# Targeting kupffer cells with antisense oligonucleotides

Ponnappa, Biddanda C.

Israel, Yedy

© 2002 Frontiers in Bioscience. All rights reserved.During proinflammatory reactions such as endotoxemia, ischemia-reperfusion and immune reactions, excessive amounts of cytokines and prostanoids are released resulting in liver injury. In the liver, Kupffer cells are the primary source of cytokines and prostanoids. Obliteration of Kupffer cells prevents experimentally-induced liver damage, suggesting a major role for Kupffer in the pathogenesis of liver diseases. Pretreatment of experimental animals with antibodies directed against cytokines such as tumor necrosis alpha (TNF-alpha) prevented experimentally-induced liver damage. In recent years, antisense oligonucleotides (ASOs) directed against specific mRNAs have been tested as an alternative therapy to control the excessive production of inflammatory peptides. Although ASOs have great potential against gene expression, their design, in vivo delivery and stability, have posed significant challenges. Computer-aided configurational anal