Abstract

RAS is a signal transducer, a molecular switch with two states: an “on” state, which contains the GTP nucleic acid, and an “off” state, which contains the GDP nucleic acid. The “switch” is turned on by growth factor receptors such as epidermal growth factor (EGF) and results in Ras binding GTP. Once in the “on” state, Ras interacts with another growth activator, the Raf oncogene. Activation of Raf initiates a cascade of kinases that leads to an increase in gene expression and stimulation of cell growth.

In order to terminate the Ras activation signal, GTP is hydrolyzed to GDP resulting in Ras-GDP, the “off” state of Ras. This is accomplished with the help of a GTPase activating protein, NF1. The action of NF1 is to turn off Ras and hence it is a tumor suppressor. NF1 is also called Neurofibromin. The loss of NF1 via genetic mutations causes a cancer called neurofibromatosis.

Our project explores how the Ras protein interacts with NF1 to stimulate the hydrolysis of GTP to turn off the Ras oncogene protein. Scientists are interested in this interaction because it contributes to the understanding of cancer and potentially the design of drugs for Neurofibromatosis.

Cancer

• Uninhibited growth of cells due to mutations
• Activators initiate cell division
  • Ex: RAS
• Inhibitors, found in cells, stop cell division
  • Ex: NF1
• Cancer results from the inappropriate expression of these activators and/or inhibitors.

Neurofibromatosis

• Cancer of the nervous system
• NF1 (a tumor suppressor) encodes Neurofibromin, a protein that inhibits the RAS oncogene’s function.
• 1NF1, a neurofibromin, contains a mutant structure that fails to suppress the RAS oncogene
• This failure to suppress the RAS oncogene causes unrestricted cell proliferation, which can form tumors if the cells are mutated.

Symptoms and Treatment

- tumor growth and skin or bone irregularities
  • inherited by birth
  • 30-50% of new cases arise through mutations in NF1
- symptoms include headache, facial pain and numbness from pressure of tumors
- treatment includes removal of tumors but no effective cure has been found

Bibliography

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