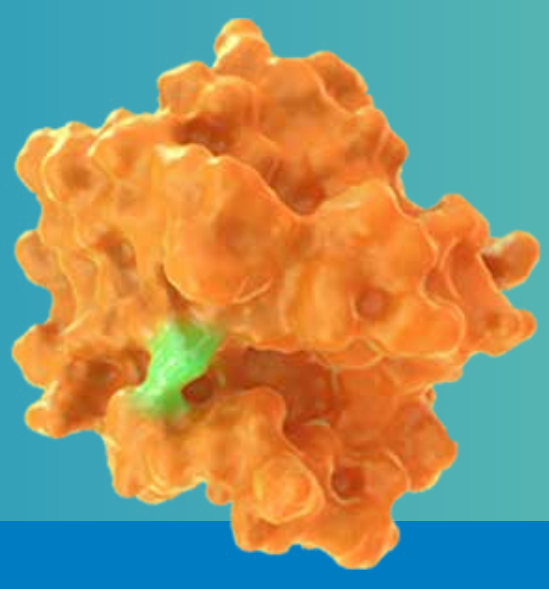
AMGEN®

Oncology

RAS FAMILY: *KRAS* (***K****IRSTEN* ***RA****T* ***S****ARCOMA)*

The *RAS* gene family, which has been the subject of almost four decades of research, is the most frequently mutated oncogenic family in human cancers, which includes *HRAS*, *NRAS* and *KRAS*.[1,2]



Globally, it is estimated that some 19% of all tumors in patients with cancer harbor a *RAS* mutation. There are roughly 3.4 million new cases of cancer with a *RAS* mutation diagnosed worldwide each year.[3]

KRAS PREVALENCE IN SOLID TUMORS

- Approximately 86% of the *RAS* mutations in CRC are *KRAS*.[1]
- ~90% of all pancreatic cancers has a *KRAS* mutation.[1]
- *KRAS* accounts for virtually all *RAS* mutations in lung adenocarcinoma.[1]

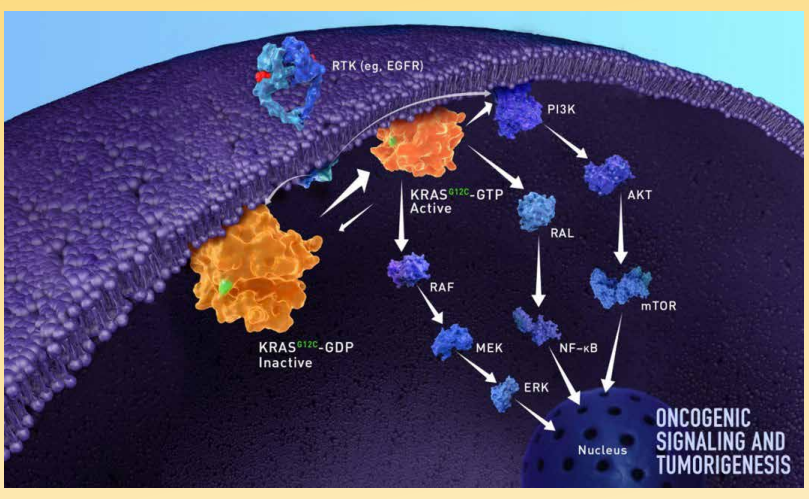
When the *KRAS* gene functions correctly it contributes to normal cell development. However, this gene can mutate and lead to uncontrolled growth of cells and to cancer.[1]

FAST FACTS

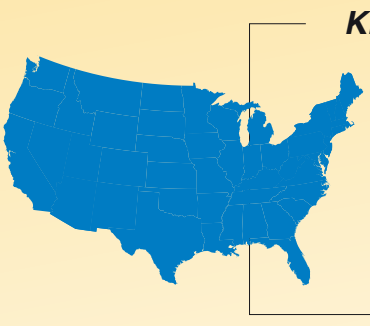
- *KRAS* is a protein involved in cell signaling pathways that control cell growth, cell maturation and cell death.[4]
- One of the most prominent mutated forms of the *KRAS* gene is called *KRAS G12C*.[5]
- *KRAS G12C* can be found in some of the most common cancers, including lung, colorectal and pancreatic cancers.[4]
- Further investigations may provide insights into a potential narrow pocket on KRAS^{G12C} that may be susceptible to targeting.[6,7]
- Amgen is investigating one of cancer research's toughest challenges of the past 40 years.[1]

KRAS G12C : One of the Broadest Subgroups of Patients with *KRAS*-mutated Solid Tumors[1]

One of the most prominent mutated forms of the *KRAS* gene is called *KRAS G12C*, and is a major driver of tumor growth, occurring broadly across solid tumor indications.[5] Normally *KRAS* alternates between an active state and an inactive state, however, the *KRAS G12C* mutation favors the active state, leading to uncontrolled multiplication of cells and ultimately to the development of cancer.[1]



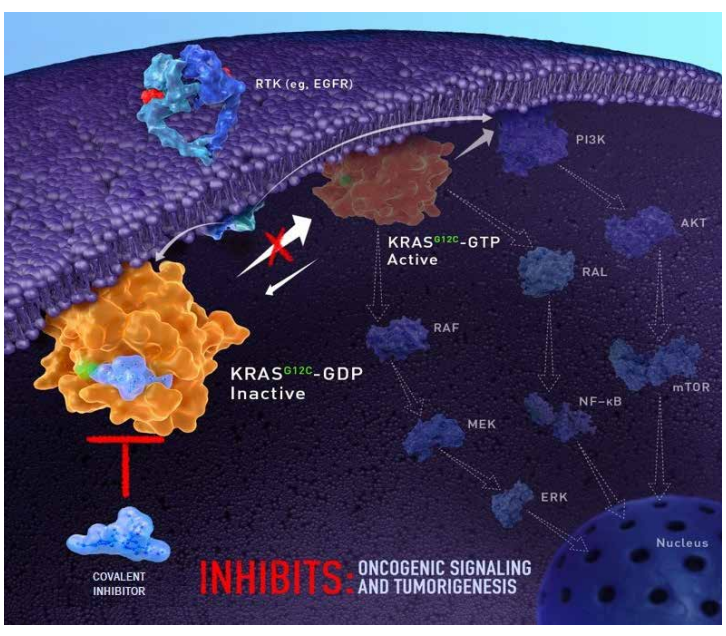
KRAS G12C Mutation Prevalence in the U.S.



In the U.S., about 13% of patients with non-squamous non-small cell lung cancer harbor the *KRAS G12C* mutation.[8] It is also found in approximately 3-5% of colorectal cancers and 1-2% of numerous other solid tumors, making this among the most broadly represented mutations across cancer patient subgroups.[6, 9-12]

The high prevalence of *KRAS G12C* highlights the importance of finding options for patients who harbor this mutation.[2]

Scientific Advancements



Novel covalent inhibitors are under investigation with the intent to specifically and irreversibly bind to cysteine-12 in a small pocket of the KRAS^{G12C} protein.[6,7]

Investigating a unique surface groove in the KRAS^{G12C} protein, Amgen is exploring the potential in KRAS^{G12C} inhibition across multiple tumor types for patients. Advances in understanding the structure of *KRAS* has prompted further investigations.[1]

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