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## Bone metastasis in prostate cancer : a cancer stem cell perspective

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## **Statements:**

1. Selecting prostate cancer cells for high ALDH activity enriches for tumor-initiating and metastasis-initiating cell phenotypes (dit proefschrift).
2. av integrins are functionally involved in the maintenance of an invasive phenotype by the formation of prostate cancer stem/progenitor cells (dit proefschrift).
3. Blocking of av integrins in preclinical models by non-peptide antagonists impairs metastasis by direct anti-cancer effects and interference with the supportive bone/bone marrow micro-environment (dit proefschrift).
4. Members of the TGF- $\beta$  superfamily strongly affect ALDH7A1 gene expression in human prostate cancer cell lines (dit proefschrift).
5. The tumor stem cell is the original cell of the tumor, responsible for tumorigenesis, tumor differentiation, tumor maintenance, and also for tumor spread and tumor relapse. This is analogue to a stem cell being the original cell of an organ, responsible for organogenesis and organ maintenance (F.R. Moltzahn et al. Urologic Oncology 2008;581-589).
6. EMT could generate tumor cells with stem/progenitor-like properties, which are not only critically involved in prostate cancer initiation and progression but also in colonization and metastasis formation (Mani et al. Cell 2008;133:704-15).
7. An altered integrin pattern allows the cancer cells to recognize variable matrices, but it may also lead to altered signaling and changes in gene expression (Koistinen and Heino, Landes Biosciences 2000)
8. Cancer cells trigger a reactive response in the stroma and the locally activated host microenvironment in turn modifies the proliferative and invasive behavior of the tumor cells by secreting additional growth factors and proteases. This shows that the tumor microenvironment is not just an innocent bystander in the process of carcinogenesis and metastasis formation (Liotta et al. 2001;411:375-9).
9. BMP7 stimulates the maintenance of an epithelial phenotype, antagonizes TGF- $\beta$  signaling, counteracts EMT responses and even induces MET, leading to strong inhibition of bone metastasis
10. De wetenschap is een prachtig iets zolang je er je brood niet mee hoeft te verdienen (Albert Einstein)

11. Vooruitgang in de wetenschap is als het beklimmen van een berg, pas boven zie je een ander berg die nog hoger is (Charles Spearman)
12. Life is what happens to you while you are busy making other plans (John Lennon)
13. Eigenwijs is ook wijs

Christel van den Hoogen