

# Review of: "Somatic evolution of Cancer: A new synthesis"

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The published manuscript addresses a very interesting and promising hypothesis, connecting the mechanisms and pathways involved in wound healing with the tumorigenesis process. The authors refer some compelling evidence about the close association between both processes, and propose explanations for some missing links, as neoantigens not being detected in wound healing. Some valuable testable predictions of their hypothesis are presented as well as some very relevant experimental evidence that can be acquired in dedicated tests.

One aspect that is not clear, and should be discussed in detail, is the the overall point of view of carcinogenesis, of adopting a cell-centric approach (the rogue cancer cell that has acquired a number of mutations and proliferates in an uncontrolled way) or a tissue based proposal (where the loss of regulation/communication led to uncontrolled cellular proliferation). As the experimental evidence stands, in particular when comparing with the complex wound healing development, the last perspective looks much more productive and realistic. The recommendation is to consider some aspects of the Tissue Organization Field Theory to explain and correlate the experimental evidence.

Related to the the questions of cell mutations in cancer, it is not clear if mutations are a cause of tumorigenesis or if this is a consequence of rapid and uncontrolled cell proliferation, when the normal DNA check mechanisms don't act in time. This outlook could also be very fruitful in the interpretations of results. The tissue organization paradigm is also very hopeful when addressing therapeutical interventions, where an effort of normalization of tissue organization can drive the cancer reversal to a normal tissue behavior.

A systematic and complete review is presented, comparing the wound healing process with cancer development, and is given a list of wound healing functions of cancer related genes and of gene differentially expressed during various phases of wound healing and their involvement in cancer. The text would benefit in being more compact and focused, with reduced repetition of some ideas, but it is, in general, clear and well explained.