**LITERATURE SURVEY**

**1) Clinical applications of nanomedicines in lung cancer treatment**

**AUTHORS:**  M. Norouzi and P. Hardy

Lung cancer is the leading cause of cancer mortality worldwide. Owing to a lack of early-stage diagnosis, most lung cancers are detected in advanced stages, limiting the available therapeutic options. Moreover, extensive systemic chemotherapy of lung tumors is often associated with severe off-target toxicity and drug resistance of cancer cells, thus diminishing the outcomes of chemotherapy modalities. In this light, nanomedicines have opened an alternative avenue to develop more efficacious therapeutic platforms while addressing several current challenges. Clinical findings have revealed that nanomedicines improve the pharmacokinetics and biodistribution of the therapeutic agents while decreasing their systemic toxicity. This review provides an update on nanomedicines that have been clinically approved or are undergoing clinical trials for treatment of lung cancer. By discussing the clinical findings of the current nanoformulations, this review provides prospects for the development of more efficacious nanomedicines to improve the clinical outcomes of lung cancer treatment.

**2) Gene-expression profiles predict survival of patients with lung adeno- carcinoma**

**AUTHORS:** D. G. Beer, S. L. Kardia, C.-C. Huang, T. J. Giordano, A. M.

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Histopathology is insufficient to predict disease progression and clinical outcome in lung adenocarcinoma. Here we show that gene-expression profiles based on microarray analysis can be used to predict patient survival in early-stage lung adenocarcinomas. Genes most related to survival were identified with univariate Cox analysis. Using either two equivalent but independent training and testing sets, or 'leave-one-out' cross-validation analysis with all tumors, a risk index based on the top 50 genes identified low-risk and high-risk stage I lung adenocarcinomas, which differed significantly with respect to survival. This risk index was then validated using an independent sample of lung adenocarcinomas that predicted high- and low-risk groups. This index included genes not previously associated with survival. The identification of a set of genes that predict survival in early-stage lung adenocarcinoma allows delineation of a high-risk group that may benefit from adjuvant therapy

**3) Computational detection of a genome instability-derived lncrna signature for predicting the clinical outcome of lung adenocarcinoma**

**AUTHORS:** C.-R. Guo, Y. Mao, F. Jiang, C.-X. Juan, G.-P. Zhou, and N. Li

Evidence has been emerging of the importance of long non-coding RNAs (lncRNAs) in genome instability. However, no study has established how to classify such lncRNAs linked to genomic instability, and whether that connection poses a therapeutic significance. Here, we established a computational frame derived from mutator hypothesis by combining profiles of lncRNA expression and those of somatic mutations in a tumor genome, and identified 185 candidate lncRNAs associated with genomic instability in lung adenocarcinoma (LUAD). Through further studies, we established a six lncRNA-based signature, which assigned patients to the high- and low-risk groups with different prognosis. Further validation of this signature was performed in a number of separate cohorts of LUAD patients. In addition, the signature was found closely linked to genomic mutation rates in patients, indicating it could be a useful way to quantify genomic instability. In summary, this research offered a novel method by through which more studies may explore the function of lncRNAs and presented a possible new way for detecting biomarkers associated with genomic instability in cancers.

**4) Proteogenomic Characterization Reveals Therapeutic Vulnerabilities in Lung Adenocarcinoma**

**AUTHORS:** Michael A Gillette et.al.

To explore the biology of lung adenocarcinoma (LUAD) and identify new therapeutic opportunities, we performed comprehensive proteogenomic characterization of 110 tumors and 101 matched normal adjacent tissues (NATs) incorporating genomics, epigenomics, deep-scale proteomics, phosphoproteomics, and acetylproteomics. Multi-omics clustering revealed four subgroups defined by key driver mutations, country, and gender. Proteomic and phosphoproteomic data illuminated biology downstream of copy number aberrations, somatic mutations, and fusions and identified therapeutic vulnerabilities associated with driver events involving KRAS, EGFR, and ALK. Immune subtyping revealed a complex landscape, reinforced the association of STK11 with immune-cold behavior, and underscored a potential immunosuppressive role of neutrophil degranulation. Smoking-associated LUADs showed correlation with other environmental exposure signatures and a field effect in NATs. Matched NATs allowed identification of differentially expressed proteins with potential diagnostic and therapeutic utility. This proteogenomics dataset represents a unique public resource for researchers and clinicians seeking to better understand and treat lung adenocarcinomas.

**5) Primary large cell neuroendocrine carcinoma of the parotid gland report of a rare case**

**AUTHORS:** K. I. Tosios, V. Papanikolaou, D. Vlachodimitropoulos, and N. Goutas

Primary neuroendocrine carcinomas of the salivary glands are very rare neoplasms that present light microscopic, ultrastructural, and immunohistochemical features of neuroendocrine differentiation. Twelve cases have been published in the English language literature. We describe the pathologic features of a case of primary large cell neuroendocrine carcinoma of the parotid gland in a 91-year old male and summarize the immunophenotype of previously reported LCNECs of the major salivary glands. It is concluded that primary LCNEC of the salivary glands presents as a high-grade undifferentiated carcinoma, whose diagnosis may be hindered by its rarity and non-specific light microscopic features. A high level of awareness, immunohistochemical staining for neuroendocrine markers synaptophysin and CD56, and a thorough diagnostic work-up in order to exclude metastasis from a primary neuroendocrine carcinoma will allow its diagnosis.