Hypermethylation of tumor suppressor genes (TSG) is an early and frequent event in most neoplasias, including non-small cell lung cancer (NSCLC). Evidences have showed that hypermethylation of TSGs can be detected in precursor lesions of lung cancer, even in sputum of cancer-free individuals at high risk of lung cancer. Our results revealed *APC* (adenomatous polyposis coli) promoter hypermethylation would be a promising diagnosis biomarker, and better diagnosis efficiency was found for *APC* methylation test in serum sample than that in tissues, suggesting the methylation status of *APC* would be an excellent diagnosis biomarker in remote non-invasive media. In addition, *APC* methylation test has better diagnosis ability in adenocarcinoma (Ad) than that in squamous cell carcinoma (Sc). Therefore, Ad and Sc might have different biomarkers, and thus they should be considered separately in future biomarker discovery research.