A genetic polymorphism associated with lung cancer progression

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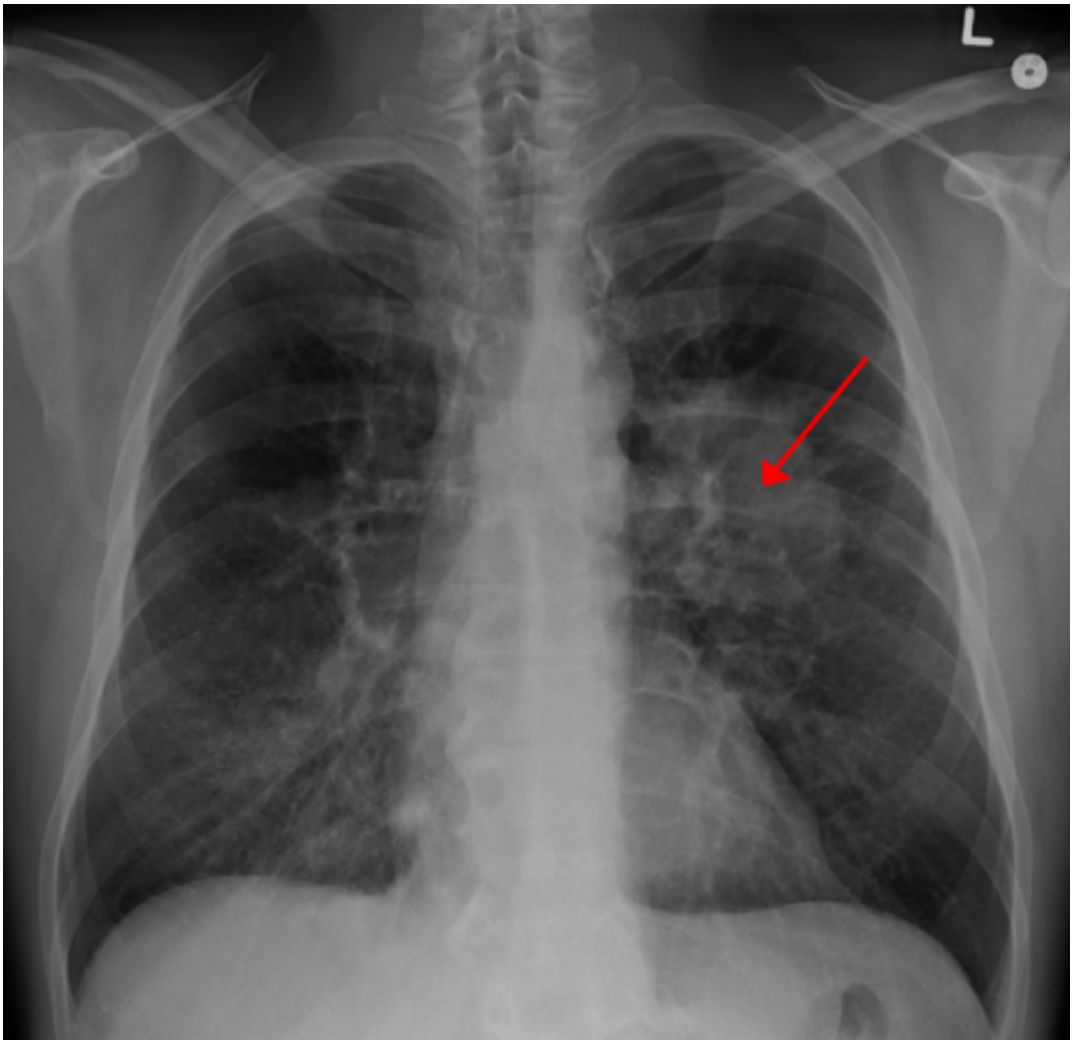

Lung CA seen on CXR. Credit: CC BY-SA 4.0 James Heilman, MD/Wikipedia

Genetic polymorphisms associated with cancer progression lead to variations in gene expression and may serve as prognostic markers for lung cancer. Researchers at the Hiroshima University and Saitama Medical University found that in patients with lung cancer, a single nucleotide polymorphism (SNP) may regulate gene and protein expression and be associated with poor prognosis. To establish this genetic polymorphism as a useful clinical prognostic marker and to further clarify its molecular mechanism, large-scale clinicopathological studies of lung cancer and/or other types of cancer are required for additional insights.

Hypoxia-inducible factor-2 alpha (HIF-2 alpha or EPAS1) is important for cancer progression, and its overexpression is considered a putative biomarker for poor prognosis in patients with lung cancer. However, molecular mechanisms underlying EPAS1 overexpression are not fully understood. Recently, several SNPs of EPAS1 have been reported to be associated with the development of various diseases including cancer.

Dr. Keiji Tanimoto of the Hiroshima University and his collaborators focused on SNPs within EPAS1. They examined the roles of these SNPs in regulation of EPAS1 gene expression and the association of these SNPs with prognosis of lung cancer patients by bioinformatics analyses.

"Several SNPs of EPAS1 have been shown to correlate with various diseases, but their mechanism has scarcely been known," said Dr. Tanimoto. He continued, "the SNP within the EPAS1 intron 1 region may affect EPAS1 gene and protein expression, and having the A (adenine) allele of EPAS1 rather than the G (guanine) allele is associated with poor prognosis in lung cancer patients."

The association of the SNP within the EPAS1 region with overall survival for patients with lung cancer was assessed. The median survival time of patients with at least one A allele was significantly shorter than

that of patients with the G allele (28.0 months vs. 52.5 months).

Moreover, cancer cells with the A allele of EPAS1 showed higher EPAS1 gene and protein expression in in vitro experiments. It was suggested that the A allele of EPAS1 plays an important role in lung cancer progression by regulating EPAS1 gene and protein expression.

"Besides lung cancer, other cancers such as colorectal and head and neck cancers were also reported to have poor prognosis associated with the over-expression of EPAS1. On confirmation of our observation by large-scale studies in the future, genotyping for the EPAS1 SNP may become a clinically useful tool in personalized health examinations and cancer therapy." Dr. Tanimoto explained.

More information: "The A Allele at rs13419896 of EPAS1 Is Associated with Enhanced Expression and Poor Prognosis for Non-Small Cell Lung Cancer," *PLOS ONE*, 2015, DOI 10.1371/journal.pone.0134496

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