INTERNATIONAL SYMPOSIUM ON INFECTIOUS DISEASES AND VACCINES

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Culture filtrateproteins from Mycobacterium bovisBCG act as adjuvants for cytotoxic T lymphocyte induction

Abstract: Mycobacterium bovis bacilli Calmette-Guérin (BCG) is a licensed vaccine against tuberculosis (TB). Although this bacterium has been used as an effective vaccine against infant TB for a long time, its efficacy in adult pulmonary TB has been limited. This has rendered it ineffective in the global fight against TB. It requires live bacteria to be effective, possibly because actively secreted proteins play a critical role in inducing anti-TB immunity. BCG also functions as an effective adjuvant. Moreover, the effects of BCG components as adjuvants are not comparable with those of live BCG, which is practically used in cancer immunotherapy. However, the role of the secreted proteins in anticancer immunity remains unclear. To understand mycobacterial secreted proteins' function, we investigated immuneresponses to BCG culture filtrate proteins (CFP).

Although purifiedprotein derivatives did not induce antigen-specific CD8+ T cell, CFP strongly induced both antigen-specific CD4+ and CD8+ T cells, which may be functional cytotoxic T lymphocytes (CTLs). In this study, we clearlydemonstrated that CFP acts as an adjuvantfor CTL induction against specificco- administered proteins and propose CFP as a new protein adjuvant. The CTL response shows potent anticancer effects in mice. A detailed mechanism analysis is required to better understand the CTL adjuvanticity of the CFP. However, CFP is a mixture of >100 proteins. Therefore, the verification of CTL adjuvanticity for each protein and identification of the "key protein" warrant further study. Several candidateproteins were obtainedas active components which showed enhancement of ovalbumin-specific CTL induction. These proteins could be developed as a novel CTL adjuvant for production of vaccines against various infectious diseases and cancers where antigen-specific CTL function is involved.

Keywords: BCG, culturefiltrate proteins, CTL, anti-cancer immunity

Biography: I started mycobacterial research in 1986 and first I cloned alpha antigen (antigen 85B) gene from BCG (J. Bacteriol., 1988). Based on it, I established a foreign antigen secretion system in BCG vaccine strain (Infect. Immun., 1990). This was the first report on a recombinant BCG secreting exogeneous antigen. By using this system, Ihave been working on anti-HIV vaccine development since 1994, and developed a prime-boost vaccine using BCG and vaccinia vectors (J. Virol., 2005, J. Virol., 2021). Currently, I'm working on anti-TB vaccine development using the CFP adjuvant (Front. Immunol., 2023) in IVReD, Hokkaido University.

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