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Studying DNA methylation changes of CpG islands in different stages of prostate cancer by pyrosequencing

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Prostate cancer is one of the most common forms of cancer in men. Our lab is currently investigating changes in DNA methylation that occur during cancer progression, and in response to the soy phytoestrogen genistein treatment. We analyze genome-wide methylation differences by using the mouse DMH (mouse-Differential Methylation Hybridization) assay, a form of microarray. We are specifically looking at broad sets of CpG islands, areas rich in cytosine-guanine dinucleotides, that are subject to epigenetic modifications. The hypermethylation of CpG islands is correlated with the silencing of a gene while hypomethylation is correlated with a gene being actively transcribed. We were looking for potential new oncogenes or tumor suppressors. To study these genes we have a mouse model called TRAMP (TRansgenic Adenocarcinoma of the Mouse Prostate), which is a good model to study the progression of prostate cancer and metastasis because it is similar to human prostate cancer. We are using double transgenic mice that are WT or KO for the transcription factor estrogen receptor alpha, on a TRAMP background. The removal of ER α has been correlated with DNA methylation changes. These methylation changes showed up in our microarray screen that led us to find a set of genes that were differentially methylated across cancer progression. We selected one gene: Kinesin superfamily protein 9 (K3_E17) which has been shown on our microarrays to be methylated in well differentiated carcinoma and unmethylated in hyperplasia and poorly differentiated carcinoma. To confirm the methylation status we performed pyrosequencing, a new method to specifically study short sequences of DNA for methylation at specific CG sites. Our hypothesis is that in well differentiated carcinoma Kinesin 9 is hypermethylated, which will correlate with this gene being turned off. This would mean that Kinesin 9 might be acting as a tumor suppressor.