Role of CD82 in prevention of prostate cancer metastasis

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Prostate cancer is one of the most commonly diagnosed forms of cancer in males; it is the second most frequent cause of cancer related death in the United States. A diagnosis of a malignant tumor is divided into four stages. During stage one, the cancer cells remains localized within the tumor itself. As the tumor grow and progress into stage two, cells break through the basement membrane guarding the surrounding tissue, and in stage three they migrated to the nearest lymph nodes. Once the cancer has invaded the lymph nodes then it has free access to the bloodstream, and the prognosis significantly diminishes. Cancer is deadliest during stage 4 because at this stage, cancerous cells can be found throughout the body system, making it nearly impossible to combat. Stages 1-3 is also considered a primary stage, and during this stage the cancer is confined to the prostate gland only, so it is treatable. In the metastatic stage, the cancer spreads beyond the prostate which increases the mortality rate.

One factor that has been identified that leads to metastasis is the activation of the c-Met signalling pathway. The c-Met signalling pathway has been implicated in many functions including metastasis. The only known ligand of the c-Met receptor is hepatocyte growth receptor (HGF). HGF has been shown to promote the invasiveness of cancer cells by increasing matrix adhesion, which encourages the migration of tumor cells from the point of origination as well as secretion of cancer specific enzymes that allow the cancer cells to break through the basement membrane.

Previous studies have shown CD82 to be an active metastasis suppressor in normal, healthy cells. What is not known is how the loss of CD82 in cancer cells enables them to metastasize beyond their original tissue. CD82 is a known metastasize tumor suppressor in prostate cancer and it was first identified by Dong et.al. Previous rat studies have shown that CD82 prevents metastasis but does not affect tumor formation. In a normal cell CD82 is highly expressed especially in the spleen, thymus, prostate, lungs, kidneys and other vital organs. However, in a cancerous cell CD82 is under-expressed and downregulated which allows the tumor to progress. Loss or low expression of CD82 has been observed in many invasive and metastatic tumors, which means loss of CD82 is correlated with changes in cytoskeleton structure of the cells. Some of the changes may allow cells to move freely (no longer adhering) and be invasive as well as help with cell migration. The proposed research looked into how the reintroduction of CD82 in metastatic prostate cancer would prevent cell motility and affect cell signalling and cell adhesion. Understanding the mechanism by which re-introduction of CD82 affect cell signalling, cell adhesion and cytoskeleton structure rearrangement propose a greater potential for controlling the mechanism of metastasis. If metastasis could be controlled, it would provide a huge step towards preventing metastatic cancer.

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