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Caspase 3 in Dying Tumor Cells Mediates Post-Irradiation Angiogenesis

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Cytotoxic radiotherapy unfavorably induces tumor cells to generate various proangiogenic substances, promoting post-irradiation angiogenesis (PIA), which is one of major causes of radiotherapy failure. Though several studies have reported some mechanisms behind PIA, they have not yet described the beginning proangiogenic motivator buried in the irradiated microenvironment. In this work, we revealed that dying tumor cells induced by irradiation prompted PIA via a caspase 3 dependent mechanism. Proteolytic inactivation of caspase 3 in dying tumor cells by transducing a dominant-negative version weakened proangiogenic effects *in vitro* and *in vivo*. In addition, inhibition of caspase 3 activity suppressed tumor angiogenesis and tumorigenesis in xenograft mouse model. Importantly, we identified vascular endothelial growth factor (VEGF)-A as a downstream proangiogenic factor regulated by caspase 3 possibly through Akt signaling. Collectively, these findings indicated that besides acting as a key executioner in apoptosis, caspase 3 in dying tumor cells may play a central role in driving proangiogenic response after irradiation. Thus, radiotherapy in combination with caspase 3 inhibitors may be a novel promising therapeutic strategy to reduce tumor recurrence due to restrained PIA.

Biography:

Xiao Feng has acquired the Doctor's Degree in Oncology from Shanghai Jiao Tong University in july 2017. Xiao Feng has been focusing on unrevealing the mechanisms of how dying tumor cells promote tumor repopulation after radiotherapy from the perspective of neovascularization. Similarly, not only in colorectal cancer, we have also discovered important role of caspase 3 in post-irradiation angiogenesis in glioma cells. Therefore, we may hypothesized that it might be a biologically conservative signaling pathway in the process of tumor recurrence after radiotherapy. We hope this interesting phenomenon could be known by more researchers.