

An Innovative Therapy for Inflammatory Diseases (BGN)

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Inflammation often named "the secret killer" is a key factor in a large group of diseases affecting and killing millions of people every year. Examples of inflammatory diseases or diseases with key inflammatory components include Arthritis, Alzheimer, Parkinson, ALS, Peritonitis, Colitis, Obesity & Insulin resistance and several types of cancer. Currently, anti-inflammatory drugs, both NSAIDs and steroidal, fail to deliver a solution because they tackle only parts of the inflammatory cascade and induce unacceptable side effects. There is a strong need for specific and efficient anti-inflammatory drugs with minimal side effects. This need is recognized by the pharmaceutical industry which struggles to develop such drugs.

Our Solution

cPLA2 is a major participant in the inflammatory cascade and cPLA2 over production is a major cause of inflammation. We have developed an antisense oligonucleotide based therapy that reduces the overproduction of cPLA2 and successfully combats inflammation as shown in several inflammatory diseases.

Applications

Colon cancer -The administration of the antisense oligonucleotides (AS) but not the corresponding sense oligonucleotides (SE) significantly inhibit cPLA2 protein expression and reduce HT-29 cell proliferation by inducing cell arrest.

Alzheimer's Disease - Our studies demonstrate that cPLA2 is regulating the production of A β and that both neuronal cPLA2 directly, and microglia cPLA2 indirectly, contribute to apoptotic neuronal death. The presence of our antisense oligonucleotides (AS) not only inhibit the excessive production of A β but also prevents the indirect and direct neuronal death in culture, indicating towards an efficient treatment for Alzheimer's disease.

Rheumatoid Arthritis - In-vivo intravenous administration of the antisense oligonucleotides (AS), after development of severe arthritis in a mouse model of CIA, induced remarkable recovery after only a short treatment, as determined by clinical score and by the histological examination of the inflamed joints.

Obesity Induced Insulin Resistance - Initiating obesity and impairment of liver insulin signaling in a mouse model of High Fat Diet was accompanied by neutrophil recruitment to the intra-abdominal fat. Intravenous administration of antisense against cPLA2 prevented the severe liver insulin signaling impairment.

ALS - The elevated expression and activity of cPLA2 in brain and spinal cord of both sporadic and familial ALS patients and in spinal cord of the mouse model of ALS, with SOD1 mutation suggests that cPLA2 may have an important role in the pathogenesis of the disease in all ALS patients. The role of cPLA2 up regulation has been demonstrated also in caspase mediate apoptotic neuronal death induced by oxidative stress. We have shown that inhibition of cPLA2 up regulation that inhibited caspase activation prevented neuronal death, and extended survival of ALS mice.

Patent Status

Patent Pending

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