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## 钛颗粒和炎症因子对人滑膜细胞MMP-2表达的影响:

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Title: Effect of titanium particles and inflammatory cytokines on MMP-2 expression in human knee joint synovial cells

作者: 符纯锋; 黄伟; 梁熙; 胡宁; 宋国立; 谢静; 陈荣富; 王春莉; 林良波; 王志强; 陈诚

重庆医科大学附属第一医院骨科; 重庆大学生物工程学院; 美国加州大学圣地亚哥分校骨科与生物工程系

Author(s): Fu Chunfeng; Huang Wei; Liang Xi; Hu Ning; K-L Paul Sung; Xie Jing; Chen Rongfu; Wang Chunli; Lin Liangbo; Wang Zhiqiang; Chen Cheng

Department of Orthopaedics, First Affiliated Hospital, Chongqing Medical University, Chongqing, 400016, China; College of Bioengineering, Chongqing University, Chongqing, 400044, China; Department of Orthopaedics and Bioengineering, University of California at San Diego, California, CA92093-0412, USA

关键词: 钛颗粒; 滑膜; 炎症因子; 基质金属蛋白酶; 无菌性松动

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摘要: 目的 研究钛颗粒和炎症因子(TNF- $\alpha$ 、IL-1 $\beta$ )对人滑膜细胞基质金属蛋白酶<sup>2</sup>(MMP-2)表达及活性的影响,探讨滑膜在钛磨损颗粒诱导的金对金人工关节假体周围骨溶解中的可能机制。方法 用钛颗粒和TNF- $\alpha$ 、IL-1 $\beta$ 处理体外培养的人膝关节滑膜细胞,处理后12、24、48、72 h收集培养上清液,用明胶酶谱法检测MMP-2的活性。结果 直径最小的钛颗粒( $\leq 5 \mu\text{m}$ )能刺激人滑膜细胞MMP-2蛋白表达达4倍于对照组;与对照组相比,钛颗粒、TNF- $\alpha$ 、IL-1 $\beta$ 及相互联合作

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用均明显增加了MMP-2的表达 ( $P<0.01$ ), 三者联合作用更明显 ( $P<0.01$ )。钛颗粒和TNF- $\alpha$ 、IL-1 $\beta$ 能够刺激人膝关节滑膜细胞增加MMP-2蛋白活性,并具有协同效应。 结论 金对金人工关节置换术后, 磨损钛颗粒可能和炎性因子协同刺激滑膜细胞, 增加骨细胞外基质的降解, 导致假体的骨性支持结构力学性能下降, 促使假体无菌性松动的发生。

**Abstract:** Objective To determine the effect of titanium (Ti) particles, and cytokines TNF- $\alpha$  and IL-1 $\beta$  on the expression and activity of MMP-2 in human synovial cells so as to explore the probable mechanism of post-operative osteolysis of metal-on-metal total joint arthroplasty in human synovial cells induced by Ti particles. Methods Human synovial cells were freshly isolated and cultured from normal knee joint synovium, and then those at passage 4 were treated with Ti particles in size of  $\geq 10$ ,  $>5$ - $<10$ , and  $\leq 5$   $\mu\text{m}$  respectively for 12, 24, 48 or 72 h. TNF- $\alpha$ , and IL-1 $\beta$  at different doses were used to treat the cells in presence or absence of Ti particles for above time periods. Gelatin zymography was performed to detect the activity of MMP-2 in the cell supernatant. Results Compared with the cells without any treatment, the expression level of MMP-2 treated by Ti particles in size of  $\leq 5$   $\mu\text{m}$  was significantly increased by 4 times, that treated by Ti particles, TNF- $\alpha$ , and IL-1 $\beta$  respectively or combined of any 2 agents were also increased significantly ( $P<0.01$ ), and that treated by the combination of the 3 agents