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Exhaled Breath Condensate in Lung Cancer: A Non-Invasive Sample for Easier Mutations Detection by Next Generation Sequencing

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Abstract : Exhaled breath condensate (EBC) is a unique sample that allows studying different genetic changes in lung carcinoma through a non-invasive way. With the aid of next generation sequencing (NGS) technology, analysis of genetic mutations has been more efficient with increased sensitivity for detection of genetic variants. In order to investigate the possibility of applying this method for cancer diagnostics, mutations in EBC DNA from lung cancer patients and healthy individuals were studied by using NGS. The key aim is to assess the feasibility of using this approach to detect clinically important mutations in EBC. EBC was collected from 20 healthy individuals and 9 lung cancer patients (four lung adenocarcinomas, four 8 squamous cell carcinoma, and one case of mesothelioma). Mutations in hotpot regions of 22 genes were studied by using Ampliseq Colon and Lung cancer panel and sequenced on Ion PGM. Results demonstrated that all nine patients showed a total of 19 cosmic mutations in APC, BRAF, EGFR, ERBB4, FBXW7, FGFR1, KRAS, MAP2K1, NRAS, PIK3CA, PTEN, RET, SMAD4, and TP53. In controls, 15 individuals showed 35 cosmic mutations in BRAF, CTNNB1, DDR2, EGFR, ERBB2, FBXW7, FGFR3, KRAS, MET, NOTCH1, NRAS, PIK3CA, PTEN, SMAD4, and TP53. Additionally, 45 novel mutations not reported previously were also seen in patients' samples, and 106 novel mutations were seen in controls' specimens. KRAS exon 2 mutations G12D was identified in one control specimen with mutant allele fraction of 6.8%, while KRAS G13D mutation seen in one patient sample showed mutant allele fraction of 17%. These findings illustrate that hotspot mutations are present in DNA from EBC of both cancer patients and healthy controls. As some of the cosmic mutations were seen in controls too, no firm conclusion can be drawn on the clinical importance of cosmic mutations in patients. Mutations reported in controls could represent early neoplastic changes or normal homeostatic process of apoptosis occurring in lung tissue to get rid of mutant cells. At the same time, mutations detected in patients might represent a non-invasive easily accessible way for early cancer detection. Follow up of individuals with important cancer mutations is necessary to clarify the significance of these mutations in both healthy individuals and cancer patients.

Keywords : exhaled breath condensate, lung cancer, mutations, next generation sequencing
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