Review Article
Volume 17:3, 2023

Journal of Molecular and Genetic Medicine

ISSN: 1747-0862 Open Access

The Gene's Function in Regular Cellular Signalling Pathways

Veronese Dwan*

Department of Genetic Studies, University of Yat-Sen, Indianapolis, USA

Abstract

In the realm of cancer research, few genes have garnered as much attention and significance as KRAS. KRAS mutations are among the most common genetic alterations found in human cancers, particularly in pancreatic, colorectal and lung cancers. The discovery of these mutations has revolutionized our understanding of cancer biology and opened new avenues for targeted therapies. In this article, we will delve into the world of KRAS mutations, exploring their impact on cancer development and discussing the recent advancements in therapeutic approaches. KRAS, an acronym for Kirsten rat sarcoma viral oncogene homolog, is a proto-oncogene that plays a vital role in cell signalling pathways. This gene encodes a protein involved in transmitting signals from cell surface receptors to the cell nucleus, thereby regulating critical cellular functions such as proliferation, differentiation and apoptosis. However, when mutated, KRAS becomes an oncogene, driving uncontrolled cell growth and promoting tumour formation. KRAS mutations are known to confer aggressive tumour behavior and resistance to conventional cancer therapies. Studies have shown that KRAS-mutated tumors tend to be more resistant to chemotherapy and radiation, posing significant challenges in the clinical management of these cancers. Additionally, KRAS mutations are associated with poor prognosis and reduced overall survival rates in several cancer types, underscoring the urgent need for effective targeted therapies.

Keywords: Epidemiology • KRAS mutations • Target identification • Dysplasia • Prognosis • Human cancer

Introduction

KRAS mutations are characterized by alterations in the DNA sequence of the KRAS gene, resulting in a dysfunctional protein. The most common KRAS mutations involve a substitution of a single amino acid at position 12, 13, or 61 in the protein sequence, known as KRASG12, KRASG13 and KRASQ61 mutations, respectively. These mutations lead to a constitutively active KRAS protein, which remains persistently "switched on" even in the absence of external signals, driving cell proliferation and survival. KRAS mutations are prevalent in several malignancies, with pancreatic, colorectal and lung cancers being the most affected. Approximately 90% of pancreatic cancers and 50% of colorectal cancers harbour KRAS mutations, highlighting their significance in these diseases. In lung cancer, KRAS mutations are present in about 30% of cases, mainly in adenocarcinomas.

Literature Review

The presence of KRAS mutations has far-reaching implications for cancer biology. Firstly, KRAS mutations are frequently early events in tumorigenesis, often occurring at the precancerous stage, known as dysplasia. These mutations drive the transition from normal tissue to pre-malignant lesions and subsequently to invasive cancers. The early and persistent activation of KRAS protein sets in motion a cascade of signalling events, leading to uncontrolled cell growth, evasion of apoptosis and angiogenesis. For many years, KRAS was deemed "undruggable" due to its complex structure and lack of suitable binding sites for small molecules. However, recent breakthroughs have offered new hope in the quest to develop KRAS-targeted therapies. Scientists have discovered novel strategies to directly inhibit the mutated KRAS protein or its downstream effectors, aiming to disrupt the aberrant signalling pathways driving tumour growth.

One promising avenue is the development of small-molecule inhibitors targeting KRASG12C, a specific mutant form of KRAS found in approximately 14% of lung adenocarcinomas. These inhibitors selectively bind to the mutant KRASG12C protein, locking it in an inactive state and preventing downstream signalling. Early clinical trials have shown encouraging results, with some patients achieving durable responses, raising hopes for this novel class of targeted therapies [1]. Moreover, efforts are underway to develop inhibitors that target other KRAS mutations, such as KRASG12D and KRASG13D, which are prevalent in pancreatic and colorectal cancers. These inhibitors aim to block the function of the mutated KRAS protein, impeding its oncogenic activity and inhibiting tumour growth. Another strategy involves targeting downstream effectors of KRAS signalling, such as MEK and ERK. These proteins play a crucial role in transmitting signals from activated KRAS to the nucleus, regulating cell growth and proliferation. Inhibitors that target MEK or ERK have shown promise in preclinical and early clinical studies, demonstrating their potential to disrupt KRAS-driven pathways and inhibit tumour growth [2].

Combination therapies are also being explored to overcome the inherent resistance of KRAS-mutated tumors. By combining KRAS inhibitors with other targeted agents or conventional chemotherapy, researchers hope to enhance treatment efficacy and overcome resistance mechanisms. Additionally, immunotherapy approaches, such as immune checkpoint inhibitors, are being investigated in combination with KRAS-targeted therapies to harness the power of the immune system in fighting cancer [3].

Discussion

The significant progress has been made in targeting KRAS mutations, several challenges remain. One major hurdle is the development of resistance to KRAS-targeted therapies. Cancer cells can acquire secondary mutations or activate alternative signaling pathways to bypass the effects of KRAS inhibitors. Understanding the mechanisms of resistance and developing strategies to overcome it are critical for long-term treatment success. The heterogeneity of KRAS mutations poses a challenge. Different KRAS mutations may respond differently to targeted therapies, necessitating the development of mutation-specific inhibitors or combination therapies to address the diversity of KRAS-driven cancers. In addition, early detection of KRAS mutations and monitoring of treatment response are crucial for optimizing patient outcomes. Advances in

***Address for Correspondence:** Veronese Dwan, Department of Genetic Studies, University of Yat-Sen, Indianapolis, USA, E-mail: dwanv66@edu.in*

Received: 01 May, 2023, Manuscript No. Jmgm-23-102724; **Editor Assigned:** 03 May, 2023, Pre-QC No. P-102724; **Reviewed:** 15 May, 2023, QC No. Q-102724; **Revised:** 20 May, 2023, Manuscript No: R-102724; **Published:** 27 May, 2023, DOI: 10.37421/1747-0862.2023.17.607

liquid biopsies and non-invasive imaging techniques hold promise in identifying KRAS mutations and assessing treatment response, providing valuable tools for personalized cancer management [4-6].

Conclusion

KRAS mutations represent a significant challenge in the field of cancer research and treatment. Their prevalence in various malignancies, coupled with their role in driving aggressive tumour behavior and therapeutic resistance, underscores the urgent need for effective targeted therapies. Recent breakthroughs in developing KRAS inhibitors have revitalized the field and ignited hope for improved treatment options. While there is still much work to be done, the progress made in understanding KRAS mutations and developing targeted therapies is remarkable. Continued research and collaboration between scientists, clinicians and pharmaceutical companies are essential to unravelling the complexities of KRAS-driven cancers and bringing novel therapies to the clinic. In the future, personalized treatment strategies that consider the specific KRAS mutation, combination therapies and immunotherapeutic approaches hold great promise in improving patient outcomes and transforming the landscape of cancer care. With each step forward, we move closer to taming this formidable oncogene and offering new hope to patients affected by KRAS-mutated cancers

Acknowledgement

We thank the anonymous reviewers for their constructive criticisms of the manuscript. This manuscript was supported by a grant from the Americas Health Foundation (AHF), responsible for the development, organization and implementation of the consensus conference, along with independently selecting the experts to serve on the panel.

Conflict of Interest

The Author declares there is no conflict of interest associated with this manuscript.

References

1. Cannataro, Vincent L., Stephen G. Gaffney, Carly Stender and Zi-Ming Zhao, et al. "Heterogeneity and mutation in KRAS and associated oncogenes: Evaluating the potential for the evolution of resistance to targeting of KRAS G12C." *Oncogene* 37 (2018): 2444-2455.
2. Cook, Joshua H., Giorgio EM Melloni, Doga C. Gulhan and Peter J. Park, et al. "The origins and genetic interactions of KRAS mutations are allele-and tissue-specific." *Nat Commun* 12 (2021): 1808.
3. Watterson, Alex and Matthew A. Coelho. "Cancer immune evasion through KRAS and PD-L1 and potential therapeutic interventions." *Cell Commun Signal* 21 (2023): 45.
4. Bryant, Kirsten L., Joseph D. Mancias, Alec C. Kimmelman and Channing J. Der. "KRAS: Feeding pancreatic cancer proliferation." *Trends Biochem Sci* 39 (2014):91-100.
5. Zimmermann, Gunther, Björn Papke, Shehab Ismail and Nachiket Vartak, et al. "Small molecule inhibition of the KRAS–PDEδ interaction impairs oncogenic KRAS signalling." *Nat* 497 (2013): 638-642.
6. Brady, Anna K., Jonathan D. McNeill, Brendan Judy and Joshua Bauml, et al. "Survival outcome according to KRAS mutation status in newly diagnosed patients with stage IV non-small cell lung cancer treated with platinum doublet chemotherapy." *Oncotarget* 6 (2015): 30287.

How to cite this article: Dwan, Veronese. “The Gene's Function in Regular Cellular Signalling Pathways.” *J Mol Genet Med* 17 (2023): 607.