In this manuscript by Nie et al., authors have collected miRNA expression data of non-small cell lung cancer (NSCLC) from publicly available databases. After some initial screening they identified 5 miRNAs and performed PPI analysis using STRING to identify 61 hub genes. Finally, they found that *GTF2F2* is one of the hub genes that is independently regulated by miR-708-5p. Pathway analysis of *GTF2F2*, as expected, shows that it can regulated RNA pol II mediated transcription. Based on this the authors propose miR-708-5p can be used as a marker for lung cancer.

The hypothesis proposed by the authors is reasonable and well-known that independent regulation mode is more "fragile" and "influential" and so is worth the chase. The reviewer appreciates that authors have used multiple datasets for the screening process which makes a robust analysis. Computational screening for SDE miRNAs using stringent parameters such as $|\log2 (FC)| \geq 1$, p-value < 0.05, SNR, NOG ≥ 3, and AUC ≥ 0.9 is also appreciated. The reviewer feels that conclusions derived downstream of this screening are somewhat biased and oversee other potential findings.

Comments:
1. Of the 5 miRNAs identified after AUC and NOG cutoff, why was only miR-708-5p chosen for downstream screening? Why not miR-218-5p, miR-1-3p or miR-183-5p even though they had NOG values of 19,14 and 6 respectively and all had AUC > 0.9?
2. As a follow-up to previous comment, wouldn't it make more sense, according to the initial hypothesis, to identify a hub gene related to these three miRNAs since they would have a more "fragile" network?
3. In table S4 which shows 61 hub genes with their degree of connectivity, there are 3 other genes with their respective degrees in the 90s. These are *BTRC* (degree=97), *TCEB2* (degree=92) and *RNPS1* (degree=90). Which miRNAs regulate these genes? Why did the authors consider the 4th candidate on the list?
4. DAVID functional analysis of any general transcription factor would yield similar results as they are well documented to play role in RNA pol II mediated transcription. The extrapolation from miR-708-5p to *GTF2F2* to accelerated tumor growth is overstated.

Unfortunately, most information presented downstream of identifying miR-708-5p seems to be selective. If the authors believe their conclusion about miR-708-5p to be true despite of this, it would be worthwhile performing some experiments on NSCLC cell lines or tissue samples to prove their hypothesis.