Epithelial-to-mesenchymal transition enhances cancer cell sensitivity to cytotoxic effects of cold atmospheric plasmas in breast and bladder cancer systems

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Cold atmospheric plasma (CAP) has emerged as a highly selective anti-cancer agent, most recently in the form of plasma-activated medium (PAM). Since epithelial mesenchymal transition (EMT) has been implicated in metastasis and resistance to various cancer therapies, we assessed whether EMT status associated with PAM response. Mesenchymal breast cancer cell lines as well as the mesenchymal variant in an isogenic EMT/MET human breast cancer cell system (PMC42-ET/LA), were more sensitive to PAM treatment than their epithelial counterparts, contrary to their responses to other therapies. The same trend was seen in luminal bladder cancer model (TSU-Pr1/B1/B2) and the basal 5637 bladder cancer cell line. Three-dimensional spheroid cultures of the bladder cancer cell lines were less sensitive to the PAM treatment compared to their 2-dimensional counterparts; however incrementally better responses were seen in more mesenchymally-shifted cell lines. This study provides evidence that PAM preferentially inhibits mesenchymally-shifted carcinoma cells, which have been associated with resistance to other therapies. Thus, PAM may represent a novel treatment that can selectively inhibit triple-negative breast cancers, which tend to be more mesenchymal, and may be selectively active against metastasis. Our approach may potentially be utilized for other aggressive cancers exhibiting EMT and opens new opportunities for CAP and PAM as a promising new onco-therapy.