

Review of: "The role of pH in cancer biology and its impact on cellular repair, tumor markers, tumor stages, isoenzymes, and therapeutics"

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I like the basic idea of the paper. It is basically a quick review paper, and that's OK, especially to get a start on a very complicated field.

What I don't like about the paper is that it pretty much glosses over the details of how cancer cells maintain a cell environment that is quite different from normal cells, both internally and in the nearby environs. This is fundamentally interesting, but complex. Is that environment always different or only sometimes different? Does that environment include gradients? and if so, how strong are those gradients? What are the dynamics involved e.g. are cancer proton pumps more numerous, or do they pump faster, or slower, or both? What about ionic gradients? those seem equally as important as proton gradients. pH depends strongly on local environment e.g. succinic acid is both more and less acidic than acetic acid...because of local effects. Picking up on that theme, how spatially dispersed are the pH effects in the paper - nm, um, mm? without a sense of scale it is difficult to interpret what is being discussed. Are these pH effects manifested for a single cancer cell, or only for macro-assemblies of cancer cells, is there a critical size at which pH effects manifest?

In short, the enzymatic/molecular basis for the paper is largely lacking. A paper must always stand on it's own merits, being complete in and of itself, references are nice, and the interested reader will follow those up, but a precis in and of itself is not a paper. The paper has a thesis, but doesn't do a good job of supporting that thesis. It has to be fleshed out in more detail, and with more specifics. The path for that is probably to narrow it down considerably...it's too broad in it's current incarnation, too superficial. It needs to tell a more focused, more precise story, a deeper dive into the specifics. If the paper is about using derivatized sugars to control cancer pH...great...talk about that...but only that. The rest is extraneous and detracts from the paper.