



Title	Hydroxypropyl Cellulose Enhances Immune Responses to the Current Seasonal Influenza Vaccine in Mice
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Citation	大阪大学, 2026, 博士論文
Version Type	
URL	https://hdl.handle.net/11094/105740
rights	
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論文内容の要旨
Synopsis of Thesis

氏名 Name	KAEWAROON Nantaporn
論文題名 Title	Hydroxypropyl Cellulose Enhances Immune Responses to the Current Seasonal Influenza Vaccine in Mice (ヒドロキシプロピルセルロースによる現行季節性インフルエンザワクチンの免疫応答増強効果)
論文内容の要旨 〔目的(Objective)〕 1) To assess the potential adjuvant ability of hydroxypropyl cellulose for the current seasonal influenza split HA vaccine. 2) To evaluate the protective and cross-protective efficacy of hydroxypropyl cellulose adjuvant against homologous and heterologous virus (A/H1N1 pdm09) challenge. 〔方法ならびに成績(Methods/Results)〕 Hydroxypropyl cellulose (HPC) is an injectable excipient that has been reported to have adjuvant ability for split influenza HA vaccines for the 2015/2016 and 2016/2017 seasons in the previous screening report in 2019. However, antigenic drift of the influenza virus and mutations in the HA segment, a major antigen of the influenza vaccine, can lead to reduced vaccine efficacy. Therefore, re-assessment of the remaining adjuvant potential, as well as evaluation of cross-protective efficacy, is necessary. In this study, I evaluate the adjuvanticity of HPC and its efficacy in combination with the quadrivalent split HA vaccine for the 2023–2024 influenza season, which contains the current strain of influenza A/H1N1 pdm09 and three other strains of influenza viruses. Using a mouse model, I performed immunogenicity studies and assessed protective and cross-protective efficacy in BALB/c mice following challenge with homologous and heterologous H1N1pdm09 virus strains. The results of immunization in BALB/c suggested that HPC in combination with the HA vaccine generated higher virus-specific IgG antibody titers compared to the vaccine alone. The level of virus-specific IgG induction by the HPC-adjuvanted vaccine was comparable to that of the alum-adjuvanted vaccine, even though the HPC ratio in the vaccine combination was five-fold lower than alum. The adjuvanted vaccine provided complete protection against homologous challenge and enhanced viral clearance from respiratory organs. Notably, both HPC- and alum-adjuvanted vaccines demonstrated cross-protective efficacy against heterologous H1N1pdm09 virus challenge, improving survival rates compared to the vaccine alone. 〔総括(Conclusion)〕 This study reveals that hydroxypropyl cellulose (HPC) has adjuvant potential for the current seasonal influenza vaccine (2023–2024 season) and effectively enhances vaccine-induced humoral immune responses when combined with the split HA vaccine. Overall, the HPC-adjuvanted vaccine showed immunogenicity and protective efficacy comparable to those of the alum-adjuvanted vaccine. The HPC adjuvanted vaccine provided complete protection in BALB/c mice against homologous challenge and conferred cross-protective efficacy against heterologous H1N1pdm09 virus challenge. These findings indicate that HPC can enhance both strain-matched and cross-reactive influenza vaccine efficacy. HPC enhances vaccine efficacy, although the precise mechanism underlying its adjuvant activity remains unclear and requires further investigation. To clarify the adjuvant potential of HPC for the HA vaccine, future evaluation including dose optimization and assessment of cell-mediated immunity, including T cell responses, should be addressed.	

論文審査の結果の要旨及び担当者

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論文審査の結果の要旨 本論文は、毎年世界的な流行を引き起こすインフルエンザに対し、既存の不活化スプリットHAワクチンの効果向上を目的として、新規アジュバント候補であるヒドロキシプロピルセルロース（HPC）の有効性を検討した研究である。申請者は、2023-2024シーズンの4価スプリットHAワクチンを用い、マウスモデルにおいて免疫原性および感染防御効果を詳細に解析した。その結果、HPC併用ワクチンは、ワクチン単独と比較してウイルス特異的IgG抗体価を有意に増強し、ワクチン株と一致するウイルスに対して完全な防御効果を示した。さらに、抗原的に異なるH1N1pdm09ウイルスに対しては限定的ながらも防御効果が認められ、生存率の改善が示された。本研究は、安全性の高い既存添加物を用いた新たなアジュバント戦略を提示するものであり、季節性インフルエンザワクチンの有効性向上に資する重要な知見を提供している。以上より、本論文は博士（医学）の学位授与に値するものと認める。				