

Stepwise refinement refers to the progressive refinement in small steps of a program specification into a program. Sometimes, it is called top-down design.

While accumulating studies have investigated coding [gene-associated biomarkers](#) in [malignant glioma](#), research on comprehensive coding and [non-coding RNA](#)-associated biomarkers is lacking. Furthermore, few studies have illustrated the [crosstalk signaling pathways](#) among these biomarkers and mechanisms in detail.

Huang et al. identified differentially expressed genes and [Competing endogenous RNA](#) (ceRNA) networks in [malignant glioma](#) and then constructed [Cox/Lasso regression models](#) to further identify the most valuable genes through [stepwise refinement](#). Top-down comprehensive integrated analysis, including functional enrichment, SNV, immune infiltration, transcription factor binding site, and molecular docking analyses, further revealed the regulatory maps among these genes. The results revealed a novel and accurate model (AUC of 0.91 and C-index of 0.84 in the whole malignant gliomas, AUC of 0.90 and C-index of 0.86 in LGG, and AUC of 0.75 and C-index of 0.69 in Glioblastoma) that includes twelve ncRNAs, 1 MicroRNA, and 6 coding genes. Stepwise logical reasoning based on top-down comprehensive integrated analysis and references revealed [crosstalk signaling pathways](#) among these genes that were correlated with the [circadian rhythm](#), [tumor immune microenvironment](#), and [cellular senescence](#) pathways. In conclusion, the work reveals a novel model where the newly identified biomarkers may contribute to a precise diagnosis/prognosis and subclassification of [malignant glioma](#), and the identified cross-talk signaling pathways would help to illustrate the noncoding RNA-associated epigenetic regulatory mechanisms of [glioma tumorigenesis](#) and aid in [targeted therapy](#) ¹⁾.

¹⁾

Huang Y, Gao X, Yang E, Yue K, Cao Y, Zhao B, Zhang H, Dai S, Zhang L, Luo P, Jiang X. Top-down [stepwise refinement](#) identifies coding and noncoding RNA-associated [epigenetic](#) regulatory maps in malignant glioma. J Cell Mol Med. 2022 Feb 22. doi: 10.1111/jcmm.17244. Epub ahead of print. PMID: 35194922.

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