

Review of: "[Research Note] Semaglutide, a GLP-1 Agonist Like Ozempic, and Its Potential Role as a Preventive Anti-Cancer Agent"

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Potential competing interests: No potential competing interests to declare.

In this research note, the authors tried to promote the repurposing of Semaglutide as a cancer prevention agent. The authors have well-explained the shared signalling pathways involved in both diabetes and cancer, such as activation of cell proliferation and inflammatory response pathways like MAPK, NF-kB, and JAK-STAT. This provides justification to utilize Semaglutide to prevent cancer progression, including uncontrolled cell proliferation, angiogenesis, and metastasis, by targeting these malignant signalling pathways. However, there are a few comments and concerns as listed below:

- One must take note that the reported anticancer activities of GLP-1 agonists were limited to Semaglutide target organs such as the pancreas and colorectal, which future studies should focus on for these organs with a possible higher success rate.
- 2. The angiogenesis references that had been quoted by the authors indicate that GLP-1 promotes angiogenesis in human endothelial cells in a dose-dependent manner, through the Akt, Src, and PKC pathways, instead of the reported "interfering with pro-angiogenic factors, these agonists create an inhospitable microenvironment for tumor growth, undermining the critical support network required for sustained malignancy." This is misleading.
- 3. There are also some clinical studies that reported the possible higher risk of developing medullary thyroid cancer and pancreatic cancer associated with the consumption of GLP-1 agonists. Although almost an equal number of studies stated no direct association of Semaglutide with cancer, one must exercise caution regarding the possibility that this drug might promote malignant neoplasms.

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