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GRHL2 as a epigenetic response biomarker for targeted EGFR therapies in NSCLC

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Introduction: Lung cancer (LC) is the leading cause of cancer related death worldwide and responsible for mortality of 1.7 million people by 2015. Although signifi cant progress has been made in the comprehension of LC biology, survival rates remain very low due to the lack of early prediction tools and personalized therapies. Our laboratory has carried out high-throughput screening for the identifi cation of epigenetic biomarkers in non-small cell lung cancer (NSCLC) using DNA methylation microarrays, finding that methylation levels in the promoter regions of genes LAD1 and GRHL2, were associated with the response to EGFR tyrosine kinase inhibitors (ITQs).

Materials and methods: We have in vitro validated the functional role of these genes and their possible relationship with resistance to ITQs in NSCLC cell lines directed by EGFR activating mutations (HCC827 NCBI1975 and HCC4006). In addition, given the relationship of both genes to the epithelial phenotype, we studied whether their repression could induce EMT (Epithelial-Mesenchymal Transition).

Results: Our results indicate that GRHL2 silencing increases the expression of the mesenchymal markers and decreases epithelial markers, confirming that the GRLH2 promoted EMT phenotype is associated with a higher resistance to ITQs.

Conclusion: GRHL2 constitutes not only a biomarker for response, but also appears as an important modulator EMT.

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