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以Pam2CSK4为佐剂的减毒活疫苗D39△CPS-TA可保护幼鼠抵抗肺炎链球菌感染

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Title: A live attenuated vaccine D39△CPS-TA with Pam2CSK4 as adjuvant elicits protection against pneumococcal infection in infant mice

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关键词：肺炎链球菌；疫苗；佐剂；安全性

Keywords: *Streptococcus pneumoniae*; mucosal adjuvant; vaccine; safety

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摘要：

目的　评价新型减毒肺炎链球菌疫苗株D39△CPS-TA与佐剂Pam2CSK4联用时在幼鼠模型中的免疫保护效果及安全性。　方法　D39△CPS-TA、D39△CPS-TA+霍乱毒素（cholera toxin，CT）、D39△CPS-TA+Pam2CSK4经鼻免疫C57/BL6幼鼠，每周1次，共4次。末次免疫后1周，酶联免疫吸附法（ELISA）测定抗体及细胞因子水平。末次免疫后2周，采用19F型和2型肺炎链球菌攻毒，观察免疫保护效果。生存率实验评价D39△CPS-TA的安全性；从体质量变化和肺组织病理学改变2个角度，评价Pam2CSK4的安全性。　结果　D39△CPS-TA+Pam2CSK4免疫幼鼠可有效引起抗原特异性IgG升高，其中以IgG1为主；能有效促进IFN-γ、IL-4、IL-10和IL-17A水平升高；能有效抵抗19F型肺炎链球菌在小鼠鼻咽部定植；能有效提高小鼠经2型肺炎链球菌攻毒后的生存

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率。高剂量D39△CPS-TA可被幼鼠耐受，Pam2CSK4较CT安全。　结论　D39△CPS-TA+Pam2CSK4经鼻免疫幼鼠可安全有效地刺激其体液免疫和细胞免疫，进而对抗肺炎链球菌感染。

Abstract: Objective To evaluate the safety and efficacy of a novel pneumococcal attenuated vaccine strain D39△CPS-TA when delivered intra-nasally with adjuvant Pam2CSK4 in a infant mice model of pneumococcal infection. Methods C57/BL6 infant mice were intra-nasally administrated on days 0, 7, 14 and 28 with 1 dose of D39△CPS-TA+ cholera toxin (CT) or Pam2CSK4, with D39△CPS-TA alone or with one of selected adjuvant alone. In 1 week after the last immunization, antibodies and cytokines levels were measured by enzyme-linked immunosorbent assay (ELISA). In 2 weeks after the last immunization, mice were challenged with pneumococcal serotype 19F or 2 and protective effects were observed. Furthermore, the safety of D39△CPS-TA was measured by a survival experiment and the safety of Pam2CSK4 was evaluated by monitoring body weight and pathological analysis. Results Intranasal immunization with D39△CPS-TA+Pam2CSK4 in infant mice induced IgG1-based rise in antigen-specific IgG, increase of IFN-γ, IL-4, IL-10 and IL-17A, clearance of nasal colonization of pneumococcal serotype 19F and protective effects against lethal infection of pneumococcal serotype 2. High dose of D39△CPS-TA was tolerated by infant mice and Pam2CSK4 was safer than CT. Conclusion Intra-nasal immunization with D39△CPS-TA+Pam2CSK4 in infant mice stimulates humeral and cellular immune responses safely and effectively, and protects mice against pneumococcal infection.

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