

## Review of: "Targeting Cancer Cell Signaling Using Precision Oncology Towards a Holistic Approach to Cancer Therapeutics"

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Potential competing interests: No potential competing interests to declare.

pg2 (Introduction): line 1: change "causing" to "responsible for". Also change "huge physical, psychological, and economic" to "multifaceted".

pg2, line 3-4: change "an early diagnosis and improving prevention and treatment strategies for the disease" improving patient prognosis, diagnosis and treatment response".

If you decide to include the sentence above, you could not include the sentence in lines 4-6 "It requires...across the alobe."

pg2, line 8: change "pancreas" to "pancreatic".

pg2, line 7-10: "Most cancers...and neuroblastomas", i feel like you could not include this part, it feels like it is way too detailed. I could be wrong.

pg2, line 11: "They are", which are? Also, the whole sentence is too simplistic. Consider changing it to "These malignancies, rank amongst the most prevalent cancer categories, exacting a substantial toll in terms of both human lives and economic resources on a global scale". Although, i would try to not use the word "toll", so maybe find another way to phrase it.

pg2, line 12: change "towards fighting the menace of cancer" to "against cancer".

pg 2, line 14: Why is Richard Nixon mentioned?

pg2, lines 12-19: The whole part "Thus, considering...cancer development." feels unecessary.

pg 2, line 23: change "that were considered the deadliest diseases earlier" to "that were once considered".

pg 3, line 3: remove "and subtypes. Cancer types is enough. Also, you can change "prevention" to "prognosis". If you decide to follow my earlier advice, you can keep "prevention". You shouldn't repeat "prognosis".

pg 3, line 4: Cancer is not the leading cause of death (worldwide). If you meant something else, then change the text to make the correct sense.



pg 3, lines 5-6: In the original sentence, change "There are kinds" to "There have been", because you write "for quite some time" later. Also, you can include less examples of therapies, as including so many gets tiring to read.

pg 3, line 7: Avoind using "must". And in general try to not be so direct as to say "cure" for cancer. Not a big deal though, i think.

pg 3, line 11: change "spread to other parts of the body" to "metastasize to distant loci."

pg 3, line 13: remove "in reality"

pg 3, lines 13-17: The sentences "Cell proliferation requires...wound healing." and "The fundamental...and differentiation." say exactly the same thing. Also, you have already mentioned uncontrolled cell division, in line 11. You can remove the whole part of lines 13-17 that i mentioned.

pg 3, lines 18-19: change "to ascertain that cellular developments go well in time." to "to ensure proper cellular development".

pg 3, lines 20-21: change "lead the cellular...tumor formation." to "leading to aberrant cell growth and tumor formation."

pg 3, line 23: change "concerned" to "responsible"

pg 3, lines 24-26: i do not like that sentence.

pg4, line 6: change "on or off" to activated etc.

pg4, line 12: no need to say both seperate and independently. Just say "as two independent mechanisms".

pg4, line 13: "which may is not the whole" doesn't make sense.

pg4, line 19-28: "Cancer in general...every cell in the body" add more references in that part

pg 6-7, "Because the realization...without affecting normal cells". You have only one reference there (27), you should definitely add more.

You could add more biomarkers to Table 1.

pg 9, line 6-7: you can add more tumor suppressor genes, such as BRCA1-2 or PTEN.

Section 5 "Signaling Pathway Deregulation and Prospective Targets for Cancer Therapeutics". I feel like the introductory information you present, albeit correct, are a bit too long. Maybe you can shorten that part and then start mentioning the pathways.

pg 24, lines 3-4: You mention circulating DNA and extracellular vesicles. Firstly, the correct term is "circulating tumor DNA (ctDNA)". Additionally, as i specialise in the area of liquid biopsy i think it is a vastly growing field with studies focusing on Circulating Tumor Cells (CTCs), ctDNA, EVs, Cell-Free DNA (cfDNA) and microRNAs (miRNAs). Based on my knowledge i would create a seperate section in the paper focusing on liquid biopsy alone. If you don't want to do that you can add



some related information as a subsection in your Section 9.

Section 9 "Precision Oncology and Targeted Drug Therapy of Cancer". If we are talking about mAbs i think PD-L1 should definitely get a mention. Especially since you are already mentioning CTLA-4.