

A therapeutic method for treating oncogenic Ras-mediated tumor growth with L-NAME

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Unmet Need

In cancer, there are various gene mutations and amplifications that drive the survival and proliferation of tumors. One of the most mutated genes in cancer is the RAS gene family (HRAS, KRAS and NRAS). Approximately 30% of all cancers contain a RAS mutation. However, despite being a major player in tumorigenesis, targeting the RAS pathway has had low success in the clinic. Therefore, there is an unmet clinical need to identify novel therapeutics to treat cancers where RAS is essential for tumor growth and survival.

Technology

Counter and colleagues have identified a new therapeutic method for the treatment of oncogenic RAS-driven cancer. This is accomplished by treating patients with L-NAME, a nitric oxide synthase inhibitor. The researchers have identified that the oncogenic RAS-Akt pathway causes phosphorylation of endothelial nitric oxide synthase (eNOS) at site S1177. Through pre-clinical mouse studies and genetic manipulation of eNOS, Counter and colleagues showed that eNOS is required for tumor growth in RAS mutated cancer cells. Oral administration of L-NAME in mice bearing oncogenic RAS tumors showed decreased tumor growth.

Advantages

- Targeting the downstream eNOS serves as a novel, alternative strategy for treating RAS-driven cancers
- Animal studies demonstrate decreased tumor growth
- Can treat multiple cancer types including pancreatic and non-small cell lung cancer



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Links

- [From the lab of Dr. Christopher Counter](#)

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Publications

- [Treatment with the nitric oxide synthase inhibitor L-NAME provides a survival advantage in a mouse model of Kras mutation-positive, non-small cell lung cancer \(Oncotarget, 2016\)](#)
- [Evaluating the role of nitric oxide synthase in oncogenic ras-driven tumorigenesis \(Redox Biol, 2015\)](#)
- [Targeting eNOS in pancreatic cancer \(Cancer Res, 2012\)](#)
- [Tumor maintenance is mediated by eNOS \(Nature, 2008\)](#)
- [Issued Patent 8,927,598](#)

Patents

Patent Number: 8,927,598

Title: Treating Oncogenic Ras Driven Cancers

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