Polymers as Vaccine Adjuvants and Vaccine Agents against Tuberculosis

Siwarutt Boonyarattanakalin[1,*], Marisa Ponpuak[2], Harin Leelayuwapan[3], Chakree Wattanasiri[3], Haris Leelayuwapan[3], Warunda Bunthitsakda[1], Niwat Kangwanrangsan[4], Runglawan Chawengkirttikul[2], Jiraporn Paha[2], Kanokthip Boonyarattanakalin[5] and Somsak Ruchirawat[3]

[1]*School of Bio-Chemical Engineering and Technology, Sirindhorn International Institute of Technology, Thammasat University, Pathum Thani 12121, Thailand*
[2]*Department of Microbiology, Faculty of Science, Mahidol University, Bangkok 10400, Thailand*
[3]*Program in Chemical Biology, Chulabhorn Graduate Institute and the Center of Excellence on Environmental Health, Toxicology and Management of Chemicals, 54 Kamphaeng Phet 6, Talat Bang Khen, Lak Si, Bangkok 10210, Thailand*
[4]*Department of Pathobiology, Faculty of Science, Mahidol University, Bangkok 10400, Thailand*
[5]*College of Nanotechnology, King Mongkut's Institute of Technology Ladkrabang, Ladkrabang, Bangkok 10520, Thailand*

[*]*corresponding author, E-mail: siwarutt@siit.tu.ac.th; siwarutt.siit@gmail.com*

Abstract

Multivalency bindings are a key feature of interactions in biological systems. The interactions between carbohydrates and proteins are not as strong as typical protein-protein interactions. Thus, the interactions rely essentially on the multivalency bindings. The unique biopolymers – polysaccharides found on the surfaces of pathogenic bacteria are fruitful sources of antigenic compounds that may potentially be used as immune modulators to serve as vaccine agents and/or vaccine adjuvants. The extracted polysaccharides found on the outer surface of *Mycobacterium tuberculosis* (Mtb) are strong immune modulators. However, the applications of these biopolymers as a vaccine or vaccine adjuvant are limited by tedious polysaccharide isolation methods from Mtb culture, low extraction yields, and uncertain chemical identities. Genetic engineering to overexpress the polysaccharide is difficult because saccharide biosyntheses are post-translation. A traditional stepwise synthesis for the polysaccharide is almost impossible because of the macromolecular nature of the polysaccharides. The development of controlled polymerization is critically essential to practically prepare such polysaccharides. Therefore, we have aimed to develop a rapid synthetic protocol to fill up this knowledge gap. In turn, these biopolymers would be available for immunological studies and we will be able to elucidate the profound interactions between these molecules and the human immune system. Here, we report the development of controlled polymerization to practically synthesize the biopolymers. The synthetic polymers were evaluated for its immunological properties *in vitro* and *in vivo*. Systemic inflammation and the promotion of innate immune response were observed in macrophages treated with the synthetic polysaccharides. *In vivo* evaluation of IFN-γ, IL-2, and TNF-α production in mice pre-immunized with the synthetic glycan protein conjugate also indicated the enhancements of the immunological responses.

Keywords: controlled polymerization, rapid synthesis, glycoconjugate vaccine, vaccine adjuvant, mannan.