Suppression of Nitric Oxide Production by Osteopontin

Background

Nitric Oxide (NO) is a potent vasodilator produced by macrophages, endothelium and neuronal cells. NO production is important for the proper functioning of organs such as kidneys and the brain. Kidney cells such as glomerular endothelial cells and mesangial cells produce NO. Nitric oxide is synthesized by nitric oxide synthase (NOS) from arginine and oxygen. The kidney appears to have both the inducible as well as the constitutive forms of the enzyme. During inflammation or stress kidney cells are exposed to inflammatory mediators such as IFN-gamma, IL-1beta and TNF-alpha which are known to stimulate NO production. Excessive NO is cytotoxic to kidney epithelium and interferes with kidney function. Thus, down-regulation of NO production may be necessary to minimize kidney injury. **The present invention describes the use of Osteopontin, a phosphoprotein produced by many epithelial cells, in the treatment of diseases or disorders involving NO.**

Description of the Technology

UMDNJ scientists have discovered that administration of osteopontin to mouse kidney epithelial cells stimulated with IFN-gamma and LPS results in the inhibition of inducible NO-synthase (iNOS) gene induction. Furthermore, osteopontin also induced the suppression of iNOS protein. Suppression of NO production could also be obtained with a 20 amino acid fragment of osteopontin as well as a GST-osteopontin fusion protein purified from *E.coli* suggesting that the post-translational modifications characteristic of mammalian proteins are unnecessary for its activity.

Advantages:

- Effective even in low (~pM) concentrations

Applications

- For use in the treatment of diseases or disorders involving NO such as inflammation, septic shock, hypotension

Patent Status

. • United States patent granted on December 9, 1997
. • Patent Number: 5,695,761

Licensing Opportunity

This technology is available for licensing non-exclusively or exclusively.

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