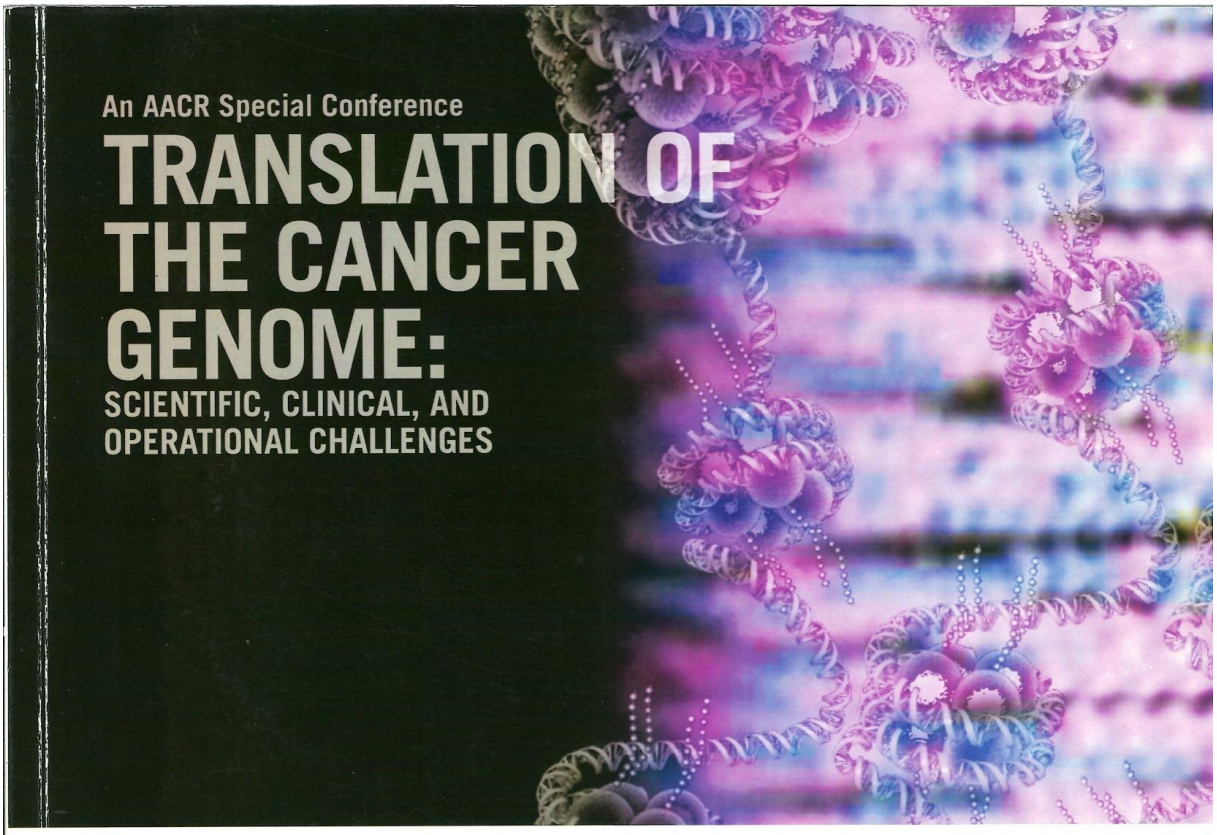

An AACR Special Conference

TRANSLATION OF THE CANCER GENOME:

SCIENTIFIC, CLINICAL, AND OPERATIONAL CHALLENGES

October 15-18, 2011
Hyatt Regency San Francisco
San Francisco, CA

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Program and Proceedings

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A18 Downregulation of NPRL2 in colon cancer. Nur Buyru, Beste Yogurtcu. Cerrahpasa Medical Faculty Department of Medical Biology, Istanbul, Turkey.

Colorectal cancer is a major cause of cancer related death all around the world. Genetic and epigenetic factors affecting DNA methylation and gene expression are known to be involved in the development of CRC, but full range of genetic alterations and many key genes involved in the pathogenesis of CRC remain to be identified.

NPRL2 is one of the candidate tumor suppressor genes identified in the human chromosome 3p21.3 region, which contains genetic abnormalities are frequently found in the early stages of various cancers. The aim of this study to evaluate the role of NPRL2 gene in the pathogenesis of colorectal cancer. Therefore we investigated NPRL2 mRNA expression in 55 normal and tumor colon tissue samples using quantitative real-time reverse transcription polymerase chain reaction analysis and the correlation between NPRL2 expression and clinicopathologic parameters.

RNA expression patterns showed that the decreased NPRL2 expression was observed in 46.15% of the patients. Unaffected NPRL2 expression was detected in 23.07 of patients. There was not a significant correlation between NPRL2 expression and in a clinicopathological parameters.

Our results suggest that the expression of NPRL2 may contribute to the progression of colon cancer however further studies are required to elucidated the role of NPRL2 in colon tumorigenesis.

A19 Genome-wide molecular and functional analysis identified LNX2 as a novel gene involved in colorectal carcinogenesis. Jordi Camps[1], Michael B. Ghadimi[2], Tim Beissbarth[2], Michael J. Difilippantonio[1], Natasha J. Caplen[1], Thomas Ried[1], Jason J. Pitt[1], Georg Emons[2], Amanda B. Hummon[1], Chanelle M. Case[1], Marian Grade[2], Tamara L. Jones[1], Quang T. Nguyen[1]. [1]National Cancer Institute, Bethesda, MD, [2]University of Medicine Göttingen, Göttingen, Germany.

Colorectal cancer (CRC) is one of the most frequent malignancies in many parts of the world and a leading cause of cancer deaths in both men and women. The identification of rationale therapeutic targets is one possibility to provide personalized medicine to cancer patients. Our approach consisted of identifying overexpressed genes located at sites of recurrent chromosomal amplifications, as these regions are likely to harbor genes required for cancer cell survival. Thirty-one colon cancers, 25 rectal cancers, and 15 CRC cell lines were analyzed by high-resolution array CGH and microarray gene expression profiling. RNA interference (RNAi)-based analysis identified a subset of genes whose loss-of-function (LOF) reduced the cellular viability of CRC cell lines. Consistent with previous reports, the vast majority of CRC assayed exhibited amplification of the chromosome band 13q12.13-q12.3. Among the genes residing within the 13q12.13-q12.3 amplified region, we focused on those showing an overexpression level of at least two-fold higher in the tumor compared to normal mucosa. Of this subset, we identified NUPL1, LNX2, POLR1D, CDX2, POMP, and SLC7A1, for which cell survival was impaired after gene silencing. As little is known about the function of these proteins, we decided to use an unbiased systems biology approach to identify genes, pathways and networks altered following RNAi-mediated LOF of each of these candidate genes. To do this, we perturbed the expression of each candidate gene through application of two or more siRNAs corresponding to each gene, followed by whole genome expression profiling to monitor cellular transcriptional responses for each gene specific LOF. One candidate, LNX2, ligand of numb-protein X 2, encodes