人工关节假体磨损颗粒对巨噬细胞游走抑制因子表达的影响

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摘　要　目的:观察人工关节假体磨损颗粒对巨噬细胞游走抑制因子表达的影响。**方法:**配制钛颗粒悬液,并培养小鼠巨噬细胞。将培养的第 3 代小鼠巨噬细胞分别进行以下实验:①将细胞分为 4 组,A 组不作任何处理,B 组加入浓度为 0.01% 的钛颗粒;C 组加入浓度为 0.05% 的钛颗粒,D 组加入浓度为 0.1% 的钛颗粒。培养 24 h 后分别用酶联免疫吸附剂测定法和聚合酶链式反应法检测各组的巨噬细胞游走抑制因子蛋白和巨噬细胞游走抑制因子 mRNA 的含量。②将细胞分 2 组,对照组不作任何处理,观察组加入浓度为 0.1% 的钛颗粒。分别在实验开始后 0 h、6 h、12 h、24 h 和 36 h 对 2 组的不同培养孔的细胞用酶联免疫吸附剂测定法和聚合酶链式反应法检测各组的巨噬细胞游走抑制因子蛋白和巨噬细胞游走抑制因子 mRNA 的含量。③将细胞分为 4 组,Ⅰ组不作任何处理,Ⅱ组加入浓度为 0.1% 的钛颗粒,Ⅲ组加入浓度为 100 μmol·mL^{-1}的吡咯烷二硫代氨基甲酸盐,Ⅳ组先加入浓度为 100 μmol·mL^{-1}的吡咯烷二硫代氨基甲酸盐,1 h 后再加入浓度为 0.1% 的钛颗粒。培养 24 h 后用酶联免疫吸附剂测定法检测各组的巨噬细胞游走抑制因子蛋白含量。④将细胞分为 2 组,a 组不作任何处理,b 组加入浓度为 0.1% 的钛颗粒。分别在实验开始后 0 h、0.5 h、1 h、3 h 和 6 h 对 2 组的不同培养孔的细胞用酶联免疫吸附剂测定法测定磷酸化 p65 的含量。**结果:**①钛颗粒浓度对巨噬细胞游走抑制因子表达的影响:各组小鼠巨噬细胞巨噬细胞游走抑制因子蛋白和巨噬细胞游走抑制因子 mRNA 含量的组间比较,差异均有统计学意义($F=207.158$,$P=0.000$;$F=64.955$,$P=0.000$)。A 组巨噬细胞游走抑制因子蛋白和巨噬细胞游走抑制因子 mRNA 的含量[(3.93±0.11)ng·mL^{-1},(0.03±0.01)]与 B 组[(4.21±0.27)ng·mL^{-1},(0.10±0.01)]比较,差异无统计学意义($P=0.167$;$P=0.223$);A 组小于 C 组[(6.56±0.27)ng·mL^{-1},(0.25±0.09)],差异有统计学意义($P=0.000$;$P=0.004$);A 组小于 D 组[(7.82±0.21)ng·mL^{-1},(0.70±0.09)],差异有统计学意义($P=0.000$;$P=0.000$);B 组小于 C 组($P=0.000$;$P=0.025$)和 D 组($P=0.000$;$P=0.000$);C 组小于 D 组($P=0.000$;$P=0.000$)。②钛颗粒刺激时间对巨噬细胞游走抑制因子的影响:对照组巨噬细胞游走抑制因子蛋白和巨噬细胞游走抑制因子 mRNA 含量各时点间比较,差异无统计学意义($F=0.310$,$P=0.865$;$F=0.065$,$P=0.991$)。观察组巨噬细胞游走抑制因子蛋白和巨噬细胞游走抑制因子 mRNA 含量各时点间比较,差异有统计学意义($F=32.857$,$P=0.000$;$F=15.621$,$P=0.000$),各时点间两两比较:6 h 时的巨噬细胞游走抑制因子蛋白和巨噬细胞游走抑制因子 mRNA 表达量[(4.14±0.24)ng·mL^{-1},(0.08±0.04)]与 0 h[(3.60±0.40)ng·mL^{-1},(0.03±0.01)]比较,差异无统计学意义($P=0.133$;$P=0.621$);12 h 的表达量[(5.61±0.47)ng·mL^{-1},(0.36±0.21)]大于 0 h,差异有统计学意义($P=0.000$;$P=0.004$);24 h 的表达量[(7.15±0.10)ng·mL^{-1},(0.71±0.12)]大于 12 h,差异有统计学意义($P=0.000$;$P=0.003$);36 h 的表达量[(5.22±0.85)ng·mL^{-1},(0.31±0.18)]小于 24 h,差异有统计学意义($P=0.000$;$P=0.004$),但高于 0 h 的表达量($P=0.000$;$P=0.003$)。③钛颗粒和吡咯烷二硫代氨基甲酸盐对巨噬细胞表达巨噬细胞游走抑制因子蛋白的影响:实验结束后 4 组小鼠巨噬细胞的巨噬细胞游走抑制因子蛋白量分别为,Ⅰ组(3.77±0.42)ng·mL^{-1},Ⅱ组(7.59±0.28)ng·mL^{-1},Ⅲ组(4.23±0.42)ng·mL^{-1},Ⅳ组(6.48±0.5)ng·mL^{-1}。析因方差分析结果提示,单独使用 0.1% 钛颗粒能促进巨噬细胞表达巨噬细胞游走抑制因子蛋白($F=153.363$,$P=0.000$);单独使用 100 μmol·mL^{-1}的吡咯烷二硫代氨基甲酸盐对巨噬细胞表达巨噬细胞游走抑制因子蛋白无影响($F=1.762$,$P=0.221$);100 μmol·mL^{-1}的吡咯烷二硫代氨基甲酸盐对 0.1% 钛颗粒促进巨噬细胞表达巨噬细胞游走抑制因子蛋白具有抑制效应($F=10.325$,$P=0.012$)。④钛颗粒浓度对巨噬细胞 NF-κB 信号通路的影响:a 组各时点磷酸化 p65 含量比较,差异无统计学意义($F=0.248$,$P=0.904$)。b 组各时点磷酸化 p65 含量比较,差异有统计学意义($F=30.217$,$P=0.000$),各时点间两两比较:0.5 h 磷酸化 p65 含量[(17.68±0.55)pg·mg^{-1}]高于 0 h[(10.38±3.18)pg·mg^{-1}],差异有统计学意义($P=0.005$);1 h 磷酸化 p65 含量[(23.31±2.05)pg·mg^{-1}]高于 0.5 h,差异有统计学意义($P=0.020$);3 h 磷酸化 p65 含量[(31.80±1.84)pg·mg^{-1}]高于 1 h,差异有统计学意义($P=0.002$);6 h 磷酸化 p65 含量[(18.42±3.61)pg·mg^{-1}]低于 3 h($P=0.000$),但高于 0 h($P=0.003$)。**结论:**人工关节假体磨损颗粒可通过 NF-κB 信号通路上调巨噬细胞游走抑制因子的表达,促进假体周围炎症反应,导致假体周围骨吸收、溶解,导致假体无菌性松动。

关键词　人工关节　巨噬细胞游走抑制因子　NF-κB　动物实验

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Effect of wear particles from joint prosthesis on the expression of macrophage migration inhibiting factor

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ABSTRACT **Objective**: To observe the effects of wear particles from joint prosthesis on the expression of macrophage migration inhibiting factors (MMIF). **Methods**: Suspension with titanium particles was prepared and mice macrophages were cultured. The following experimentations were respectively carried on the third generation of mice macrophages. ①The cells were divided into 4 groups, cells in group A were added with nothing, while cells in group B, C and D were added with titanium particles suspension (0.01%, 0.05% and 0.1%, respectively). The contents of MMIF protein and MMIF mRNA of the 4 groups were respectively detected through enzyme linked immunosorbent assay (ELISA) and polymerase chain reaction (PCR) after culturing for 24 hrs. ②The cells were divided into 2 groups, cells in control group were added with nothing, while cells in observation group were added with 0.1% titanium particles suspension. The contents of MMIF protein and MMIF mRNA of the 2 groups were respectively detected through ELISA and PCR at 0, 6, 12, 24 and 36 hrs from the beginning of the experimentation. ③The cells were divided into 4 groups, cells in group Ⅰ were added with nothing, and cells in group Ⅱ were added with 0.1% titanium particles suspension and group Ⅲ were added with pyrrolidine dithiocarbamate (PDTC) (100 μmol/ml), while cells in group Ⅳ were firstly added with PDTC (100 μmol/ml) and titanium particles suspension (0.1%) one hr later. The contents of MMIF protein of the 4 groups were detected through ELISA after culturing for 24 hrs. ④The cells were divided into 2 groups, cells in group a were added with nothing, while cells in group b were added with 0.1% titanium particles suspension. The contents of phosphorylation p65 of the 2 groups were respectively detected through ELISA at 0, 0.5, 1, 3 and 6 hrs from the beginning of the experimentation. **Results**: ①Effect of titanium particles suspension concentration on MMIF expression: There were statistical differences in the contents of MMIF protein and MMIF mRNA of macrophages among the 4 groups ($F = 207.158$, $P = 0.000$; $F = 64.955$, $P = 0.000$). There were no statistical differences in the contents of MMIF protein and MMIF mRNA between group A ((3.93 ± 0.11) ng/ml, (0.03 ± 0.01)) and group B ((4.21 ± 0.27) ng/ml, (0.10 ± 0.01)) ($P = 0.167$; $P = 0.223$); the contents of MMIF protein and MMIF mRNA of group A were lower than those of group C ((6.56 ± 0.27) ng/ml, (0.25 ± 0.09)) and there were statistical differences ($P = 0.000$; $P = 0.004$); the contents of MMIF protein and MMIF mRNA of group A were lower than those of group D ((7.82 ± 0.21) ng/ml, (0.70 ± 0.09)), and there were statistical differences ($P = 0.000$; $P = 0.000$); the contents of MMIF protein and MMIF mRNA of group B were lower than those of group C ($P = 0.000$; $P = 0.025$) and group D ($P = 0.000$; $P = 0.000$); the contents of MMIF protein and MMIF mRNA of group C were lower than those of group D ($P = 0.000$; $P = 0.000$). ②Effect of titanium particles stimulation time on MMIF expression: There were no statistical differences in the contents of MMIF protein and MMIF mRNA of control group among different time points ($F = 0.310$, $P = 0.865$; $F = 0.065$, $P = 0.991$). There were statistical differences in the contents of MMIF protein and MMIF mRNA of observation group among different time points ($F = 32.857$, $P = 0.000$; $F = 15.621$, $P = 0.000$). Further comparison between any two time points showed that there were no statistical differences in the contents of MMIF protein and MMIF mRNA between 6 hrs ((4.14 ± 0.24) ng/ml, (0.08 ± 0.04)) and 0 hr ((3.60 ± 0.40) ng/ml, (0.03 ± 0.01)) ($P = 0.133$, $P = 0.621$); the contents of MMIF protein and MMIF mRNA at 12 hrs ((5.61 ± 0.47) ng/ml, (0.36 ± 0.21)) were larger than those at 0 hr, and there were statistical differences ($P = 0.000$; $P = 0.004$); the contents of MMIF protein and MMIF mRNA at 24 hrs ((7.15 ± 0.10) ng/ml, (0.71 ± 0.12)) were larger than those at 12 hrs, and there were statistical differences ($P = 0.000$; $P = 0.003$); the contents of MMIF protein and MMIF mRNA at 36 hrs ((5.22 ± 0.85) ng/ml, (0.31 ± 0.18)) were lower than those at 24 hrs ($P = 0.000$; $P = 0.004$) and larger than those at 0 hr ($P = 0.000$; $P = 0.003$). ③Effect of titanium particles and PDTC on the expression of MMIF protein: After experimentations, the MMIF protein contents were (3.77 ± 0.42) ng/ml (group Ⅰ), (7.59 ± 0.28) ng/ml (group Ⅱ), (4.23 ± 0.42) ng/ml (group Ⅲ) and (6.48 ± 0.5) ng/ml (group Ⅳ), respectively. The results of analysis of variance of factorial design showed that single use of 0.1% titanium particles suspension could promote the expression of MMIF protein ($F = 153.363$, $P = 0.000$), while single use of PDTC (100 μmol/ml) had no influence on the expression of MMIF protein ($F = 1.762$, $P = 0.221$). PDTC (100 μmol/ml) could depress the promotive effect of 0.1% titanium particles suspension on expression of MMIF protein ($F = 10.325$, $P = 0.012$). ④Effect of titanium particles suspension concentration on NF-κB signal pathway in macrophages: There were no statistical differences in phosphorylation p65 contents among different time points in group a ($F = 0.248$, $P = 0.904$). There were statistical differences in phosphorylation p65 contents among different time points in group b ($F = 30.217$, $P = 0.000$). Further comparison showed that phosphorylation p65 contents at 0.5 hr ((17.68 ± 0.55) pg/mg) was higher than that at 0 hr ((10.38 ± 3.18) pg/mg) ($P = 0.005$); phosphorylation p65 contents at 1 hr ((23.31 ± 2.05) pg/mg) was higher than that at 0.5 hr ($P = 0.020$); phosphorylation p65 contents at

3 hrs((31.80 ± 1.84) pg/mg) was higher than that at 1 hr(P = 0.002); phosphorylation p65 contents at 6 hrs((18.42 ± 3.61) pg/mg) was lower than that at 3 hrs(P = 0.000) and larger than that at 0 hr(P = 0.003). **Conclusion**: Wear particles from joint prosthesis can up-regulate the expression of MMIF through NF-κB signal pathway and promote inflammatory reactions around prosthesis, which leads to bone absorption and osteolysis, and leads to aseptic prosthesis loosening as a further result.

Key words Joint prosthesis; Macrophage migration-inhibitory factors; NF-kappa B; Animal experimentation

人工关节假体磨损颗粒诱导的慢性炎症反应可促进假体周围骨吸收、溶解，是人工髋关节置换术后假体无菌性松动的主要原因之一[1]。巨噬细胞游走抑制因子(macrophage migration inhibiting factor, MMIF)是炎症反应上游的调控因子，为了研究人工关节假体磨损颗粒对其表达的影响，我们进行了动物实验，现总结报告如下。

1　材料与仪器

1.1　实验材料及试剂　钛颗粒(Alfa Aesar 公司)；小鼠巨噬细胞(中国科学院细胞库)；吡咯烷二硫代氨基甲酸盐(pyrrolidine dithiocarbamate, PDTC)(Sigma 公司)；RIPA 裂解液、细胞核蛋白与细胞浆蛋白抽提试剂盒(碧云天公司)；MMIF 酶联免疫吸附剂测定(enzyme linked immunosorbent assay, ELISA)试剂盒、磷酸化 p65ELISA 试剂盒(GBD 公司)；Trizol Reagent 总 RNA 提取试剂(Invitrogen 公司)。

1.2　实验仪器　SW-CJ-1FD 超净工作台(AIR TECH 公司)；TP800 聚合酶链式反应(polymerase chain reaction, PCR)仪(TaKaRa 公司)。

2　方　法

2.1　钛颗粒悬液配制　将钛颗粒用乙醇浸泡消毒后，用无菌 PBS 配成浓度为 5% 的悬液，用鲎试剂证实其无内毒素后储存在 4 ℃冰箱备用。

2.2　小鼠巨噬细胞培养　用含有 10% 胎牛血清和 100 单位 · mL^{-1} 青霉素与 100 mg · mL^{-1} 链霉素的 DMEM 高糖培养基，在 37 ℃、5% CO_2 细胞培养箱中培养小鼠巨噬细胞。每 2 ~ 3 d 更换一次培养基，待细胞铺满培养皿底部约 80% 后按 1∶10 比例进行传代培养。将第 3 代细胞按每孔 1×10^6 个细胞接种于 6 孔板中继续用 DMEM 培养基培养，待细胞铺满培养皿底部约 80% 后换无胎牛血清的 DMEM 培养基，饥饿 24 h 后进行实验。

2.3　观察指标

2.3.1　钛颗粒浓度对 MMIF 表达的影响　将细胞分成 4 组，A 组不作任何处理，B 组加入浓度为 0.01% 的钛颗粒，C 组加入浓度为 0.05% 的钛颗粒，D 组加入浓度为 0.1% 的钛颗粒。培养 24 h 后分别用 ELISA 法和 PCR 法检测各组的 MMIF 蛋白和 MMIF mRNA 的含量。

2.3.2　钛颗粒刺激时间对 MMIF 表达的影响　将细胞分成 2 组，对照组不作任何处理，观察组加入浓度为 0.1% 的钛颗粒。分别在实验开始后 0 h、6 h、12 h、24 h 和 36 h 对 2 组的不同培养孔的细胞用 ELISA 法和 PCR 法检测各组的 MMIF 蛋白和 MMIF mRNA 的含量。

2.3.3　钛颗粒和 PDTC 对巨噬细胞表达 MMIF 蛋白的影响　将细胞分成 4 组，Ⅰ组不作任何处理；Ⅱ组加入浓度为 0.1% 的钛颗粒；Ⅲ组加入浓度为 100 μmol · mL^{-1} 的 PDTC；Ⅳ组先加入浓度为 100 μmol · mL^{-1} 的 PDTC，1 h 后再加入浓度为 0.1% 的钛颗粒。培养 24 h 后用 ELISA 法检测各组的 MMIF 蛋白含量。

2.3.4　钛颗粒浓度对巨噬细胞 NF-κB 信号通路的影响　将细胞分成 2 组，a 组不作任何处理，b 组加入浓度为 0.1% 的钛颗粒。分别在实验开始后 0 h、0.5 h、1 h、3 h 和 6 h 对 2 组的不同培养孔的细胞用 ELISA 法测定磷酸化 p65 的含量。

2.4　统计学方法　采用 SPSS17.0 软件对所得数据进行统计分析，A 组、B 组、C 组及 D 组小鼠巨噬细胞 MMIF 蛋白和 MMIF mRNA 含量的组间比较采用单因素方差分析，组间两两比较采用 q 检验；对照组和观察组小鼠巨噬细胞 MMIF 蛋白和 MMIF mRNA 含量的各时间点间的组内比较采用单因素方差分析，各时点间两两比较采用 q 检验；钛颗粒和 PDTC 对巨噬细胞表达 MMIF 蛋白的影响采用析因设计方差分析；a 组和 b 组小鼠巨噬细胞磷酸化 p65 含量的各时间点间的组内比较采用单因素方差分析，各时点间两两比较采用 q 检验。检验水准 $\alpha = 0.05$。

3　结　果

3.1　钛颗粒浓度对 MMIF 表达的影响　各组小鼠巨噬细胞 MMIF 蛋白和 MMIF mRNA 含量的组间比较，

差异均有统计学意义。A 组 MMIF 蛋白和 MMIF mRNA 的含量与 B 组比较,差异无统计学意义(P = 0.167;P = 0.223);A 组小于 C 组(P = 0.000;P = 0.004)和 D 组(P = 0.000;P = 0.000);B 组小于 C 组(P = 0.000;P = 0.025)和 D 组(P = 0.000;P = 0.000);C 组小于 D 组(P = 0.000;P = 0.000)。(表 1)

表 1　钛颗粒浓度对小鼠巨噬细胞 MMIF 表达的影响

组别	MMIF 蛋白含量(ng·mL^{-1})	MMIF mRNA 含量
A 组	3.93 ± 0.11	0.03 ± 0.01
B 组	4.21 ± 0.27	0.10 ± 0.01
C 组	6.56 ± 0.27	0.25 ± 0.09
D 组	7.82 ± 0.21	0.70 ± 0.09
F 值	207.158	64.955
P 值	0.000	0.000

3.2　钛颗粒刺激时间对 MMIF 表达的影响　对照组 MMIF 蛋白和 MMIF mRNA 含量各时点间比较,差异无统计学意义(表 2)。观察组 MMIF 蛋白和 MMIF mRNA 含量各时点间比较,差异有统计学意义(表 3),各时点间两两比较:6 h 时的 MMIF 蛋白和 MMIF mRNA 表达量与 0 h 比较,差异无统计学意义(P = 0.133;P = 0.621);12 h 的表达量大于 0 h(P = 0.000;P = 0.004);24 h 的表达量大于 12 h(P = 0.000;P = 0.003);36 h 的表达量小于 24 h(P = 0.000;P = 0.004),但高于 0 h 的表达量(P = 0.000;P = 0.003)。

3.3　钛颗粒和 PDTC 对巨噬细胞表达 MMIF 蛋白的影响　单独使用 0.1% 钛颗粒能促进巨噬细胞表达 MMIF 蛋白(F = 153.363,P = 0.000);单独使用 100 μmol·mL^{-1} 的 PDTC 对巨噬细胞表达 MMIF 蛋白无影响(F = 1.762,P = 0.221);100 μmol·mL^{-1} 的 PDTC 对 0.1% 钛颗粒促进巨噬细胞表达 MMIF 蛋白具有抑制效应(F = 10.325,P = 0.012)。(表 4)

表 2　对照组小鼠巨噬细胞 MMIF 蛋白和 MMIF mRNA 表达量随时间变化的情况

观察指标	0 h	6 h	12 h	24 h	36 h	F 值	P 值
MMIF 蛋白(ng·mL^{-1})	3.93 ± 0.11	4.01 ± 0.01	4.25 ± 0.34	4.16 ± 0.15	3.95 ± 0.87	0.310	0.865
MMIF mRNA	0.03 ± 0.01	0.03 ± 0.00	0.02 ± 0.01	0.02 ± 0.01	0.03 ± 0.01	0.065	0.991

表 3　观察组小鼠巨噬细胞 MMIF 蛋白和 MMIF mRNA 表达量随时间变化的情况

观察指标	0 h	6 h	12 h	24 h	36 h	F 值	P 值
MMIF 蛋白(ng·mL^{-1})	3.60 ± 0.40	4.14 ± 0.24	5.61 ± 0.47	7.15 ± 0.10	5.22 ± 0.85	32.857	0.000
MMIF mRNA	0.03 ± 0.01	0.08 ± 0.04	0.36 ± 0.21	0.71 ± 0.12	0.31 ± 0.18	15.621	0.000

表 4　钛颗粒和 PDTC 对小鼠巨噬细胞表达 MMIF 蛋白的影响　ng·mL^{-1}

		100 μmol·mL^{-1}PDTC		合计
		不用	用	
0.1% 钛颗粒	不用	3.77 ± 0.42	4.23 ± 0.42	4.00 ± 0.45
	用	7.59 ± 0.28	6.48 ± 0.54	7.03 ± 0.72
合计		5.68 ± 2.11	5.35 ± 1.30	5.52 ± 1.68

3.4　钛颗粒浓度对巨噬细胞 NF-κB 信号通路的影响　a 组各时点磷酸化 p65 含量比较,差异无统计学意义。b 组各时点磷酸化 p65 含量比较,差异有统计学意义,各时点间两两比较:0.5 h 磷酸化 p65 含量高于 0 h(P = 0.005);1 h 磷酸化 p65 含量高于 0.5 h(P = 0.020);3 h 磷酸化 p65 含量高于 1 h(P = 0.002);6 h 磷酸化 p65 含量低于 3 h(P = 0.000),但高于 0 h(P = 0.003)。(表 5)

表 5　小鼠巨噬细胞磷酸化 p65 含量随时间变化的情况　pg·mg^{-1}

组别	0 h	0.5 h	1 h	3 h	6 h	F 值	P 值
a 组	9.57 ± 2.38	10.58 ± 2.86	10.83 ± 1.58	10.32 ± 0.61	9.68 ± 1.39	0.248	0.904
b 组	10.38 ± 3.18	17.68 ± 0.55	23.31 ± 2.05	31.80 ± 1.84	18.42 ± 3.61	30.217	0.000

4　讨　论

人工关节假体磨损颗粒诱导的慢性炎症反应可促进假体周围骨吸收、溶解,是人工髋关节置换术后假体无菌性松动的主要原因之一。钛是人工关节假体中常见的成分之一,也是假体磨损颗粒中常见的一种成分,因此科学研究中常将钛颗粒作为假体磨损颗粒[2]来进行研究。

MMIF 是重要的炎症因子,它在炎症级联反应中

处于上游位置,能够上调其它炎症因子的合成和释放,从而调控各种炎症反应过程。MMIF 可以诱导巨噬细胞、淋巴细胞表达多种炎性因子,促进炎症进展[3]。它也可上调滑膜中成纤维细胞的基质金属蛋白酶(matrix metalloproteinase-1,MMP-1)和 MMP-3 水平,破坏细胞外基质,还可促进巨噬细胞吞噬异物颗粒[4]。

NF-κB 通常指由 p65 和 p50 组成的二聚体转录蛋白,是机体内多种炎症反应的共同通道之一[5]。NF-κB 信号通路是通过一系列的信号级联反应最终激活 IκB 激酶,使 IκB 降解,p65 和 p50 磷酸化,磷酸化的 p65 转移至细胞核内,激活特定基因的转录,最终合成各种炎症因子[6]。PDTC 是 NF-κB 的特异性抑制剂,有清除氧自由基的作用,能有效抑制 NF-κB 的活性,从而降低肿瘤坏死因子 α、白细胞介素 10、白细胞介素 8 等的 mRNA 水平,阻断通过 NF-κB 信号通路产生的生物学效应。

总之,本研究的结果提示,人工关节假体磨损颗粒可通过 NF-κB 信号通路上调炎症因子 MMIF 的表达,促进假体周围炎症反应,导致假体周围骨吸收、溶解,导致假体无菌性松动。

5　参考文献

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