

Feng Qiu
Dr. sc. hum

Rolle von Mitgliedern der NF- κ B, bZIP Familie und Tissue Factor bei der Endotoxin-vermittelten Lethalität

Geboren am 27.04.1963 in HangZhou, V R China

Reifeprüfung am 01.08.1981 in HangZhou

Studiengang der Fachrichtung Biochemie vom SS 1981 bis WS 1985

Vordiplom am 01.09.1985 an der Universität: Amoy Universität, Xiamen, V R China

Diplom am 01.09.1990 an der Universität: CNRRI, HangZhou, V R China

Promotionsfach: Innere Medizin

Doktorvater: Priv.-Doz Dr. med. P. P. Nawroth

The patient study and the animal study complement each other in demonstrating that endotoxin mediated activation of the transcription factors NF- κ B and AP-1 play a central role in vivo. The transcription factors nuclear factor κ B (NF- κ B) and activator protein-1 (AP1) are believed to control genes, which play an important role in the pathogenesis of sepsis. The NF- κ B and AP1 binding activities were determined in nuclear extracts of monocytes isolated from 15 patients with sepsis (10 survivors, and 5 non-survivors). Non-survivors could be distinguished from survivors by an increase in NF- κ B ($p < 0.001$) and AP1 ($p < 0.05$) binding activities. The increase in NF- κ B and AP1 binding activities was a stronger predictor of outcome than the APACHE II score. Intravenous somatic gene transfer with an expression plasmid coding for I κ B α or mutated Jun (a form of Jun capable of binding Fos, but not DNA) was used to investigate the role of members of the NF- κ B and the basic-leucine zipper protein (bZIP) families in an animal model of sepsis. Intravenous somatic gene transfer with I κ B α and m-Jun increased survival, decreased renal NF- κ B and AP1 binding activities, decreased tissue factor expression, reduced the activation in the plasmatic coagulation system. Somatic gene transfer with an expression plasmid with tissue factor cDNA in the antisense direction (in contrast to sense or vector alone) also increased survival, decreased tissue factor expression and also reduced the activation of the plasmatic coagulation system. Somatic gene transfer with a reporter plasmid containing the functional tissue factor promoter demonstrated NF- κ B and AP1-dependent stimulation by endotoxin in vivo. Thus, members of the NF- κ B and bZIP families play an important role in endotoxin-mediated sepsis, partly due to regulation of tissue factor transcription.