

MHC CLASS I POLYPEPTIDE RELATED A (MICA) AS MARKER OF AGGRESSIVE PROSTATE CANCER.

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Background: Prostate cancer (PCa) is the second most common cancer in American men, with higher incidence and death rates in African American men (AAM) relative to Caucasian American men (CAM). MHC class I polypeptide-related sequence A (MICA) is a protein expressed in the membrane of tumor cells that binds to the NKG2D receptors in NK cells and subtypes of CD8⁺T cells, activating its cytotoxic effects. Aggressive tumors cleave MICA from the membrane and release the soluble form (sMICA) into the plasma. Reports in PCa show loss of MICA expression from the cell surface is associated to a more aggressive phenotype and increased levels of sMICA were linked to patients with Gleason score (GS) greater than 7. We hypothesized that conditions related to tumor aggressiveness in the microenvironment, would modify the levels of MICA in PCa. Likewise we speculated that, when compared to CAM, MICA would be differentially expressed in tumors from AAM.

Methods and Results: To access the different expression of MICA in AAM and CAM PCa patients we stained a TMA containing 41 CAM and 44 AAM tumor cores for MICA expression. Our results showed that CAM PCa tumor cores have increased chance for higher expression of MICA than the AAM (38% vs 7% respectively, $p=0.0076$). Moreover, the increased expression of MICA in tumor cores of CAM patients with GS greater than 7 is significantly higher than in specimens from AAM patients ($p=0.0014$). Next, we explored the effect of hypoxia, a condition known to be associated with tumor aggressiveness, on MICA surface expression. FACS analysis on C4-2B cells revealed that 1% O₂ (hypoxia) reduced MICA expression by 24.1%, relative to 20% O₂ (normoxia). Likewise, incubation of PCa cells in the presence of 100μM cobalt chloride, a compound that mimics hypoxia by inducing HIF-1/3 alpha, reduced MICA by 16.7%, relative to control conditions.

Conclusions: Our studies indicate that expression of MICA is modified by disease aggressiveness. More work is necessary to validate our results showing differential expression of MICA in minorities. Of equal interest is the progress of experiments focused on elucidation of the mechanistic involvement of tumor microenvironment on MICA-mediated tumorigenesis and immunoevasion.

Conflicts of interest: None

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