A novel protein called nischarin

Nischarin is a large protein that is present in the nucleus and cytoplasm of cells. So far, diseases associated with the *NISCH* gene include hypertension, dry mouth, morphine dependence, depression, anxiety, thick heart walls, congestive heart failure, rosacea, brain diseases, ovarian cancer, breast cancer and lung cancer. Nischarin interacts with a number of important proteins such as Rab14, IntegrinA5, Rac1, LIMK, IRS1-4, LKB1, PAK1 and PI(3)P to prevent cancer, mediate insulin signaling, lower blood pressure and protect the brain (Fig. 1).

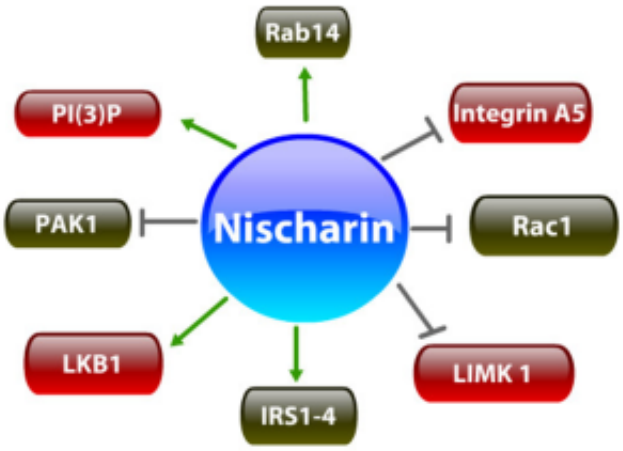

Fig 1. Nischarin interacts with a number of proteins to prevent cancer, mediate insulin signaling, lower blood pressure and protect the brain.

Nischarin prevents cancer: Nischarin plays a significant role in breast, ovarian and lung cancer cell progression. Nischarin mRNA is high in normal tissues and lower in cancer specimens. Highly invasive cancer cell lines exhibit low expression levels, moderately invasive cancer cell lines exhibit higher expression levels, and non-tumor cells have the highest amount of Nischarin expression. Nischarin expression is high in non invasive stage 0 human specimens but reduced in dangerous stage I-IV specimens. Nischarin prevents cancer by reducing tumor growth and preventing the movement of the cells to other organs. Studying Nischarin helps scientists understand how cancers form and helps find ways to treat them.

Nischarin participates in insulin signaling: Nischarin interacts with insulin receptor substrate (IRS) proteins to activate insulin signaling. After the IRS proteins are activated, they will increase glucose uptake into the cell and synthesis of fats. In muscle cells, glucose transport will increase and more glucose will be stored in the tissue as glycogen. In fat cells, more glucose will be transported in and excess fat will be created. Similarly, in the liver, more glycogen and fat will be created (Fig. 2). Without Nischarin, muscle and fat tissues have less glycogen and fat stored in them.

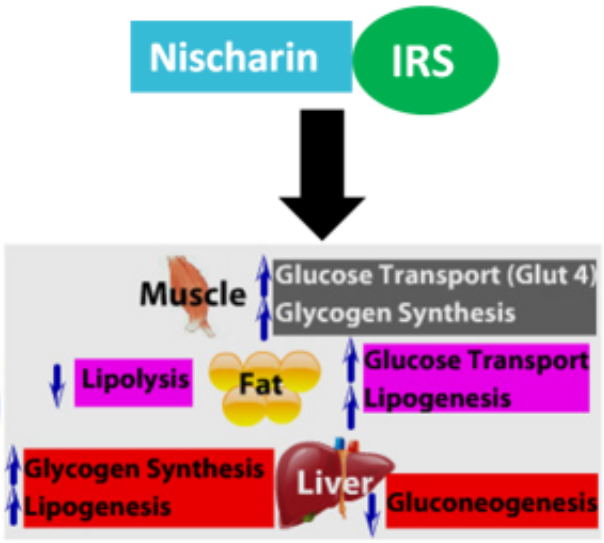

Fig 2: The activation of the IRS pathway by Nischarin increases glucose transport and glycogen synthesis in muscles. In fat cells it decreases lipolysis and increases glucose transport and lipogenesis. The liver experiences increased glycogen synthesis and lipogenesis but decreased gluconeogenesis.

Nischarin in the brain: Nischarin is highly expressed in the front of neurons, also known as the leading edge. The leading edge of neurons is important for the lengthening of neurons in the embryonic period during normal brain formation. Therefore, a reduction of Nischarin causes improper brain formation. Nischarin is also a neuroprotective protein because it induces cell death of the neuron if it is functioning improperly. Furthermore, Nischarin levels are increased in response to anxiety. A study was done that exposed cat odor to rats to make them anxious. Nischarin expression increased 1.2 fold in response to the anxiety of the rats. This is an important protein in the brain as it is also associated with morphine dependence, depression and various brain diseases.

Nischarin plays a role in hypotension: The Rostral Ventrolateral Medulla (RVLM) is a region of the brainstem that controls blood pressure. This region induces abnormally low blood pressure (hypotension) through activating the imidazoline (I_1) receptors in the brain. Nischarin has been found to increase the production of a protein called ERK1/2 to subsequently stimulate hypotension.

Further studies of the protein Nischarin will increase current knowledge in the fields of cancer biology, cell migration, cell death, intercellular trafficking, cell adhesion, signal transduction, and hypertension.

Publication

Breast Cancer Tumor Suppressors: A Special Emphasis on Novel Protein Nischarin.
Maziveyi M, Alahari SK
Cancer Res. 2015 Oct 15