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论著

Xaf1调节TNFR信号转导而诱导细胞凋亡的机制研究

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摘要 目的： 利用基因开关调节的Xaf1-Saos诱导细胞株， 检测Xaf1对TNFR信号转导通路的影响，探索Xaf1与TNF-α协同诱导细胞凋亡的机制。方法： 以免疫印迹法和RT-PCR检测Xaf1对TNFR1 表达的影响，细胞周期 DNA 含量流式细胞术检测NF-κB对Xaf1诱导细胞凋亡的影响，gel mobility shift assay 检测NF-κB的DNA结合活性， luciferase 活性检测法及RT-PCR检测NF-κB的转录活性，激酶分析法检测SAPK/JNK 激酶的活性。结果： Xaf1不影响TNFR1蛋白及mRNA水平的表达，细胞内诱导活性的NF-κB可抑制Xaf1诱导的细胞凋亡， Xaf1的表达抑制TNF-α所介导的NF-κB的DNA结合活性和转录活性，也抑制了SAPK/JNK 激酶的活性。结论： Xaf1 对TNFR信号转导的抑制是Xaf1协同TNF-α诱导细胞凋亡的机制之一。

关键词 Xaf1； 细胞凋亡； 受体,肿瘤坏死因子； 信号转导

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Xaf1 regulates TNFR signal pathway and induces apoptosis

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Abstract

<FONT face=Verdana>AIM: Xaf1-Saos inducible cell lines, which contain “gene switch” system were used to detect the effect of Xaf1 on tumor necrosis factor receptor(TNFR) signal pathway and to investigate the mechanism of cooperation between Xaf1 and TNF-α in inducing cell apoptosis.
METHODS: Xaf1 on TNFR1 expression was measured by RT-PCR and Western blotting. The effect of NF-κB on Xaf1 induced apoptosis was detected by DNA content flow cytometry after co-transfection. DNA binding activity of NF-κB was identified by gel mobility shift assay and transcription activity of NF-κB was analyzed by luciferase assay and RT-PCR. SAPK/JNK activity was checked by SAPK/JNK assay.
RESULTS: Xaf1 did not modulate TNFR1 at protein and mRNA levels. Increased NF-κB activity in cells inhibited Xaf1 induced apoptosis. Expression of Xaf1 impaired modestly TNF-α induced NF-κB DNA binding activation and transcription activation, also modestly reduced SAPK/JNK activity.
CONCLUSION: Xaf1 inhibits TNFR signal pathway, partly contributing to cooperation with TNF-α to induce apoptosis. </FONT>

Key words Xaf1 Apoptosis Receptors tumor necrosis factor Signal transduction

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