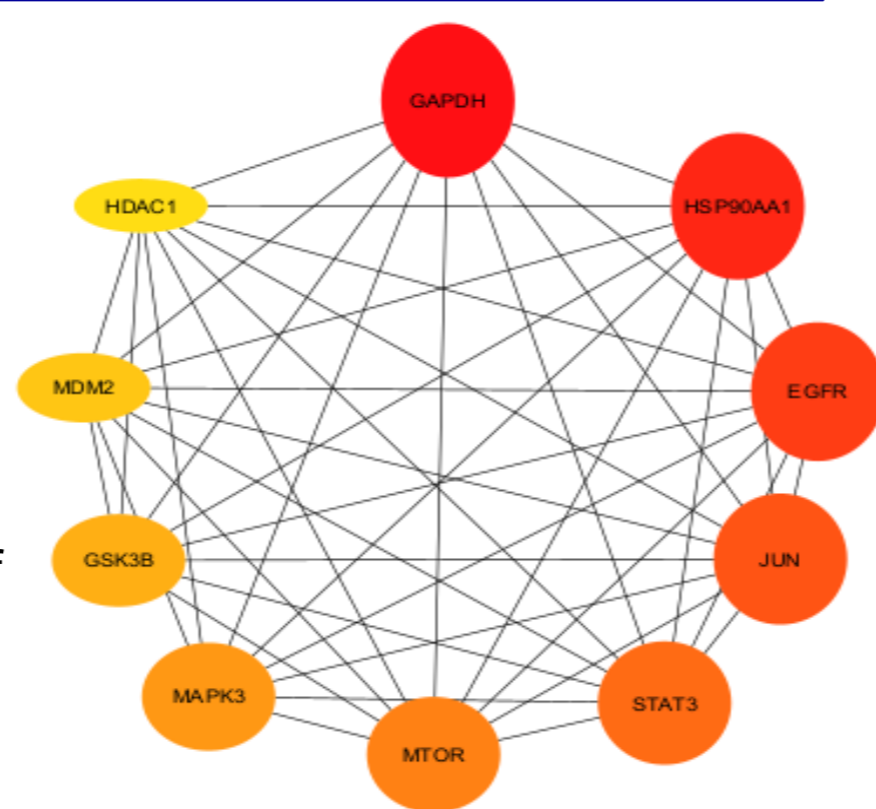
Cancer genes

### METHODS

The drug targets of 276 Meliaceae endophytes were predicted by SwissTargetPrediction. Cancer-related genes were retrieved from the GSE35972 ( $\text{LogFC} \leq \pm 2$ ,  $p < 0.05$ ). The protein-protein interaction (PPI) network of the differentially expressed genes (DEGs) was constructed using STRING and Cytoscape to identify hub genes. Functional enrichment (GO and KEGG) was performed using ShinyGO.

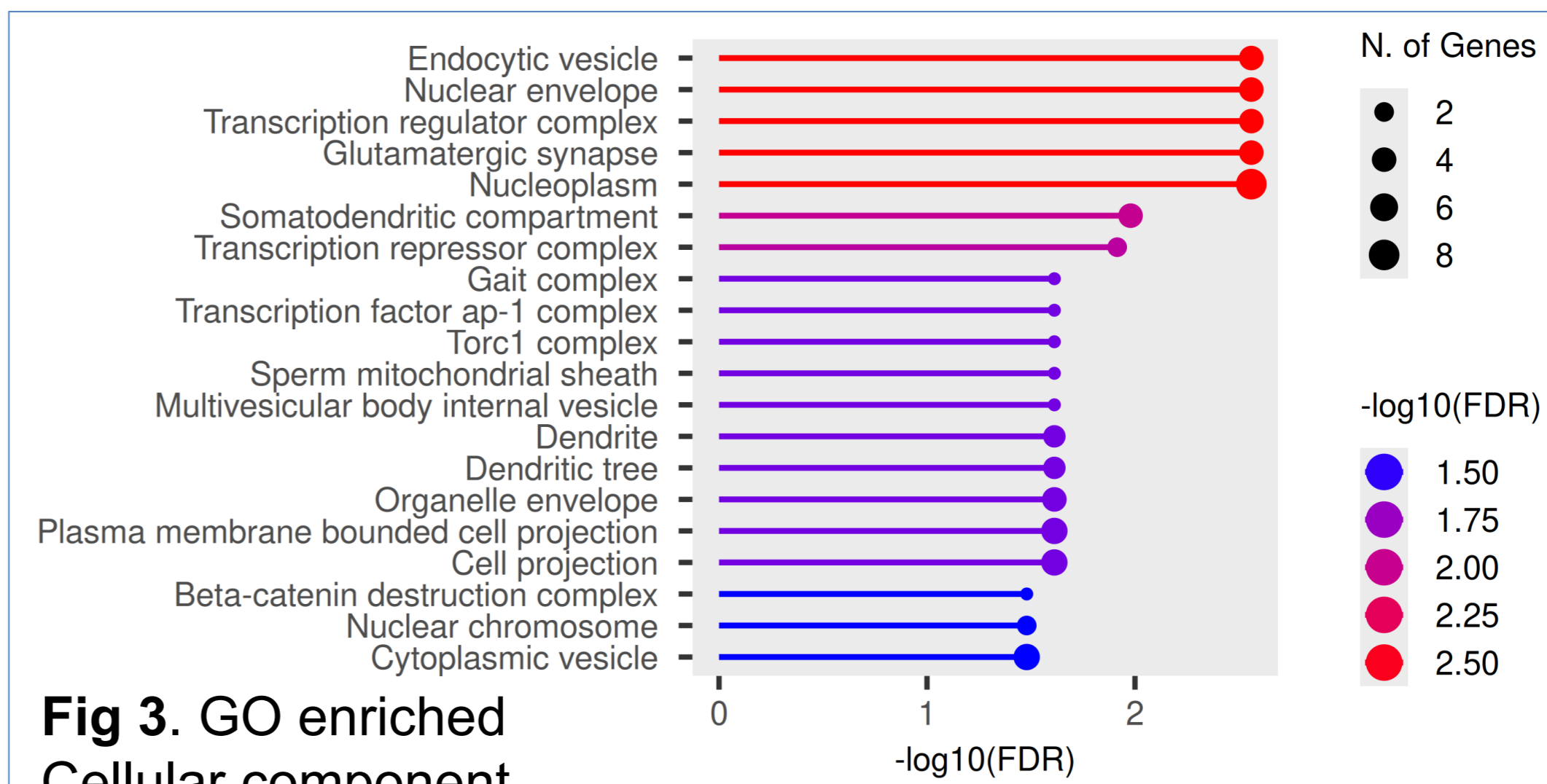


**Fig 2:** PPI network of the top 10 hub genes, analyzed



### RESULTS

326 DEGs were identified from 4,123 genes of GSE and 24007 predicted genes (Fig 1). The PPI comprised 324 nodes and 2,993 edges. The identified top hub genes included EGFR, MAPK3, JUN, MTOR, MDM2, STAT3, GSK3B, HDAC1, HSP90AA1, and GAPDH (Fig 2). The KEGG and GO enrichment analyses (Fig 3) showed pathways involved in cell growth and survival, transcriptional and epigenetic control, protein quality regulation, metabolic rewiring, apoptosis, and cell migration, with interaction of rohitukine and its analogue flavopiridol to EGFR, MTOR, and MAPK3, & emodin to EGFR, STAT3, and MDM2.



**Fig 3.** GO enriched Cellular component

### CONCLUSION

The study showed that Meliaceae endophytic fungi are a rich source of multi-target compounds that map onto central oncogenic modules. The identified hub genes and pathways provide rational priorities for experimental validation (biochemical assays, cell-based phenotyping, and in vivo models) and offer the potential for lead optimisation and combination therapy.

### REFERENCES

Mulyani Y, Sinaga SE, Supratman U. Phytochemistry and biological activities of endophytic fungi from the Meliaceae family. *Molecules*. 2023; 28(2): 778. <https://doi.org/10.3390/molecules28020778>