Reference (pubmed id)	Sample Type	Genetics/ Genomics Platform	Clinical Settings	Key Findings
a) Epigenetic Biomarkers				
Belinsky SA PNAS 1998 [59] (9751761)	Sputum, lung tissue, biopsies	Methylation - specific PCR (MSP)	Lung tissue, precursor lesions and bronchial biopsies from squamous cell carcinoma (SCC) patients and sputum from individuals with suspicion of lung cancer	CDKN2A hypermethylation more often observed in cancer patients than no cancer patients
Esteller M Cancer Res 1999 [66] (9892187)	Paired serum and lung tissue	MSP	Lung tissue and serum from patients with non-small cell lung cancer (NSCLC) and control	73% of patients had serum DNA that reflected aberrant methylation in their tumors, specifically in CDKN2A, MGMT, DAPK, GSTP1
Palmisano WA Cancer Res 2000 [60] (11085511)	Paired sputum and lung tissue	MSP	Lung tissue and sputum from smokers with SCC	CDKN2A and MGMT were hypermethylated in both sputum and tumor of patients at time of diagnosis
Russo AL Clin Cancer Res 2005 [72] (15814621)	Bronchial epithelial cells, blood lymphocytes, lung tissue	MSP	Paired blood and bronchial epithelial samples from smokers/non-smokers with preneoplastic lesions and neoplastic lesions from individuals with NSCLC versus controls	ECAD and DAPK more likely to be methylated in smoker's peripheral lymphocytes or bronchial epithelium and never methylated in non-smokers
Wang L Thorac Oncol 2010 [58] (20421821)	Peripheral blood leukocytes	Illumina Beadchip and Pyrosequencing	Smokers with recently diagnosed small cell lung cancer (SCLC) and controls	43 CpG sites were differentially methylated between SCLC and controls, and 9 of these, validated by pyrosequencing, could discriminate SCLC with AUC of 0.86
Begum S Clin Cancer Res 2011 [71] (21610147)	Paired serum and lung tissue	MSP	Paired serum and lung tissue samples from individuals with lung cancer and controls	6 gene serum panel that discriminated lung cancer patients with 75% sensitivity and 73% specificity
b) Transcriptomics Biomarkers				
Spira A Nat Med 2007 [76] (17334370)	Bronchial brushings, large airway epithelium	Affymetrix array	Bronchial brushings of cytologically normal large airway epithelium obtained from smokers undergoing bronchoscopy for suspicion of lung cancer	80 gene airway biomarker with >80% diagnostic sensitivity and specificity, and 95% sensitivity and NPV when biomarker is combined with cytology collected at bronchoscopy
Blomquist T Canc Res 2009 [78] (19887610)	Bronchial brushings, airway normal bronchial epithelial cells	(StaRT)-PCR	Normal bronchial epithelial cells of lung cancer cases and non–lung cancer controls	14 gene airway biomarker of antioxidant, DNA repair and transcription factor genes with performance in a test AUC>0.84 and an accuracy of 80%.
Showe MK Can Res 2009 [86] (19951989)	Peripheral blood mononuclear cells	cDNA array	Blood collection from smokers with newly diagnosed lung cancer confirmed by histopathology	29-gene blood signature >80% sensitivity and specificity
Gustafson AM Sci Trans Med 2010 [79] (20375364)	Bronchial brushings from airway epithelium	Affymetrix array	Bronchial airway brushings of cytologically normal epithelium from smokers with and without lung cancer or premalignancy	Gene expression signature of PI3K signaling pathway activation was differentially expressed in airways of smokers with lung cancer or dysplasia and was reversible with chemopreventive therapy
Zander T Clin Canc Res 2011 [88] (21558400)	Whole blood	Sentrix whole genome bead chips WG6 (Illumina)	PAXgene-stabilized blood samples from three independent groups consisting of NSCLC cases and controls	Genes differentially expressed in whole blood of NSCLC patients and controls was used to build a diagnostic classifier with AUC >0.82
Zhang L Cell Mol Life 2012 [85] (22689099)	Saliva	Affymetrix array	Whole saliva collected from untreated lung cancer patients with matched cancer-free controls	7 highly discriminatory transcriptomic salivary biomarker with AUC = 0.925 with >82% sensitivity and specificity
c) MicroRNA Biomarkers				
Xing L Mod Pathol 2010 [93] (20526284)	Sputum	RT-qPCR	Sputum from squamous lung cancer patients and healthy controls	Three miRNA diagnosed stage I squamous cell lung cancer with AUC 0.87
Yu L Int J Cancer 2010 [94] (21351266)	Sputum	RT-qPCR	Sputum from lung adenocarcinoma patients and healthy controls	Four miRNA diagnosed stage I lung adenocarcinoma with AUC 0.90
Foss KM J Thorac Oncol 2011 [107] (21258252)	Serum	Genoexplorer microRNA expression system	Serum from patients with lung cancer versus healthy controls	Two miRNA discriminated individuals with early stages NSCLC with AUC 0.77
Bianchi F EMBO Mol Med 2011 [103] (21744498)	Serum	Taqman Low Density Arrays RT-qPCR	Serum from asymptomatic NSCLC patients and healthy smokers. Patients were screened by low doses CT and sera were collected at the time of diagnosis before the surgery.	32 miRNA predicted risk of developing lung cancer in asymptomatic high-risk individuals with accuracy of 80%
Boeri M PNAS 2011 [109] (21300873)	Plasma	Taqman Low Density Arrays RT-qPCR	Multiple plasma samples were collected before and at the time of disease, from two independent spiral CT-screening trials	Fifteen miRNA predicted the risk of lung cancer with AUC 0.85 and 13 miRNA diagnosed lung cancer in undetermined CT nodules with AUC 0.88
Shen J Lab Invest 2011 [110] (21116241)	Plasma	RT-qPCR	Plasma from patients with lung cancer versus healthy controls	Four miRNAs discriminated patients with NSCLC with AUC 0.93
Chen X Int J Cancer 2012 [105] (21557218)	Serum	RT-qPCR	Serum from patients with lung cancer versus healthy controls	Ten miRNAs discriminated patients with NSCLC with AUC 0.97