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Genetic polymorphisms may serve as prognostic markers for lung cancer

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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.

Source:
Hiroshima University