Genetic variant implicated in lung cancer development also linked with improved outcomes among affected patients

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Lung cancer is the most common cause of cancer death in much of the industrialized world, including Japan. While cigarette smoke is most

frequently the source of the disease, genetics can also play a role. Scientists have identified a handful of genetic variants associated with an increased susceptibility to lung cancer among Asian women who do not smoke. A research team led by Toshihisa Ishikawa and colleagues from the RIKEN Center for Life Science Technologies has now identified another gene mutation that puts non-smoking Japanese women at elevated risk of lung cancer, but which is also linked to better prognosis for those who develop the disease.

Genetic variants, referred to by geneticists as single nucleotide polymorphisms (SNPs), can be useful as prognostic biomarkers for guiding diagnoses and personalizing therapies. Ishikawa and his colleagues set out to test whether variants in the NRF2 gene, which encodes a transcription factor involved in cellular antioxidant defense mechanisms, could predict the likelihood of someone developing lung cancer. The researchers analyzed DNA samples from a total of 387 Japanese lung cancer patients—43% women and 40% non-smokers—using a rapid isothermal genetic test developed specifically for this study. The team's rapid genotyping does not require DNA to be isolated or polymerase chain reaction (PCR) amplification and takes only 30–45 minutes to complete.

Looking at position –617 in the NRF2 gene, the researchers identified 24 patients who had two copies of the adenine nucleotide; the rest had at least one cytosine at this location. Of these 24 individuals, 16 were female non-smokers, and all had a type of lung cancer known as adenocarcinoma.

Notably, patients of either gender who carried two copies of adenine at position –617 of the NRF2 gene also had significantly better survival outcomes than other patients. These same individuals were more likely to carry the most common, or 'wild type', version of MDM2, a gene regulated by NRF2 that encodes a negative regulator of p53, an

important tumor suppressor protein. Both the –617A variant in the NRF2 gene and the wild-type version of MDM2 are more often found in east Asian populations.

"Genetic testing of these SNPs should be performed to predict the prognosis of lung cancer patients in east Asian countries, such as Japan, South Korea and China," suggests Ishikawa. "It would be desirable to include such genetic information in each patient's record as guidance for medical doctors to provide individualized treatment."

More information: Okano, Y., et al. SNP (–617C>A) in ARE-like loci of the NRF2 gene: A new biomarker for prognosis of lung adenocarcinoma in Japanese non-smoking women, *PLoS One* 8, e73794 (2013). dx.doi.org/10.1371/journal.pone.0073794

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