Review of: "Metabolic Reprogramming and Cancer: 2022"

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Potential competing interests: The author(s) declared that no potential competing interests exist.

The author's review is based on misunderstandings of foundational cancer cell biology. Vague ideas on how diet might influence metabolic reprogramming or manage cancer is another weakness.

A number of grammatical errors also detract from the information reviewed.

Major Issues

1. The author states on page 4, first paragraph, "biological research have proved that many of the signaling pathways changed by gene mutations regulates cancer cell metabolism, and can lead to conditions, like aerobic glycolysis or 'Warburg effect'. Reports evidence aberrations in the proto-oncogenes, Myc or Ras leading to glycolytic phenotype by HIF 1α – mediated metabolic reprogramming." The author should recognize that the gene mutations, aerobic glycolysis (Warburg effect), and aberrations in the proto-oncogene expression are all down stream effects of dysfunctional OxPhos (https://doi.org/10.3390/metabo11090572)[1].
2. The author should also recognize that the EMT/MET hypothesis is inconsistent with concepts of evolutionary biology. The EMT/MET hypothesis has yet to explain how random somatic mutations could transform an epithelial cell into a biologically distinct mesenchymal cell (EMT), and then have these random mutations be suppressed or reversed to allow a transition of the mesenchymal phenotype back to an epithelial phenotype (MET) (https://doi.org/10.3390/metabo11090572)[1]. Consequently, most of the information presented dealing with the EMT/MET, which involves much of the review, will require reevaluation and reinterpretation especially related to the origin of metastasis.
3. The author cites reference 54 which suggests that cancer cells can switch from glycolysis to OxPhos based on the EMT/MET concept. The information in this reference is based on the misunderstanding that oxygen consumption is a biomarker for OxPhos in cancer cells, which is no longer the case (doi.org/10.1016/j.molmet.2021.101389; doi.org/10.3390/metabo11090572)[2][1].
4. No information is presented on how dietary factors could alter reprogramming in cancer cells and normal cells. The issue of dietary factors is vague. No information is presented showing how specific dietary factors or diets could reprogram cancer cell metabolism to manage or control dysregulated growth.

References

1. [a, b, c] *Thomas N. Seyfried, Christos Chinopoulos. (2021). Can the Mitochondrial Metabolic Theory Explain Better the Origin and Management of Cancer than Can the Somatic Mutation Theory?. Metabolites, vol. 11 (9), 572. doi:10.3390/metabo11090572.*
2. [^] *Tomás Duraj, Josefa Carrión-Navarro, Thomas N. Seyfried, Noemí García-Romero, et al. (2021). Metabolic therapy and bioenergetic analysis: The missing piece of the puzzle. Molecular Metabolism, vol. 54 , 101389. doi:10.1016/j.molmet.2021.101389.*