2939 The Matricellular Protein, Periostin, Negatively Impacts Radiation Response in Head and Neck Cancer Models

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Purpose /Objective(s): Despite improvements in surgery, chemotherapy, and radiation, overall survival of patients with head and neck squamous cell carcinomas (HNSCC) has remained stable for 30 years. Inherent or radiation-induced signaling pathways within HNSCC likely promote resistance to therapy. Periostin, is a component of the tumor microenvironment that can alter cancer signaling. This matricellular protein has been shown to play a predominantly pro-tumorigenic role in many cancers, increasing cancer cell survival, invasion, and metastases. Since the role of periostin in the context of radiation has not been investigated, we sought to determine its importance in relation to radiation response.
Materials/Methods: Human derived HNSCC cell lines (Fadu, UMSCC-1, UMSCC-6) and murine derived microvascular endothelial cells (2H11 and 3B11) were analyzed in response to ionizing radiation with or without recombinant periostin (100-1000ng/ml). Periostin mRNA expression was determined by RT-PCR using human and murine primers from Applied Biosystems. Western blotting for periostin, Akt, phospho-Akt, GAPDH, and actin were performed. Cellular proliferation was measured using Quickcell Assay Kit (Genscript) and clonogenic assays. Chick chorioallantoic membrane (CAM)-HNSCC xenografts were generated for tumor vascular proliferation experiments using matrigel/gelfoam plugs to quantitate the number of vessels intersecting the tumor at 72 h.
Results: Periostin expression was induced at the level of mRNA and protein level in HNSCC cell lines in response to 0-8 Gy irradiation. Radiation (0-8 Gy) also promoted increased periostin protein expression in microvascular endothelial cells in as little as 48 h. The addition of recombinant periostin promoted Akt phosphorylation in both irradiated and non-irradiated HNSCC while significantly protecting the cells from radiation cytotoxicity. Similar radiation protection was seen with the addition of recombinant periostin in the microvascular endothelial cells. When HNSCC tumor xenografts were implanted within CAM's, recombinant periostin generated a significant increase in tumor vasculature (p=0.0013).
Conclusions: We have shown in our model systems that periostin expression is induced by ionizing radiation in HNSCC and tumor microvascular cells. We further show that periostin itself can trigger pro-survival signaling pathways as demonstrated by enhanced phospho-Akt resulting in radiation protection. Furthermore, exogenous periostin also promoted angiogenesis in CAM-xenografts of HNSCC tumors. Ongoing studies of periostin are aimed and studying its role in modulating radiation sensitivity in HNSCC and its vasculature. Thus, periostin may represent a new target for therapeutic development.

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