

## Review of: "Metabolic Reprogramming and Cancer: 2022"

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The present review of Susinjan Bhattacharya dealt with the mechanism of metabolic reprogramming which is an adaptation to low nutrient and oxygen conditions in the tumor microenvironment for enabling cancer cells of diverse origin to hyperproliferate. The concept is interesting. However, some of the problems need addressal for better comprehension. Some of the suggestions are as follows:

- 1. In the Abstract section, full name of EMT and VM needs to be mentioned as per convention.
- 2. The term Thermodynamic change that has been mentioned in the abstract means what is not clearly mentioned. Is it the fact that the thermodynamic behaviour of metabolic enzymes gets dysregulated? Dysregulated metabolism is one of the most common and recognizable features of cancer. Within the main manuscript Thermodynamic constraints is not explicitly mentioned.
- 3. It is not clearly mentioned in the manuscript that which cue is giving an indication of requirement of metabolic reprogramming in cancer.
- 4. The title is based on metabolic reprogramming. However, the authors are majorly concentrating on EMT.
- 5. The term should be 'vasculogenic mimicry' instead of 'vascular mimicry'
- 6. It is not clear how gut microbiome comes into the picture. How it is related with metabolic reprogramming is not clear.
- 7. Since the author is concentrating on metabolic reprogramming; the author should concentrate on the involvement of following events in driving metabolic rewiring
- a). Altered redox homeostasis
- b). Deregulated signaling pathways
- c). Glutamine metabolism
- d). Hexose monophosphate shunt
- e). Lipid metabolism
- f). TCA cycle
- g). One carbon metabolism.
- 8. The information under each topic is superficial; not elaborated properly. It would have been wiser and better if the author would explain the mechanisms underlying metabolic reprogramming under broader subheadings as discussed.