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Letter

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Hypoxia in prostate cancer

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Dear Editor,

I have read with great interest the review "Current challenges and opportunities in treating hypoxic prostate tumors" by McKenna *et al.*[1]. In this review, the authors present, as a key information in Table 1 of their article, values of oxygen partial pressures (pO_2) in human tumors and the respective normal tissues, published earlier by our group[2,3] and "adapted" by McKeown[4] later.

In their article, McKenna *et al.*[1] have reviewed current knowledge about the impact of the "hallmark feature" hypoxia on pathways promoting cancer growth, malignant progression, therapeutic resistance and tumor immune escape[5-7]. Certainly, this information is of utmost interest to experimental and clinical oncologists. However, since this review contains some misleading/inappropriate oxygenation data, some additional information that may be of interest for the distinguished readership of this highly reputed journal, may serve for clarification.

In Table 1 of their review, McKenna *et al.*[1] present oxygen partial pressure (pO_2) values together with oxygen concentration (cO_2) data. When reviewing the biological role of hypoxia in malignant tumors, authors lacking an expertise in respiratory physiology often convert - without any need - the *in vivo* pO_2 values, originally measured in tumors (and in normal tissues) using pO_2 histography[2], into O_2 concentrations using either Dalton's law (only valid for gas mixtures within the airways) or Henry's law for gases dissolved in solutions, which cannot describe the relationship between partial pressures and concentrations of gases in heterogeneous media (e.g., tissues with lipid-rich membranes, the cytosol and the extracellular space, the latter with a high content of free water in cancers). Therefore, it is strongly suggested to avoid any conversion of measured pO_2 values into cO_2 data since the O_2 solubility coefficient is: (1) highly dependent on the tissue water content; and (2) usually not known for heterogeneous cancer tissues in patients. In this context, it has

to be mentioned that authors not familiar with respiratory physiology often use "local O_2 concentrations" by mistake, although pO_2 values have been measured in the original studies[2,3] (for typical examples see Table 1 in the review by McKenna *et al.*[1]).

Considering Henry's law ($cO_2 = \alpha \times pO_2$; α: oxygen solubility coefficient), McKenna *et al.*[1] have communicated questionable oxygenation data grounded on wrong/doubtful O_2 solubility values for malignant and normal tissues, which originally have been communicated for blood plasma, i.e., irrelevant data when heterogeneous tissues such as prostate cancer are considered[8].

Oxygen solubility coefficients for heterogeneous tissues (e.g., for experimental tumors[9]) are significantly lower than those for blood or blood plasma[10]. Due to this misconception, the O_2 concentration data of Table 1 in the review by McKenna *et al.*[1] are misleading/not correct and should, therefore, be removed from the table. There is no need to present concentration data in this comprehensive review.

DECLARATIONS

Authors' contributions

Vaupel P contributed solely to the paper.

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Conflicts of interest

There are no conflicts of interest.

Patient consent

Not applicable.

Ethics approval

Not applicable.

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