Assessing Response to Photodynamic Therapy and its Foundation

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Abstract:

Our primary research focus is the investigation of photodynamic therapy (PDT) for the treatment of solid malignancies. PDT involves the local illumination of tumors that have accumulated a photosensitizer following exogenous administration of a photosensitizer or its precursor. The light-excited photosensitizer interacts with oxygen in the treated tissues (tumor) to produce reactive oxygen species that damage the tissue and its associated stroma, including the supporting vascular network. Thus, vascular damage composes a major mechanism of therapeutic effect by PDT with many photosensitizers and light delivery protocols. PDT damage to the tumor-supporting blood vessels can ultimately lead to tumor cell death through nutrient/oxygen deprivation, while it can also trigger the activation of protective responses. We have investigated the mechanisms through which the structure of tumor vessels and the composition of their network serve as effectors of PDT response. For example, the collagen composition of vascular basement membrane can influence the sensitivity of tumor blood vessels to PDT. Moreover, the activation of survival signaling secondary to vascular and tumor damage can rescue tumor blood vessels from the comprehensive shutdown necessary to impact treatment outcome. Indeed, inhibitors of this signaling can increase the propagation of vascular damage after PDT. Overall, our investigations have revealed specific mechanisms by which the structural and molecular composition of the vascular microenvironment can alter tumor response to PDT. They open the door to the development of new possibilities toward exploiting tumor microenvironment for improved application of PDT.