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Genome-wide enhancer signature predicts metastatic potential of bladder cancer

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Bladder cancer is the 4th most common cancer in men in the US and metastatic disease carries poor prognosis. To date, only few driving mutations have been identified in this tumor type, but altered gene expression involving an estimate of >2,300 coding sequences involving many chromatin modifiers. These data indicate that chromatin organization plays an important role in bladder cancer development and progression. We compared whole exome sequencing and mRNA expression with analysis of DNase I hypersensitivity combined with deep sequencing (DHS-seq) on multiple cell lines developed by *in vivo* selection. Bioinformatics of DHS-seq was performed using algorithms developed at LRBGE. Analysis of microarray expression was performed using Ingenuity Pathways (IPA). Only few additional mutations and gene expression marked the progression to metastatic phenotype and these did not correspond to specific pathways. In contrast, enhancers analysis assigning to nearest neighbor gene identified genes involved in cell-to-cell interaction, with a decrease in genes involved in cell adhesion and increase in genes associated with EMT. Gene expression profile correlated with nearby chromatin remodeling of regulatory regions. Genome-wide analysis of DHS showed large-scale changes in chromatin landscape during tumorigenesis indicating massive reprogramming of regulatory networks. Thus, combination of global unbiased chromatin landscape, exome sequencing, and microarray profiling opens a new valuable view of enhancers signature for establishing biomarkers, analysis of tumor progression and understanding the biology of bladder cancer.

Biography

Lyuba Varticovski has completed her Undergraduate training and started her Medical Schooling. She has finished Internal Medicine training in Albany MC, Albany, NY. Her Hematology and Oncology fellowship was done at the New England Medical Center in Boston, MA, where she has continued as an Academic and Clinical Faculty Member for 20 years. She has joined NCI Center for Cancer Research in 2003. She is currently an Associate Staff in the Laboratory of Receptor Biology and Gene Expression, NCI, NIH. She is Board-certified in Internal Medicine and Hematology/Oncology and has published over 100 peer-reviewed manuscripts, 14 book chapters and has several patents.

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