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A Systematic Review on Lung Cancer and its Evolutionary Challenges in the Emerging Future

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Short Communication

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ABSTRACT

Lung cancer incidence has dramatically risen in the past decades. It is one of the most common malignancies worldwide and a leading cause of cancer-related deaths both among men and women. Approximately 1.5 million people worldwide die from lung cancer every year. The disease has an extremely poor prognosis and there has been no noticed improvement in the 5-year survival rate in the last 30 years. Unfortunately currently available treatments do not prevent the progressiveness of the disease. There has been lack of optimism regarding treatment advances in the last ten years, and progress in treating or predicting the risk for lung cancer has been very slow. The present review discusses about the lung cancer, its stages and causes and the preventive steps to be taken to challenge the relentless progression of the disease.

Lung Cancer

Lung cancer is the leading cause of cancer death due to insufficient therapeutic options, which resulted in the equaling of morbidity with mortality rates and causing an unsolved health problem [1-3]. It is one of the most common malignancies in the US and worldwide and a leading cause of cancer-related deaths.

It is a disease that occurs due to unwanted growth in tissues of the lung. The growth which spreads beyond the lung is a process known as metastasis and it can also spread into other parts of the body [4,5]. Most cancers that begin its growth in lung are known as carcinomas and are derived from

epithelial cells. If uncontrolled growth can be detected successfully at early stages, it helps to proceed with many treatment options, which reduces risk of invasive surgery and increased survival rate [6-8]. Possible treatments of the disseminated disease include surgery, chemotherapy, and radiotherapy. Survival of the patient depends on stage, overall health, and other factors, but overall only 14% of people who are diagnosed with lung cancer can survive only for five years after their diagnosis [9].

Lung cancer basically consists of heterogeneous groups in terms of pathological features and is classified into two major types namely [10],

Small Cell Lung Carcinoma (SCLC) and

Non-Small Cell Lung Carcinoma (NSCLC).

NSCLC includes squamous cell carcinoma and adenocarcinoma. Vascular Endothelial Growth Factor (VEGF) and Basic Fibroblast Growth Factor (BFGF) produced by Non-Small Cell Lung Carcinoma (NSCLC) [11-13]. VEGF is known to promote the vascularization and growth of the tumor through mobilizing circulating endothelial cell precursors to the nascent blood vessels and plays a major role in establishing new metastatic foci. BFGF in addition to its involvement in tumor growth may have the potential to predict early-stage NSCLC recurrence following tumor resection [14-17].

Among the neuroendocrine tumors which constitute approximately 20% of lung cancers, SCLC comprises the majority of cases. It is a highly malignant tumor and originates from neuroendocrine cells (Amine Precursor Uptake and Decarboxylation/APUD cells) [18] of the bronchus called Feyrter cells and in addition to its rapid growth, early dissemination and progression to drug resistance after successful first-line therapy treatment of SCLC has very limited efficacy [19-22]. Lung cancer is the most preventable cancer worldwide owing to the fact that the fore-most and predominant risk factor is tobacco consumption and along with men, women are also increasingly being affected [23-25]. Non-neuroendocrine lung tumors which are known as non-SCLC (NSCLC), including adenocarcinoma, squamous cell carcinoma and large cell carcinoma, differ by a lower growth fraction and aggressiveness from SCLC [26-28].

Characterized Symptoms of Lung Cancer

Lung cancer is generally characterized and can be detected by some symptoms which include:

1. Coughing, especially if it persists or becomes intense
2. Pain in the chest, shoulder, or back unrelated to pain from coughing [30]
3. A change in color and volume of sputum
4. Shortness of breathing
5. Changes in the voice or hoarseness [31]
6. Harsh sounds with each breath (stridor)
7. Recurrence of lung problems, such as bronchitis or pneumonia
8. Coughing up phlegm or mucus, especially if it is with blood
9. Coughing up blood

The above symptoms are usually observed in the chest and the following symptoms may occur elsewhere in the body:

1. Loss of appetite or unexplained weight loss
2. Cachexia [33]
3. Fatigue
4. Headache, bone or joint pain
5. Bone fractures
6. Neurological symptoms [34], such as unsteady gait or memory loss
7. Neck or facial swelling
8. General weakness
9. Bleeding
10. Blood clots

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Cancer Stem Cells- Origin

It is believed that the existence of Cancer Stem Cells (CSCs) [35-37] within the tumors is a responsible factor for the majority of biological characteristics that are associated with the severity of tumors/ cancer cells [38]. A CSC theory proposes that a tumor cell subpopulation has self-renewal capacity, cancer-initiating ability and multi-potent differentiation ability. In recent years, many experimental evidences came into prevalence in support of the role of CSCs [39]. There are many concepts in cancer which can be explained by the stem cell theory like tumor self-renewal, tumor heterogeneity, and tumor relapse after treatment and resistance to conventional chemotherapies. CSCs were firstly described in human hematopoietic cancer [40-42].

According to a debated concept, CSCs are generally known as rare population of undifferentiated cells driving tumor initiation, maintenance and spreading [43]. CSCs tend to have unlimited proliferation potential, self-renewal ability and capacity to generate a progeny of differentiated cells, responsible for the major tumor populations [44]. Cells which resemble CSCs' characteristics have been detected from leukemia, and a wide range of solid tumors, which include melanoma, breast, prostate, pancreatic, and colon carcinomas. These cells have the tendency to expand in vitro as tumor spheres, like mamma- and neurospheres, and produce original tumors in immunodeficient mice at lower cell numbers than the unfractionated tumor cell population [45-47]. Brain, hematopoietic, prostate and colon cancer CSCs feature the membrane antigen CD133, whose expression is shared by normal stem cells of different lineages [48].

The origin of CSCs is still a hot topic which is widely being discussed. One theory is the malignant transformation of normal stem cells particularly in rapidly dividing tissues, where the stem cell is available throughout life and it might undergo different mutations [49].

In a combined model of complex tumor development integrating the stochastic and CSC model, genetically distinct CSCs are known to exist on top of each heterogenous tumor subclone [50, 51]. Most therapies are targeted at the bulk of rapidly dividing tumor cells but not the slowly dividing CSCs. CSCs are well-resistant to both radiation therapy and chemotherapy, and, therefore, this subpopulation persists following therapy being responsible for relapses which occur in some cases [52-55]. The CSCs' resistance to therapy is a complex, multistep process that occurs with the short-term, inherent plasticity of subpopulations of cancer cells. The cytotoxic stimuli which results from inhibiting a target can result in enhanced expression/activity of stemness factors in the persisting subpopulations of cells [56-58]. These stemness factors results in genetic plasticity that allows these cells to remain in a dormant, drug-tolerant state. Since the role of CSCs is still not well established, these cells are also alluded to as tumor initiating cells [TICs], cancer initiating cells [CICs] and tumor propagating cells [TPCs] [59,60].

Recently, independent studies using lineage-tracing technique in mouse models have proposed the existence of CSCs in brain, skin and intestinal tumors [61-64]. Eradicating CSCs, in addition or instead of the fast growing tumor mass seems to constitute a promising approach to achieve a long-lasting response and thereby improving cancer therapy. Therefore, studies looked at the cell response to injury as a means to find if the stem cell characteristics can be characterized [65-68].

Stem cell populations are established in niches, which resemble the microenvironment that interacts with stem cells to regulate stem cell self-renewal and differentiation [69]. It remains unexplained whether CSCs form their own microenvironment/niches or depend on the pre-existing tissue environment. The solid microenvironment is composed of different mesenchymal cell types which are recruited by cancer cells to enhance their survival, growth, invasion and dissemination [70,71]. These include endothelial cells of the blood and lymphatic circulation, inflammatory cells, fibroblasts and others. Fibroblasts produce different chemokines that modulate tumor expansion, invasion, angiogenesis, and activation of extracellular matrix associated cytokines and growth factors. Some of them are commonly associated with self-renewal [72-75].

Lung Cancer- Diagnosis and Treatment

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Computed tomography (CT) and Positron Emission Tomography (PET) are able to define the level of the disease, both anatomically & functionally. PET and CT are the two medical imaging techniques which are used to find out affected part in accurate manner [76-79].

The existing system shows how PET/CT was used to detect the lung cancer and various ways for managing the respiratory motion in medical manner [80]. It also explains the workflow of the imaging technique. Algorithms are not used in the existing system. Two concepts are combinedly integrated into patient-specific workflows i.e. are PET/CT guided radiotherapy and motion managed radiotherapy [81-83]. A scanned image of PET/CT is shown in the figure 1 for example [84]. Imaging with PET/CT becomes a standard care in the lung cancer staging, but it is still underused in its direct integration to therapy planning. The most frequent application of PET and CT to lung cancer patient care is used for diagnosis and also to know the stages of the disease in accurate and precise manner [85-87].

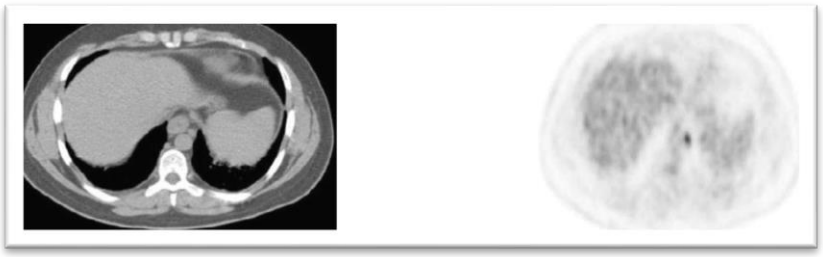

Figure 1: CT and PET scan image

In patients with SCLC, combination chemotherapy produces results that are clearly superior to single-agent treatment with objective response rates of 65 to 90% and total response rates ranging from 45 to 75% [88-90]. A combination of etoposide and cisplatin/carboplatin chemotherapy with concurrent chest irradiation is standard and achieves median survivals of 18 to 24 months and 40% to 50% ranging of 2-year survival with less than a 3% treatment-related mortality [91-93]. The prognosis for patients with relapsing SCLC is exceedingly poor, with expected survival between 2 to 3 months. Topotecan [94] is the sole approved chemotherapeutic drug for second line treatment of SCLC prolonging live for several months. In summary, the treatment of SCLC is characterized by extremely short survival rates in advanced disease, that have been not seen much improvement in the past years [95,96].

Patients are currently diagnosed with lung cancer when their disease is fairly in an advanced stage, a condition where they begin to experience symptoms. Unfortunately, at this stage, surgery or radiotherapy is usually not viable options, and chemotherapy is usually commenced. The importance of prediction of lung cancer at an early stage is therefore of utmost and primary importance. Other potential targeted therapies are under investigation which includes BRAF, HER-2, c-KIT and EML4-ALK [97]. Emerging genetic markers of lung cancer risk have also been reported. From the numerous studies that have emerged over the past decade, a Single Nucleotide Polymorphism (SNP) at chromosome 13q31.3, and Endothelial Growth Factor, EGF=61 A>G polymorphisms [98] have emerged as promising markers of NSLC risk, but further studies are required. To offer the most effective targeted therapy for the lung cancer, it is now essential to sub-classify NSLC and perform molecular analyses. In terms of the rapid recurrence of SCLC after primary therapy 99, this tumor entity is ideally suited to test clinical efficacy of CSC-directed therapies [100] in combination with the elimination of the tumor bulk using conventional chemotherapy.

REFERENCES

1. Hodge S. Lung Cancer: Future Challenges and Opportunities. J Pulmon Resp Med. 2013; S5:005.

2. Abdel Ghany SM, et al. Emerging Prognostic Biomarkers in Non Small Cell Lung Cancer Patients: Impact of Treatment with Nimesulide (COX-2 Inhibitor) Combined with Chemotherapy. J Pulmonar Respirat Med. 2011; S5:003.
3. Pusztaszeri M, et al. Cytopathological Diagnosis of Non Small Cell Lung Cancer: Recent Advances Including Rapid On-Site Evaluation, Novel Endoscopic Techniques and Molecular Tests. J Pulmonar Respirat Med. 2012; S5:002.
4. Gaber KA, et al. Ability of Lung Specialist to Predict a Diagnosis of Lung Cancer during the First Visit to a Fast Track Clinic. J Pulmon Resp Med. 2012; S5:004.
5. Lamelas IP. Long-Term Lung Cancer Survival in a Province of Spain. J Pulmonar Respirat Med. 2012; S5:001.
6. de Mello RA. EGF+61 A>G Polymorphisms and Lung Cancer Risk: Future Directions. J Pulmonar Respirat Med. 2012; S5:e001.
7. Said AF, et al. Prognostic Value of CYFRA 21-1 and Carcinoembryonic Antigen in Non-Small Cell Lung Cancer. J Clin Cell Immunol. 2015; 6:316.
8. Mortara L, et al. Polarization of Tumor Infiltrating Leukocytes from Innate Immunity and their role in the Pro-angiogenic Phenotype in NSCLC. J Clin Cell Immunol. 2015; 6:312.
9. Adamowicz K. Combining Systemic Therapies with Radiation in Non-Small Cell Lung Cancer. J Cancer Sci Ther. 2015; 7:102-110.
10. Sushma B and Ravalli R. Recent Developments in Cancer. J Develop Drugs. 2015; 4:R001.
11. Saida Y, et al. Recurrent Interstitial Lung Disease Induced By Various Therapies for Non-Small Cell Lung Cancer. J Clin Case Rep. 2014; 4:471.
12. Verma A, et al. EBUS-TBNA: Are Two Needle Revolutions (Back and Forth Movement of the Needle Inside the Lymph Node) Adequate for Diagnosis of Lung Cancer?. J Pulm Respir Med. 2015; 5:239.
13. Chung C. Tyrosine Kinase Inhibitors for EGFR Gene Mutation-Positive Non-Small Cell Lung Cancers: An Update for Recent Advances in Therapeutics. J Pharmacovigilance. 2015; 2:155.
14. Fournel L, et al. Thoracic Myelolipoma: A Rare Case of Mistake in Lung Cancer Staging. J Clin Exp Pathol. 2014; 5:202.
15. Chen YM and Luo YH. Interstitial Lung Disease Induced by Targeted Therapy for Non-Small Cell Lung Cancer: A Review of Diagnosis, Workup, and Management. J Palliat Care Med. 2015; 5:204.
16. Onuigbo BW. The Visionary Views of Medical Masters of Yester Years on Natureâ€™s Norms Point to Present Prospects in the Target Therapy of Cancer. Biol Med (Aligarh). 2015; 7:221.
17. Karthikeyan S, et al. Resveratrol Modulates Expression of ABC Transporters in Non-Small Lung Cancer Cells: Molecular Docking and Gene Expression Studies. J Cancer Sci Ther. 2014; 6:497-504.
18. Crvenkova S. Influence of Prognostic Factors on Survival in Locally Advanced Non-Small Cell Lung Cancer Patients Treated with Combination of Chemoradiotherapy. J Nucl Med Radiat Ther. 2014; 5:200.
19. Nobuhiro Kanaji and Nobuki Nanki. Delayed onset, Long-term Efficacy of S-1 Monotherapy for an Elderly Patient with Squamous Cell Lung Cancer. Chemotherapy. 2014; 4:140.
20. Lee MH, et al. Combination Treatment with Apricoxib and IL-27 Enhances Inhibition of Epithelial-Mesenchymal Transition in Human Lung Cancer Cells through a STAT1 Dominant Pathway. J Cancer Sci Ther. 2014 ; 6:468-477.
21. Monirul Islam KM, et al. Developing a Web-Based, Patient-Centered Data Collection and Management Approach for a Multi-Center Lung Cancer Study. J Integr Oncol. 2014; 3: 121.
22. Konno S, et al. New Scoring System Available at Home Health Care for Prediction of 14 Days Survival in Lung Cancer Complicated with Lymphangitic Carcinomatosis. J Palliat Care Med. 2014; 4:200.
23. Liu M, et al. Cervical Muscular Metastasis from Squamous Lung Cancer. Intern Med. 2014; 4:i002.
24. Hanagiri T, et al. Indoleamine2,3-Dioxygenase as A Prognostic Factor in Patients with Non-Small Cell Lung Cancer. J Clin Cell Immunol. 2014; 5:260.

25. Bittner N, et al. The EGFR and KRAS Mutation Status and Correlations with the Prevalence of Bone Metastases - The Results of Three Year Retrospective Analysis. J Carcinog Mutagen. 2014; 5:184.
26. Sung HJ, et al. Clinically Applicable Diagnostics Assay Development for Lung Cancer Biomarker, SAA. J Proteomics Bioinform. 2014; 7:303-309.
27. Parikh R and Jeganathan N. A Short Review: Complementary and Alternative Medicine in Lung Cancer. J Anc Dis Prev Rem. 2014; 2:115.
28. Kumar Nagi B, et al. Chemoprevention Trial Feasibility Using Botanicals in Exceptionally High Risk Populations for Lung Cancer. J Clin Trials. 2014; 4:180.
29. Chen YT, et al. Over-diagnosis in Lung Cancer Screening using the MSKC-LCSP Data. J Biomet Biostat. 2014; 5:201.
30. Gironés R. Communication of Diagnosis in Elderly Lung Cancer Patients: Who is Informed, What Information is Given and What Patients Know and Want to Know. J Palliat Care Med. 2014; 4:184.
31. Nehls W, et al. Communication Skills Training Significantly Improves Lung Cancer Patient`s Understanding. J Palliat Care Med. 2014; 4:182.
32. Vasic N, et al. Amiodarone-Induced Pulmonary Toxicity Mimicking Metastatic Lung Disease: Case Report. J Pharmacovigilance. 2014; 2: 137.
33. Stone A, et al. c-Met: A Potential Target for Current Non-Small-Cell Lung Cancer Therapeutics. Chemotherapy. 2014; 3:136.
34. Marx G, et al. Understanding the Needs and Perspectives of Patients with Incurable Pulmonary Disease at the End of Life and their Relatives: Protocol of a Qualitative Longitudinal Study. J Palliat Care Med. 2014; 4:177.
35. Meisenberg C, et al. TDP1/TOP1 Ratio as a Promising Indicator for the Response of Small Cell Lung Cancer to Topotecan. J Cancer Sci Ther. 2014; 6:258-267.
36. Dhillon SS, et al. 2014 Metformin and Not Diabetes Influences the Survival of Resected Early Stage NSCLC Patients. J Cancer Sci Ther. 2014; 6:217-222.
37. Zhang Y, et al. Correlation of a Serological Proteome and Lung Cancer Prognosis. Transcriptomics. 2014; 2:103.
38. Onuigbo WIB. Lymphangiogenesis in Cancer: A Review. Biochem Physiol. 2014; 3:138.
39. Coats V, et al. Exercise-Based Rehabilitation for People with Lung Cancer. J Pulm Respir Med. 2014 ; 4:183.
40. Hsu CP, et al. Effects of Targeted Anticancer Medicines on Post-Cell Removal Surface Morphology of Cancer Cells Cultivated on 3-Aminopropyltriethoxysilane Surface. Med chem. 2014 ; S1: 007.
41. Kaladhar DSVGK, et al. Evaluation of Anti-inflammatory and Anti-proliferative Activity of Abutilon indicum L. Plant Ethanolic Leaf Extract on Lung Cancer Cell Line A549 for System Network Studies. J Cancer Sci Ther. 2014; 6: 195-201.
42. Onuigbo W. Is There A Natural Translational System Suitable for the Target Therapy of Lung Cancer?. Transl Med (Sunnyvale). 2014; 4:130.
43. Tang Y, et al. The Anticancer Mechanism of an Approved Disease Modifying Herb Medicine: Total Glucosides of Paeony Target both EGFR and HER-2 in Lung Cancer Cell Lines. Transl Med (Sunnyvale). 2014; 4:129.
44. Berardi R, et al. Hedgehog (Hh) Signaling is a Predictor of Clinical Outcome for Advanced Non-Small Cell Lung Cancer (NSCLC). J Carcinog Mutagen. 2014; 5:175.
45. Lotayef M, et al. A Clinico-Epidemilogical Study of Cases of Locally Advanced Non-Small Cell Lung Cancer (NSCLC) that Received Radiotherapy at NCI Cairo in the Periodfrom 2001-2010. J Cancer Sci Ther. 2014; 6:151-155
46. Benbrahim Z, et al. Metastatic Non-Small Cell Lung Cancer in the Young: A Retrospective Comparative Analysis. J Cancer Sci Ther. 2014; 6:148-150.

47. Cooper WA and O'Toole SA. Detecting ALK Gene Rearrangements in Lung Cancer Cytology Specimens. J Cytol Histol. 2014; 5:216.
48. Wang M, et al. Secreted Clusterin (sCLU) Gene Silencing Enhances Chemosensitivity of A549 Cells to Cisplatin through AKT and ERK1/2Path ways *In Vitro*. J Clin Exp Pathol. 2014; 4:162.
49. Kulig K, et al. Predictive and Prognostic Value of ALK Gene Rearrangement in Non-Small Cell Lung Cancer. Epidemiol. 2014; 4:146.
50. Loudon JA. Preventing and Correcting Communicable and Non-Communicable Chronic Disease via Amlexanox â€" Dual â€˜No-Nonsenseâ€™ and Inflammatory Axis Targeting. J Bioanal Biomed. 2013; 5:138-179.
51. Kunos CA, et al. Lung Cancer Motion Management-Cinema at Its Best?. OMICS J Radiology. 2013; 3:e124.
52. Berardi R, et al. Prognostic Factors in Early Stage Non-Small Cell Lung Cancer: The Importance of Number of Resected Lymph Nodes and Vascular Invasion. Chemotherapy. 2013; 2:120.
53. Choudhary M, et al. Graphene Oxide based Label Free Ultrasensitive Immunosensor for Lung Cancer Biomarker, hTERT. J Biosens Bioelectron. 2013 ; 4:143.
54. Potprommanee L, et al. Human Urinary GM2-activator Protein as a Potential Biomarker for Lung Cancer. J Proteomics Bioinform. 2013; 6:264-270.
55. Kadoya N, et al. Investigation of Correction Method of Recovery Effect and Motion Blur for SUV Quantification in FDG PET/CT in Patients with Early Lung Cancer. J Nucl Med Radiat Ther. 2013; 4:162.
56. Patra S, et al. Protocatechualdehyde Induces Apoptosis in Human Non-Small-Cell Lung Cancer Cells by up Regulation of Growth Arrest and DNA Damage-Inducible (GADD) Genes. Mol Biol. 2013; 2:113.
57. Nakamichi S and Kubota K. Evolving Management with Molecular- Targeted and Bone-Targeted Medicine in Patients with Advanced Nonâ€"Small Cell Lung Cancer. General Med. 2013; 1:120.
58. Gomez-Cabrero A, et al. NF-κB Inhibitor IMD-0354 Targets Human Non-Small Cell Lung Cancer Stem Cells and Combined with Chemotherapy Reduces Multidrug Resistance. J Cancer Sci Ther. 2013; 5:300-312.
59. Ma HT, et al. Proteomics Characterization of Haptoglobin Alpha-2 Subunit in Non-Small Cell Lung Cancer Serum and Various Human Materials. J Proteomics Bioinform. 2013; 6:187-196.
60. Berman Abigail T, et al. Dietary Flaxseed in Non-Small Cell Lung Cancer Patients Receiving Chemoradiation J Pulm Respir Med. 2013; 3:154.
61. Hamilton G and Olszewski U. Chemotherapy-induced Enrichment of Cancer Stem Cells in Lung Cancer. J Bioanal Biomed. 2013; S9:003.
62. Javid J, et al. Biological and Clinical Implications of Functional Promoter Polymorphism of CASPASE 9 Gene in Non Small Cell Lung Cancer Patients. J Mol Biomarkers Diagn. 2013; S8:007.
63. Moss LAS and Stevenson WGS. Influence of Stromal Components on Lung Cancer Carcinogenesis. J Carcinogene Mutagene. 2013; S13:008.
64. Ohno S, et al. A Survey of Non-Small Cell Lung Cancer Patients with Meningeal Carcinomatosis in Japan: Incidence and Medical Resource Consumption. Adv Pharmacoepidem Drug Safety. 2013; 2:133.
65. Middleton GD. A Report of Two Cases of Metastatic Lung Cancer Simulating Gout. Rheumatol Curr Res. 2013; S16:001.
66. Reyzer ML, et al. MALDI MS Profiles Distinguish ER-Negative Breast Cancers from Lung Adenocarcinoma. J Proteomics Bioinform. 2013; S6:004.
67. Hussein ZA, et al. Measurements of Indoor Radon-222 Concentration inside Iraqi Kurdistan: Case Study in the Summer Season. J Nucl Med Radiat Ther. 2013; 4:143.
68. Koh H, Kamiishi N, et al. A Rare Case of Persistent Pneumothorax in Non-Small Cell Lung Cancer on Bevacizumab Therapy. J Pulmon Resp Med. 2013; S14:001.

69. Alpana S, et al. TP53 is a Mutational Target in Non Small Cell Lung Cancer Patients and its Pro/Pro Variant is Potentially Contributing to Cancer Susceptibility. J Carcinogene Mutagene. 2013; 4:138.
70. Ahn JM and Cho JY. Current Serum Lung Cancer Biomarkers. J Mol Biomark Diagn. 2013; S4:001.
71. Salama R, et al. Lung Cancer Stem Cells: Current Progress and Future Perspectives. J Stem Cell Res Ther. 2012; S7:007.
72. Javid J, et al. Clinical and Prognostic Significance of R282W p53 gene mutation in North India Patients with Non Small Cell Lung Cancer. Transl Med. 2012; 2:110.
73. Lever JR. Opioid Receptors and Ligands: Targets for Cancer Imaging and Therapy. Med chem. 2012; 2:142-147.
74. Hassan BAR. General Overview on Leukemia. Overview on Lung Cancer. Pharmaceut Anal Acta.2012; 3:e132
75. Tanaka T and Tamura K. Recent Advances in Molecular Targeted Therapy for advanced Colorectal Cancer and Non–Small Cell Lung Cancer. J Phys Chem Biophys. 2012; 2:108
76. Horii N, et al. Structure of Life Adjustments by Lung Cancer Patients with Decreased Performance Status. J Nurs Care. 2012; S5:001.
77. Mehrotra A and Pandit JK. Critical Process Parameters Evaluation of Modified Nanoprecipitation Method on Lomustine Nanoparticles and Cytostatic Activity Study on L132 Human Cancer Cell Line. J Nanomed Nanotechol. 2012; 3:149.
78. Sharma R and Sharma A. Multidrug Resistance (MDR) in Lung Cancer: Finding the Holy Grail of MDR Reversal. J Cancer Sci Ther. 2012; S11:e001.
79. Javid J, et al. Impact of MDM2 SNP309T>G Polymorphism: Increased Risk of Developing Non Small Cell Lung Cancer and Poor Prognosis in Indian Patients. J Cancer Sci Ther. 2012; 4: 341-346.
80. Franco R, et al. ALK Rearrangement in Lung Cancer: Is Patients Filtering Possible? J Clin Exp Pathol. 2012; 2:e111.
81. Fanggiday JC, et al. Solitary Bone Metastasis Appearing outside the Usual Range of FDG PET/ CT in Stage III Lung Cancer: Is Total Body FDG PET/CT Imaging Mandatory? J Nucl Med Radiat Ther. 2012; 3:135.
82. Kim S, et al. Efficacy of Dual Lung Cancer Screening by Chest X-Ray and Sputum Cytology Using Johns Hopkins Lung Project Data. J Biomet Biostat. 2012; 3:139.
83. Elayouty HD, et al. Radiotherapy with or without Concomitant Chemotherapy as Pre- or Post-operative Therapy in Non-small Cell Lung Cancer. J Cancer Sci Ther. 2012; 4: 084-087.
84. Didem K, et al. Critical Normal Structures Doses for Non Small Cell Lung Cancer using 3-D Conformal Radiotherapy. J Nucl Med Radiat Ther. 2012; 3:128.
85. Javid J, et al. Clinical and Prognostic Significance of Promoter Polymorphism (-31GC) of Anti Apoptotic Gene Survivin (BIRC5) in North India Patients with Non Small Cell Lung Cancer. J Cancer Sci Ther. 2012; 4: 276-280.
86. Baianu IC. Clinical Trials in Cancer and Pharmacogenomics: A Critical Evaluation. J Clin Trials. 2012; 2:109.
87. Yoshimasu T, et al. Serum KL-6 Levels in Patients with Lung Cancer. J Pulmonar Respirat Med. 2012; 2:118
88. Andrade FM, et al. Lung Cancer Staging. J Cancer Sci Ther. 2012; S11:004.
89. Hubaux R, et al. MicroRNAs as Biomarkers for Clinical Features of Lung Cancer. Metabolomics. 2012; 2:108.
90. Al-Naggar RA. Knowledge and Practice towards Lung Cancer among University Students. J Community Med Health Edu.v 2012; 2:134.
91. Sunaga N, et al. MK615, A Compound Extract from the Japanese Apricot â€œPrunus mumeâ€ Inhibits In vitro Cell Growth and Interleukin-8 Expression in Non-small Cell Lung Cancer Cells. J Cancer Sci Ther. 2011; S11:002.

92. Velez M, et al. Mutations and Tumorigenesis Pathways Driving Personalized Treatment in Non-Small Cell Lung Cancer. J Clinic Experiment Pathol. 2012; S5:002.
93. Pusztaszeri M, et al. Cytopathological Diagnosis of Non Small Cell Lung Cancer: Recent Advances Including Rapid On-Site Evaluation, Novel Endoscopic Techniques and Molecular Tests. J Pulmonar Respirat Med. 2012; S5:002.
94. Liu J, et al. Papillary Thyroid Carcinoma with Prominent Hobnail Features Diagnosed Preoperatively by Fine Needle Aspiration and Demonstrating Constitutive Activation of mTOR Signaling Pathway: A Case Report. J Clin Exp Pathol. 2013; 3:152.
95. Baldwin DR and Hubbard RB. Lung Cancer: Early Diagnosis and Screening. J Cancer Sci Ther. 2012; S7:002.
96. Mehta RS. Role of Race in Survival among Patients Who Refuse the Recommended Surgery for Early Stage Non-Small Cell Lung Cancer: A Seer Cohort Study. J Clinic Res Bioeth. 2011; 2:123.
97. Serfin J, et al. Outcome Prediction Using Markers of Aerobic Glycolysis (the Warburg effect) Varies Between Tumor Regions in Stage I Non-Small Cell Lung Cancer. J Mol Biomark Diagn. 2011; 2:116.
98. Dalhaug A, et al. Scylla or Charybdis: Case Report on Radiation Tolerance of the Spinalcord. J Nucl Med Radiat Ther. 2011; 2:114.
99. Wampfler JA, et al. Determining the Optimal Numbers of Cores Based on Tissue Microarray Antibody Assessment in Non-Small Cell Lung Cancer. J Cancer Sci Ther. 2011; 3: 120-124.
100. Tran TT, et al. Changes of Serum Glycoproteins in Lung Cancer Patients. J Proteomics Bioinform. 2008; 1: 011-016.