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- **p.G12C KRAS mutation prevalence in non-small cell lung cancer: Contribution from interregional variability and population substructures among Hispanics**

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ABSTRACTO: Background: The KRAS exon 2 p. G12C mutation in patients with lung adenocarcinoma has been increasing in relevance due to the development and effectiveness of new treatment medications. Studies around different populations indicate that regional variability between ethnic groups and ancestries could play an essential role in developing this molecular alteration within lung cancer. Methods: In a prospective and retrospective cohort study on samples from lung adenocarcinoma from 1000 patients from different administrative regions in Colombia were tested for the KRAS p.G12C mutation. An analysis of STR populations markers was conducted to identify substructure contributions to mutation prevalence. Results: Included were 979 patients with a national mean frequency for the KRAS exon 2 p.G12C mutation of 7.97% (95%CI 6.27-9.66%). Variation between regions was also identified with Antioquia reaching a positivity value of 12.7% (95%CI 9.1-16.3%) in contrast to other regions such as Bogota DC (Capital region) with 5.4% (2.7-8.2%) and Bolivar with 2.4% (95%CI 0-7.2%) (p-value = 0.00262). Furthermore, Short tandem repeat population substructures were found for eight markers that strongly yielded association with KRAS exon 2 p.G12C frequency reaching an adjusted R2 of 0.945 and a p-value of < 0.0001. Conclusions: Widespread identification of KRAS exon 2 p.G12C mutations, especially in cases where NGS is not easily achieved is feasible at a population based level that can characterize regional and national patterns of mutation status. Furthermore, this type of mutation prevalence follows a population substructure pattern that can be easily determined by population and ancestral markers such as STR.