

Az NF-κB funkciót befolyásoló 26 gombafaj, valamint további metabolitjaik és ezek aktivitása

Lényegre törően és nagyon lerövidítve:

Az IKK/NF (nukleáris faktor)-κB jelátviteli rendszer molekulái meghatározó szerepet töltenek be többek között a gyulladásos és immunológiai folyamatokban, továbbá egyike azon tényezőknek, amelyek felelősek a sejtes kemorezisztenciáért.

Az emlősöknél az NF-κB csoport fehérjéi az alábbi öt tagból állnak:

p65 (RelA)
RelB
c-Rel

p50 (NF-κB1)
p52 (NF-κB2)

Az NF-κB fő aktivátora az alábbi IκB kináz komplex (IKK):

IKK-α
IKK-β
IKK-γ (NEMO, szabályozó alegység)

Az NF-κB alábbi három fő inhibitora (IκB) /fehérjék, lelassítják az enzimek által katalizált reakciók sebességét/:

IκBα
IκBβ
IκBε

Alább olvasható az NF-κB funkciót modulálni képes 26 gombafaj, valamint további metabolitjaik és ezek aktivitása.

Table I. Fungal species affecting the NF-κB function, including additional fungal compounds and their activities.

No.	Species	IC ₅₀ ^a (μg/ml)	Effects on IκBα and phospho-IκBα ^b	Known activities	Bioactive compounds	References
1	<i>Agrocybe aegerita</i> (edible)	>125	Moderately inhibits IκBα degradation and IκBα phosphorylation	Anti-tumor Anti-tumor and immunostimulating Anti-tumor (apoptosis induction) Inhibitor of COX and anti-oxidant activities	α-(1-3)-β-glucan Glucan Lectin Fatty acid fraction, palmitic acid ergosterol, manitol, threhalose, etc.	15 16 17 18
2	<i>Cordyceps sinensis</i> (non-edible)	110	A strong inhibitor of IκBα degradation and a moderate inhibitor of IκBα phosphorylation	Anti-tumor Immunomodulating Inhibition of proliferation and differentiation of human leukemic U937 cells Anti-tumor (against various tumor cell lines, such as the K562 (CML), Jurkat (T-lymphoblastic), HL-60 (promyelocytic leukemia), WM1341 (malignant melanoma) and RPMI (multiple myeloma) Anti-oxidant and anti-tumor activities; inhibit cell proliferation, induce apoptosis in colorectal and hepatocellular cancer	Polysaccharides, sterols, lipids, nucleosides, and deoxy-nucleosides Polysaccharides Polysaccharide fraction from ethanol-precipitable aqueous extraction Sterols Polysaccharides (ethanolic extract), cordycepin	53 54 55 56 57

3	<i>Cyathus striatus</i> (non-edible)	<2	Dose-dependently inhibits both I κ B α phosphorylation and degradation	Anti-bacterial	Striatins	35
				Inhibition of protein, RNA and DNA synthesis	(antibiotics - diterpenoids)	
				Anti-bacterial and fungicidal Anti-microbial and cytotoxic properties	Striatins Cyathins (antibiotics - diterpenes)	20 20, 34
4	<i>Fomes fomentarius</i> (non-edible)	>125	Strongly inhibits I κ B α degradation and moderately inhibits I κ B α phosphorylation	Anti-tumor	A polysaccharide fraction from culture filtrate	40
				Anti-microbial	-	41
				Anti-tumor	β -glucan	27
				Inhibition of iNOS and COX expression due to down-regulation of NF- κ B binding activity to DNA	Methanol extract	11
5	<i>Ganoderma</i> spp. (non-edible)	>125	Moderately inhibits I κ B α degradation. A strong inhibitor of I κ B α phosphorylation	G1 cell cycle arrest	Alcohol extract	22 ^c
				Inhibits breast and prostate cancer cell proliferation <i>in vitro</i>	Spore extract	23 ^c
				Inhibition of AP-1 and NF- κ B activity	Spores and FB extracts	24, 25 ^c
				G1 arrest in androgen-dependent prostate cancer cell lines	Organic extract	26 ^c
6	<i>Marasmius oreades</i> (edible)	>125	A strong inhibitor of I κ B α phosphorylation	Anti-microbial and phytotoxic properties	Agrocybin and drimane sesquiterpenes	20
				Renal thrombotic microangiopathic lesions	Lectin	21
7	<i>Phallus impudicus</i> (edible only immature)	>125	Strongly inhibits I κ B α degradation	Anti-tumor	PI-2 glucomannan (FB and culture mycelium)	27
				Reducing the metastases in Lewis lung carcinoma	FB extract in the form of small particle spray	50
				Prevention of thromboembolic complications in cancer patients	Juice from fresh FB	51
8	<i>Pleurotus ostreatus</i> (edible)	>125	A strong inhibitor of I κ B α phosphorylation	Anti-tumor	β -glucan	27
					Heteroglucan	
				Anti-tumor	Polysaccharide fractions	28
				Anti-tumor, hypocholesterol effects and hypotensive activity	FB extracts	29
				Cancer protective (cytostatic) and anti-inflammatory effects	FB extracts	30
				<i>In vitro</i> activity against rodent mammary adenocarcinoma 755	Fermentation products	31
				Suppression of aromatase activity	FB extract	32
				Inhibition of proliferation and differentiation of K562 human leukemia cells	Low-molecular-weight substances from mushroom crude extract	33
9	<i>Pleurotus pulmonarius</i> (edible)	>125	Strongly inhibits I κ B α degradation and weakly inhibits I κ B α phosphorylation	Anti-tumor	Protein-containing polysaccharides; p-anisaldehyde, (4-methoxyphenyl)-1,2-propandiol	37
				Hematological and cardiovascular effects	-	39
				Anti-fungal, nematocidal and cytotoxic properties	S-coriolic (linoleic) acid	20
				Anti-tumor	Xyloglucan(FB) Xylanprotein (FB)	27
				Anti-oxidant, anti-inflammatory and anti-tumor	Methanol extract of FB	38

10	<i>Sparassis crispa</i> (edible)	>125	Strongly inhibits I κ B α degradation	Enhancing the hematopoietic response	β -glucan fraction (CA1)	47
				Anti-tumor (improvement in lung, stomach, colon, breast, ovarian, uterine, prostate, pancreas and liver cancer)	β -glucan	48
				Immunomodulating (complete response in breast cancer patients)	1,3- β -D-glucan	49
11	<i>Schizophyllum commune</i> (edible)	40	A strong inhibitor of I κ B α phosphorylation	Squalene synthetase inhibition	Schizostatin	20
				Anti-tumor and immunomodulating	β -glucan (schizophyllan)	27
12	<i>Trametes gibbosa</i> (non-edible)	>125	A very strong inhibitor of both I κ B α degradation and phosphorylation	Anti-tumor	β -glucan (FB) Hot-water extracts (FB)	36
13	<i>Trametes zonata</i> (non-edible)	>125	Strongly inhibits I κ B α degradation. Weakly inhibits I κ B α phosphorylation	Inhibition of the growth, promotion of apoptosis and induction of erythroid differentiation of the K562 (CML), inhibition of the growth of the LNCaP (prostate cancer) cell line	Mycelial extract	52
14	<i>Agaricus bisporus</i> (edible)	-	Not included	Inhibits NF- κ B binding to DNA	CAPE	9
				Suppression of aromatase activity	-	32
15	<i>Agaricus brasiliensis</i> (edible)	-	Not included	Suppresses the activity of NF- κ B and AP-1	Crude polysaccharides	42
16	<i>Chaetomium sub-spirale</i> (non-edible)	2.5	Not included	Inhibits the phosphorylation of ERK1/2 kinases and the activation of NF- κ B	Oxaspirodion	46
17	<i>Cordyceps militaris</i> (non-edible)	-	Not included	Suppresses TNF- α gene expression, I κ B α phosphorylation and nuclear translocation of p65. Decreases the expression of COX-2 and iNOS due to the down-regulation of NF- κ B activation, Akt and p38 phosphorylation	Cordycepin	59
18	<i>Cordyceps pruinosa</i> (non-edible)	-	Not included	Inhibits IL-1 β , TNF- α , NO and prostaglandin E ₂ in LPS-stimulated murine macrophages and primary macrophages by suppressing gene expression of IL-1 β , TNF- α , iNOS and COX-2 through NF- κ B inhibition	Methanol extract	58
19	<i>Hericium erinaceum</i> (edible)	-	Not included	Enhances the activation of NF- κ B by inducing the IL-1 β expression	Water extract	43
				Induces macrophage activation through the activation of NF- κ B		44
20	<i>Inonotus obliquus</i> (non-edible)	-	Not included	Inhibits the DNA binding activity of NF- κ B associated with the prevention of I κ B α degradation and reduction of the nuclear p65 levels. Anti-inflammatory and anti-nociceptive activities related to the inhibition of iNOS and COX-2 expression through the down-regulation of the NF- κ B binding activity	Methanol extract	60
21	<i>Lentinus edodes</i> (edible)	-	Not included	Inhibits NF- κ B binding to DNA	CAPE	9
				Suppression of aromatase activity	-	32

22	<i>Lentinus crinitus</i> (edible)	-	Not included	Interferes with the NF- κ B-mediated signal by inhibiting the phosphorylation of I κ B α	Panepoxydone	12
23	<i>Morchella esculenta</i> (non-edible)	-	Not included	Increases NF- κ B luciferase expression in THP-1 human monocytes	Galactomannan	58
24	<i>Panus conchatus</i> (edible)	-	Not included	Panepoxydone inhibits the TNF- α - or TPA-induced phosphorylation and degradation of I κ B. Cycloepoxydon also has a potent NF- κ B inhibitory activity (shown in COS-1 cells)	Panepoxydone and cycloepoxydon	45
25	<i>Phellinus linteus</i> (edible)	-	Not included	Inhibits DNA binding of NF- κ B Induces the maturation of dendritic cells via NF- κ B, ERK and p38 MAPK signal pathways	CAPE	10 61
26	<i>Trametes versicolor</i> (non-edible)	-	Not included	Suppression of proliferation and increase in apoptosis in human U-937 and HL-60 leukemia cells. In HL-60, PSP decreased the levels of NF- κ B, p65 and p50, associated with the inhibition of COX-2 expression. PSP increased the expression of STAT-1 but decreased the expression of ERK	Polysaccharo-peptide	62

^aThe IC₅₀ values are given according to the data by Petrova *et al* (19). ^bMushroom effects on I κ B α phosphorylation and degradation are summarized and presented according to Petrova *et al* (19). ^cReferences presenting the activity of *Ganoderma lucidum*.

A meglévő vegyületek további vizsgálata, hatásmechanizmusának tanulmányozása, valamint újabb gombafajok esetleg még hatékonyabb metabolitjainak kutatása és ezen szubsztanciákból megbízható gyógyszerek előállítása ígéretes perspektíva lehet a rákkezelés területén.

/Forrás: Petrova *et al*: Fungal metabolites modulating NF- κ B activity: An approach to cancer therapy and chemoprevention (Review) - ONCOLOGY REPORTS 19: 299-308, 2008;
Az NF- κ B jelentősége a myeloma multiplex patogenezisében és kezelésében - Current Opinion in Hematology 2008, 15:391–399/

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