

“How Are Mmps Related To Pca Progression & How Can They Be Inhibited?”

MMPs - Matrix Metallo Proteinases Number 26. We will discuss MMP2; 3; 7; 8 & 9 - 4/2017 RVA Us too.

1. “MMP 2 and 9 are called Collagenases and gelatinases that are released by the tip of invadopodia that are spike projections extending out of PCa (like Gleason 7-10 cells) that breakdown extracellular matrix (ECM) collagens (I & IV). This releases growth factors from ECM and provides an escape hatch for the cells to metastasize into the rest of the body and promotes blood vessel growth to provide another escape route. However, the cancer cells are initially bound to each other as skin cells are that they are. They can't float off into the body until they can break free. This is accomplished by MMP7 which triggers an “epithelial to mesenchymal transformation” (EMT) of the cells. Mesenchymal cells are not bound together and can move throughout the body to metastasize if they find a favorable spot to grow.

2. The MMP-3 enzyme degrades [collagen](#) types II, III, IV, IX, and X, [proteoglycans](#), [fibronectin](#), [laminin](#), and [elastin](#). In addition, MMP-3 can also activate other MMPs such as [MMP-1](#), [MMP-7](#), and [MMP-9](#)

3. The MMP7 function is to break down [extracellular matrix](#) by degrading macromolecules including casein, type I, II, IV, and V [gelatins](#), [fibronectin](#), and [proteoglycan](#).^{[5][6]} The activated MMP7 can also cleave the propeptides of proMMP2 and proMMP9 to facilitate tumor invasion.^[10] MMP7 cleaves collagen III/IV/V/IX/X/XI and proteoglycan. Interleukin-17 promotes prostate cancer via MMP7-induced epithelial-to-mesenchymal transition.

<https://www.ncbi.nlm.nih.gov/pubmed/27375020>

4. MMP8 functions are degradation of ECM types I, II and III collagens.

5. MMP9's widely associated pathology is that to cancer, due to its role in extracellular matrix remodeling and angiogenesis. MMP9 has been found to be associated with the development of aortic aneurysms,^[29] and its disruption prevents the development of aortic aneurysms.^[30] [Doxycycline](#) suppresses the growth of aortic aneurysms through its inhibition of MMP9.^[31]

Treatments???

1. Doxycycline down-regulates matrix metalloproteinase (8 & 9) expression and inhibits NF-kB signaling in LPS-induced PC3 cells. FOLIA HISTOCHEMICA ET CYTOBIOLOGICA Vol. 54, No. 4, 2016 pp. 171–180. Osteotropism of Doxycycline prevention of bone mets???
2. 1a, 25-dihydroxyvitamin D3 suppresses interleukin-8-mediated prostate cancer cell angiogenesis (by lowering MMP9) Carcinogenesis vol.27 no.9 pp.1883–1893, 2006.
3. Finasteride Inhibits Human Prostate Cancer Cell Invasion through MMP2 and MMP9 Down regulation PLOS ONE 1 December 2013 | Volume 8 | Issue 12 | e84757
4. Use Curcumin to block Activation of Shh-[IL6](#)-RANKL Signaling Network Promotes Prostate Cancer Metastasis by Engaging Tumor-Stromal Cell Interactions.
5. Matrix metalloproteinase protein inhibitors: highlighting a new beginning for metalloproteinases in medicine; Metalloproteinase in medicine vol3 **2016: Pages 31–47**

6. Cyanidins from polyphenol fruit-seeds-berries block IL17 promotion of MMP7 that creates EMT that produces Mets in PCa. Green tea blocks MMP7 Consume Max polyphenols!!!