INHIBITORS OF NOX-4 FOR THE TREATMENT OF NEUROPATHIC PAIN

Introduction

Neuropathic pain, triggered by multiple insults to the nervous system often proceeds chronically and produces severe distress in the everyday life of affected patients. Myelin encloses the axons of many neurons, thereby isolating and protecting them. Damage to the myelin sheath plays an important role in a number of neurological diseases, which are often accompanied by chronic pain. The NADPH oxidase-4 (Nox4) generates reactive oxygen species (ROS) such as superoxide and hydrogen peroxide which damage myelin and Nox4 plays a role in the onset of pain, in particular neuropathic pain.

Invention

The present invention relates to the use of the enzyme Nox4 as a target for the prevention and treatment of neuropathic pain. Accordingly, the use of Nox4 inhibitors is proposed, which reduce the activity and / or expression of Nox4. Mice deficient in Nox4 demonstrate considerably reduced pain-related behavior in animal models of neuropathic pain. Moreover, dysmyelination of peripheral nerves that typically occurs after nerve injury (SNI) is reduced in Nox4-deficient mice.

Market Potential

The invention proposes the use of inhibitors of Nox4 for the treatment and prevention of neuropathic pain. Hence, Nox4 can be used as target for the therapy of pain in patients with nerve injury, postherpetic neuralgia, diabetic neuropathy, polyneuropathy, herniated disc, multiple sclerosis, infarction or cancer.

Development Status

The validity of the invention has been tested in animal experiments.

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Reduced neuropathic pain behavior in Nox4−/− mice. A: Paw-withdrawal latency times in Nox4−/− and wild-type (WT) mice after mechanical stimulation in the SNI neuropathic pain model. B: Paw-withdrawal latency times after mechanical stimulation in tamoxifen-inducible Nox4−CreERT2 knock-out mice and littermate control mice during SNI-induced neuropathic pain.