Review of: "The Stay-Or-Leave Dilemma of Cells in Punctuated Tumors"

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I got to read about this topic after a long time. Infact, the jargon of punctuated tumors is not widely-talked about. I assume that you have tried to put up a review piece putting together all the relevant models supporting your argument. I must say that this effort is unique yet not comprehensive. Detailed discussions like the article by Cajal et al. (J Mol Med,2020) shall make the article more robust.

Reasoning for statemnets like, "…by escaping the primary tumor under unfavorable contexts to reach better landscapes farther away." can not be unidimesional. such phenomenon are multifactorial, combining active and passive processes (e.g., chemotaxis, loss of apical/basal poalrity). Also, I feel that essentially being a genetic disease driven by oncogenic driver and passenger mutations, tumor microenvironmental parameters are not only reason for ITH. Clonal proliferation can be attributed to the translesion DNA synthesis, hypermutative phenotype, etc.
Also altruistic behavior is partly responsible for the survival of some clones at the expenses of others. Biological conduits like CNTs are a proof of that. "Along with high levels of chromosome complexity, punctuated tumors typically display low levels of ITH."- This may sound paradoxical but spatial and epigenetic regulations can affect individual tumor cells. The spatial effects can be attributed to the local interactions among cells. Such supporting references should be added. While mentioning the statement: "but also the edge that separates two different evolutionary patterns, i.e., linear and punctuated., you can touch upon leading/lagging duality seen in metastatic breast adca. It is also an example of edge-based metabolic reprogramming.

Overall, I beileve that this topic holds a great potential and can be expanded further.