Study identifies familial germline EGFR T790M variant in lung cancer

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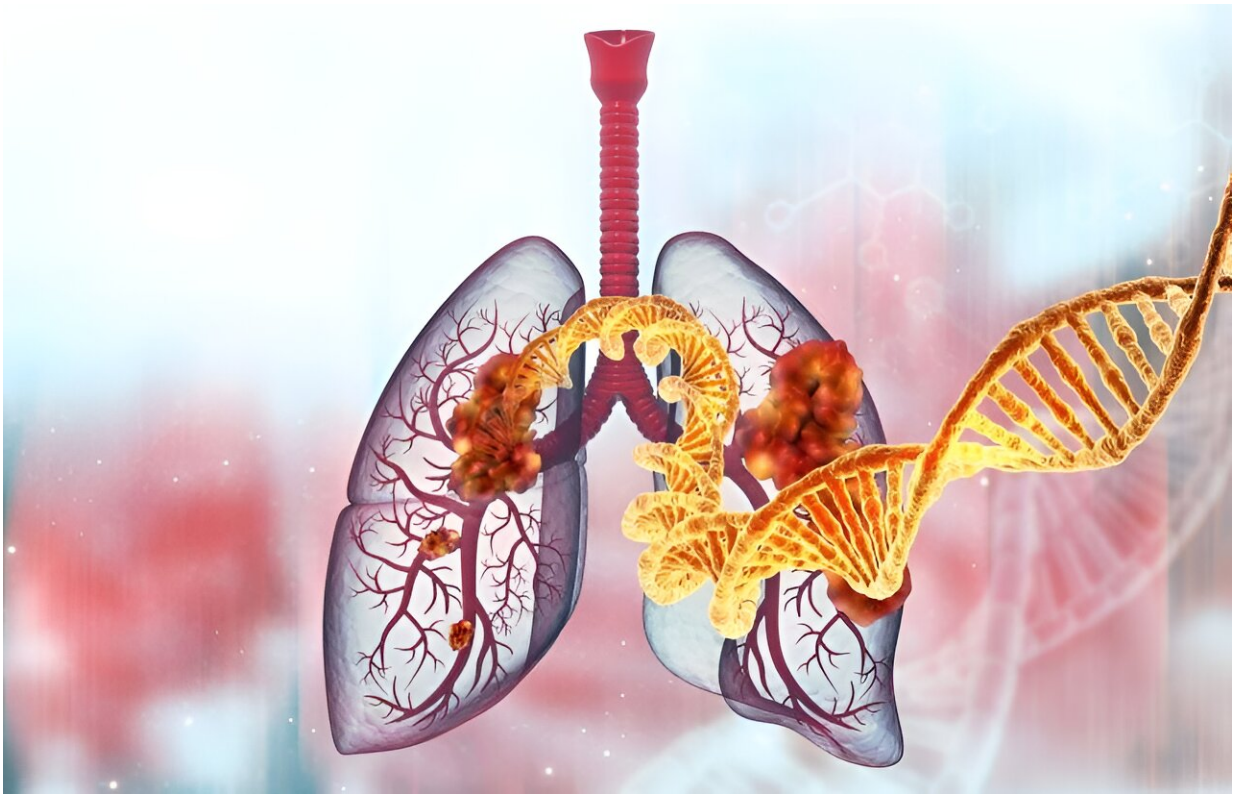

A new familial lung cancer caused by an inherited mutation in *EGFR* has been described in a study published online Oct. 23 in the *Journal of Clinical Oncology*.

Geoffrey R. Oxnard, M.D., from the Dana-Farber Cancer Institute in Boston, and colleagues enrolled patients with lung cancer whose tumor profiling harbored possible germline *EGFR* pathogenic variants (PVs) and their relatives, in person or remotely. During a five-year period, 141 participants were enrolled, including 71 percent remotely.

The researchers found that 116 participants from 59 kindreds were tested for *EGFR* T790M based on previous genotyping, demonstrating a Mendelian inheritance pattern with variable lung cancer penetrance. Fifty-five percent of the 91 confirmed or obligate carriers of a germline *EGFR* PV from 39 kindreds were affected with lung cancer; 52 percent were diagnosed by 60 years of age.

Overall, 95 percent of carriers with somatic testing of lung cancer had an *EGFR* driver comutation. Fifteen of the 36 germline carriers without a cancer diagnosis had computed tomography imaging and nine had lung nodules, including an individual aged 28 years who had more than 10 nodules. A 4.1-Mb haplotype that was shared by 89 percent of 46 carriers of a germline *EGFR* T790M was estimated to originate 223 to 279 years ago.

"The INHERIT study provides critical insight into why lung cancer develops and will ultimately expedite and advance targeted treatment for those presenting with the T790M mutation in the *EGFR* gene," coauthor Bonnie J. Addario, from Addario Lung Cancer Medical Institute in San Carlos, California, said in a statement.

Several authors disclosed ties to the biopharmaceutical industry.

More information: Geoffrey R. Oxnard et al, Germline EGFR Mutations and Familial Lung Cancer, *Journal of Clinical Oncology* (2023). DOI: 10.1200/JCO.23.01372