Accepted Manuscript

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PII: S1001-8417(17)30389-3
DOI: http://dx.doi.org/10.1016/j.cclet.2017.09.047
Reference: CCLET 4253

To appear in: *Chinese Chemical Letters*

Received date: 30-6-2017
Revised date: 18-8-2017
Accepted date: 21-9-2017

Please cite this article as: Zhifang Zhou, Han Lin, Chen Li, Zhimeng Wu, Recent progress of fully synthetic carbohydrate-based vaccine using TLR agonist as build-in adjuvant, Chinese Chemical Lettershttp://dx.doi.org/10.1016/j.cclet.2017.09.047

Review

Recent progress of fully synthetic carbohydrate-based vaccine using TLR agonist as build-in adjuvant

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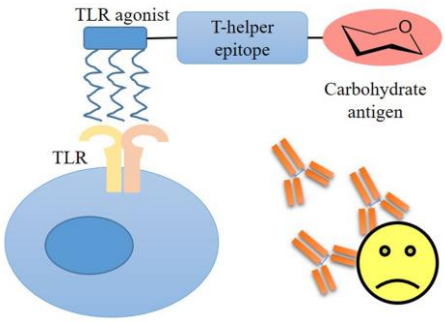
Graphical Abstract



This review highlights recent advances in developing full synthetic carbohydrate antigen based vaccines, with an emphasis on the structure-activity relationships that provide a primary basis for future vaccine design and immunotherapy developing.

ARTICLE INFO

Article history:
Received 30 June 2017
Received in revised form 18 August 2017
Accepted 19 September 2017
Available online

Keywords:
Fully synthetic vaccine
TLR agonist
Build-in adjuvant
Carbohydrate-based vaccine
TACAs

ABSTRACT

Fully synthetic vaccine, in which one or multi-molecular antigens are conjugated to a synthetic carrier with well-defined chemical structure, is a new direction to develop carbohydrate-based vaccine against cancer and pathogens. Toll like receptor (TLR) agonists with the ability to stimulate immune response have been widely investigated and been applied as build-in adjuvants to construct fully synthetic vaccines. In particular, remarkable progress has been achieved in recent years in the development of vaccines constructed with the agonists of TLR1/2, TLR2/6 and TLR4 and tumor-associated carbohydrate antigens (TACAs). These di-, tri- or multi-component vaccine candidates showed attractive immunological properties. This review highlights recent advances in developing full synthetic carbohydrate antigen based vaccines, with an emphasis on the structure-activity relationships that provide a primary basis for future vaccine design and immunotherapy developing.

1. Introduction

Since Edward Jenner discovered that cowpox could prevent human from the threat of smallpox infection, vaccine has become one of the most important and successful strategy to protect against infectious diseases [1]. Currently, the licensed vaccines in clinical are made from attenuated or killed pathogens, toxoids, proteins or polysaccharide antigens which are isolated from pathogens, and so on [2]. Despite the great achievement in vaccines, there are still some concerns and issues about them, such as limited immunological efficacy in certain populations, safety issues and lacking vaccines for some serious diseases. Among the potential immune targets, carbohydrate antigens, usually abundantly exposed on the cell surface of pathogens with highly conserved and specific chemical structures, are attractive and important targets for the development of vaccines and immunotherapy [3].

Typically, carbohydrate antigens alone only induce short-term and T cell independent immunity, especially in infants and children [3]. To overcome this problem, the conventional approach is coupling carbohydrate antigens to carrier proteins as conjugate vaccines. In this way, the immune responses induced against carbohydrate antigens can be switched to T cell dependent immunity that is more potent, functional and with immune memory [4]. This strategy is quite straightforward and has been widely applied in licensed vaccines, such as the vaccines against *Haemophilus influenzae* type b (Hib) and *Neisseria meningitidis* A, C, Y and W-135. However, the glycoprotein-based vaccine strategy still has drawbacks. One of them is that the strong immunities against the carrier proteins may

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