Human PKCδ VIII Isoform as a Biomarker in Nervous System Disorders

Researchers at the University of South Florida have demonstrated that human protein kinase C (PKC) δVIII is increased in neuronal cancer cells and decreased in patient samples from Alzheimer’s Disease (AD). This characteristic of the protein can make it a potential biomarker for nervous system disorders.

Protein kinase C (PKC) δ plays an important role in cellular proliferation and apoptosis where it is involved in the caspase-3 mediated apoptotic pathway. Cleavage of PKCδI by caspase-3 releases a catalytically-active C-terminal fragment which is sufficient to induce apoptosis. Recently, our inventors have identified a novel human PKCδ isozyme, PKCδVIII (Genbank accession number DQ516383) whose expression levels are seen highest in the brain. Expression of PKCδVIII was confirmed by real time RT-PCR analysis. Using in vivo and in vitro assays it was demonstrated that PKCδVIII is resistant to caspase-3 cleavage. Over-expression of PKCδVIII and knockdown using PKCδVIII siRNA suggests a pro-survival function for PKCδVIII isozyme.

Further, over-expression of PKCδVIII increased the expression of pro-survival proteins Bcl2 and Bcl-xL. This indicates that PKCδVIII mediates its effects via Bcl2 and Bcl-xL. Our data demonstrates that human PKCδVIII expression is increased in neuronal cancer cells and decreased in patient samples from Alzheimer’s Disease (AD).

Neurodegenerative diseases are associated with increased apoptosis whereas cancers have decreased apoptosis and increased cell proliferation. PKCδVIII is a pro-survival protein. PKCδVIII in neurons shields them from apoptosis or programmed cell death. Expression of PKCδVIII is an indicator of the levels of ongoing apoptosis in neurons. Tilting the balance of PKCδVIII isoform expression could have significant therapeutic implications. PKCδVIII serves as a biomarker for neurodegenerative diseases and neuronal cancers.

ADVANTAGES:

- PKCδVIII is an indicator of ongoing apoptosis levels in neurons
- Decreased expression as a potential indicator of Alzheimer’s
- Increased expression in cancer

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Detecting Alzheimer’s Disease and Neuronal Cancers

Fig 1: RNA extracted by RT-PCR with primers Specific for PKCδVIII. Fig 2:RT-PCR result comparison of total RNA obtained from control and Alzheimer’s patients