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论文

单剂HBsAg-PLGA控释疫苗微球小鼠体内免疫学研究

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摘要：

目的研究小鼠皮下注射重组乙型肝炎病毒表面抗原(HBsAg)-乳酸/乙醇酸共聚物(PLGA)微球后的体内抗体应答水平和免疫学机制。方法采用复乳法制备疫苗微球后，单剂注射到BALB/c小鼠皮下，在一定时间内检测全抗体、IgG抗体亚型及细胞因子的应答水平。结果HBsAg-PLGA微球在小鼠体内主要引发体液免疫应答；其中单剂注射HBsAg-PLGA50/50-COOH微球在免疫早期产生较高免疫表达，6周后降低，全抗体水平显著低于常规铝佐剂疫苗(P<0.01)；分别单剂注射HBsAg-PLGA50/50微球及HBsAg-PLGA75/25微球后产生的免疫应答在18周内与铝佐剂疫苗相当(P>0.05)。结论PLGA微球作为乙肝疫苗的长效缓释可生物降解载体，具有一定潜在优势。

关键词： 乙肝病毒表面抗原 乳酸/乙醇酸共聚物微球 控释 单剂疫苗 免疫学

Immunogenicity of single-dose HBsAg-PLGA controlled release microspheres in mice

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Abstract:

AimTo investigate the level of immune response and the immune mechanism of the single-dose hepatitis B surface antigen (HBsAg)-poly (*d,l*)-lactide-co-glicolide acid (PLGA) microspheres in BALB/c mice. MethodsThree kind of HBsAg-PLGA microspheres, HBsAg-PLGA50/50-COOH microspheres, HBsAg-PLGA75/25 microspheres and HBsAg-PLGA50/50 microspheres, were prepared by double emulsion microencapsulation technique used three kinds of PLGA with different L/G ratio. The single-dose of HBsAg-PLGA microspheres was subcutaneously injected into BALB/c mice at the dose of 7.5 μg HBsAg per mouse. The conventional aluminum-adjuvant vaccine was subcutaneously injected at 0, 1 and 2 month as positive control. In certain time interval, the induced immune level of total antibody was detected by enzyme linked immunosorbent assay (ELISA). For subclass of IgG antibody and cytokines studies, the dose of HBsAg was 2.5 μg per mouse. ResultsThe HBsAg-PLGA microspheres could successfully induce a humoral immune response in BALB/c mice. Compared with the conventional aluminum-adjuvant vaccine, the antibody response of the HBsAg-PLGA50/50-COOH microspheres was significantly lower than the group received three injections of aluminum-adjuvant vaccine (P<0.01) except for a higher priming response during the early 6 weeks. The results were ascribed to the relatively rapid degradation charactics of PLGA50/50-COOH polymer. The immune response for the HBsAg-PLGA50/50 microspheres and HBsAg-PLGA75/25 microspheres were comparable to the group administered with aluminum-adjuvant vaccine (P>0.05) which was due to the sustained degradation of PLGA50/50 and PLGA75/25 polymer. ConclusionThe HBsAg-PLGA microsphere is a promising candidate for the controlled delivery of a vaccine which does not require multiple injections.

Keywords: poly(*d,l*)-lactide-co-glicolide acid microspheres controlled release single dose vaccine immunogenicity hepatitis B surface antigen

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