

SPECIFIC COMMENTS TO AUTHORS:

This manuscript brings forward latest knowledge on the factors underlying therapy resistance in hematological cancers. Overall the hypothesis is centered on the altered metabolism in tumor microenvironment and how it promotes the observed resistance. The authors introduce the concept of resistance followed by individually highlighting the different pathways regulating therapy resistance. Specific sub-sections are dedicated to hypoxia, PI3K/Akt/mTOR, Ras, NFκB among others. Next the authors describe different hematological cancer resistance and ways to target resistance. Newer concepts and drugs are discussed including microenvironment targeted approaches, long non-coding RNAs etc. The topic is very attractive and timely. Text is supported by 94 references. There are some minor limitations: The text is excellent. However, it should be supported by at least one table and one figure summarizing various intertwining pathways that support therapy resistance. One table could be for markers and second table for targeted drugs. Authors should carefully check the paper for typos and grammar.

Reply:

We appreciate your critical comment about our manuscript. We made a table that summarizes various signaling pathways of hematological cancers. We also made a figure that summarizes various signaling pathways of hematological cancers that induce cancer development and therapy resistance. We also checked the typos and grammar of this paper.