

# Review of: "RAS mutations that have a major impact on current cancer genomic medicine"

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**Potential competing interests:** No potential competing interests to declare.

This paper makes a significant contribution to the field of cancer genomic medicine by identifying and addressing a critical gap in the interpretation of RAS mutations. Its integration of clinical data with genomic reanalysis provides a model for advancing precision oncology. However, the study's narrow focus on KRAS Q61 mutations and the limited number of reclassified cases suggest the need for further validation and expansion to other genomic contexts. For future research, it would be beneficial to:

1. Expand the cohort size and include a broader range of cancer types and mutations.
2. Develop standardized protocols for reclassifying variants based on functional genomic data.
3. Collaborate with database curators to update classification systems in real time.

The paper effectively demonstrates the importance of reevaluating the functional impact of certain RAS mutations, with immediate implications for personalized cancer treatment.

It calls for a shift in genomic cancer medicine from static mutation lists to dynamic, evidence-based classifications.

## **Potential Weaknesses:**

1. While the study points to significant clinical implications, it does not propose specific protocols for incorporating these findings into routine practice.
2. The focus on KRAS may overlook similar issues in other oncogenes or cancer pathways.
3. The methodologies, particularly for splicing analysis and confirmation of nonfunctional KRAS variants, are not explained in sufficient detail. This omission could hinder reproducibility.