1. The rationale for conducting the meta-analysis.

Limited number of studies (Boire et al. 2017; Chi et al. 2020; Fan et al. 2018; Li et al. 2021; Ruan et al. 2020; Smalley et al. 2020; Smalley et al. 2021) investigated the differentially expressed genes (DEGs) and used multi-omics data to understand the LMC progression. Only two meta-analyses (Tewarie et al. 2021; Wang et al. 2022) were conducted to analyze potential diagnostic values and assess risk factors for LMC. Nevertheless, one of the main challenges is that these studies focused on different primary tumor sites and different aspects in LMC progression such as DEGs, tumor microenvironment, or immune landscape. Therefore, this study aims to identify possible molecular pathways that may be involved in LMC development.

1. The contribution that the meta-analysis makes to knowledge in light of previously published related reports, including other meta-analyses and systematic reviews.

This study fills the gap in the literature by conducting a meta-analysis by gathering the information of mutated genes from a total of 16 articles about LMC caused by NSCLC, breast cancer, and melanoma. The outcome enables the identification of commonly mutated genes in three primary cancers, sheds light into the molecular mechanism of LMC, and finally finds possible targets for therapy.

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