Identification of circulating tumor DNA for the early detection of small-cell lung cancer.

Research Paper

Identification of Circulating Tumor DNA for the Early Detection of Small-cell Lung Cancer

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Highlights

â€¢ CtDNA may play a crucial role in the detection of pre-clinical cancer.

â€¢ TP53 mutations are detectable in the cfDNA of SCLC patients with early-stage tumors.

â€¢ Detection of TP53 mutations in non-cancer controls poses serious challenges for the development of ctDNA screening tests.

Cell-free DNA (cfDNA) has potential for monitoring response to treatment and relapse of small-cell lung cancer. This is the first study reporting the detection of TP53 mutations in SCLC patients and non-cancer controls.
and relapse, but also for early detection. This is the first study reporting the detection of circulating-tumor DNA (ctDNA) in cases diagnosed with small-cell lung cancer (SCLC). Our results show that TP53 mutations are detectable in the cfDNA of SCLC patients including those with early-stage tumors. Importantly, we also provide evidence that cancer-like TP53 mutations are present in non-cancer controls, which poses serious challenges for the development of ctDNA screening tests.

Abstract

Circulating tumor DNA (ctDNA) is emerging as a key potential biomarker for post-diagnosis surveillance but it may also play a crucial role in the detection of pre-clinical cancer. Small-cell lung cancer (SCLC) is an excellent candidate for early detection given there are no successful therapeutic options for late-stage disease, and it displays almost universal inactivation of TP53. We assessed the presence of TP53 mutations in the cell-free DNA (cfDNA) extracted from the plasma of 51 SCLC cases and 123 non-cancer controls. We identified mutations using a pipeline specifically designed to accurately detect variants at very low fractions. We detected TP53 mutations in the cfDNA of 49% SCLC patients and 11.4% of non-cancer controls. When stratifying the 51 initial SCLC cases by stage, TP53 mutations were detected in the cfDNA of 35.7% early-stage and 54.1% late-stage SCLC patients. The results in the controls were further replicated in 10.8% of an independent series of 102 non-cancer controls. The detection of TP53 mutations in 11% of the 225 non-cancer controls suggests that somatic mutations in cfDNA among individuals without any cancer diagnosis is a common occurrence, and poses serious challenges for the development of ctDNA screening tests.

Keywords

cdNA; cfDNA; Small-cell lung cancer; TP53 mutations; Early detection; Screening
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