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Cancer therapeutic potential of the interplay between the immune system and tumor-associated vasculature

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Currently, most of the basic mechanisms governing tumor-immune system interactions, in combination with modulation of tumor-associated vasculature, are far from being completely understood. A mathematical model of vascularized tumor growth is developed, where the main novelty is the modelling of the interplay between functional tumor vasculature and effector recruitment dynamics. Parameters are calibrated on the basis of different in vivo $Rag1-/-$ and wild-type (WT) $BALB/c$ murine tumor growth experiments. The model analysis supports that vasculature normalization can be a plausible and effective strategy to treat cancer when combined with appropriate immuno-stimulation. Moreover, we find that improved levels of functional vasculature, potentially mediated by vascular normalization or stress alleviation strategies, can provide beneficial outcomes in terms of tumor burden reduction and control. Normalization of tumor blood vessels opens a therapeutic window of opportunity to augment the anti-tumor immune responses, as well as to reduce the intratumoral immunosuppression and hypoxia due to vascular abnormalities. The potential success of normalizing tumor vasculature closely depends on the effector cell recruitment dynamics and tumor sizes. Furthermore, an arbitrary increase of initial effector cell concentration does not necessarily imply tumor control, and we evidence the existence of an optimal effector concentration range for tumor shrinkage. Based on these findings, we suggest a theory-driven therapeutic proposal that optimally combines immune- and vaso-modulatory interventions.

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