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Review

The key role of rubella virus glycoproteins in the formation of immune response, and perspectives on their use in the development of new recombinant vaccines

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ABSTRACT

Rubella is a highly contagious viral disease which is mostly threatens to women of reproductive age. Existent live attenuated vaccines are effective enough, but have some drawbacks and are unusable for a certain group of people, including pregnant women and people with AIDS and other immunodeficiency. Thereby the development of alternative non-replicating, recombinant vaccines undoubtedly is needed. This review discusses the protein E1 and E2 role in formation of immune response and perspectives in development of new generation recombinant vaccines using them.

1. Introduction

Rubella is a highly contagious viral disease. The most significant consequence of rubella infection is the transfer of rubella virus to an unborn fetus, where significant birth defects often result. The death of the fetus or congenital malformations, which are known as congenital rubella syndrome (CRS), can occur in 80–85% of cases of rubella virus infection during the first trimester of pregnancy. Worldwide, it is estimated that more than 100,000 children in developing countries are born with CRS each year [1].

In recent times, due to the development and application of highly effective vaccines, there has been a major reduction in the risk of rubella virus infection. However, the rubella vaccine used nowadays consists of an attenuated strain of rubella virus that cannot be recommended during pregnancy, despite the absence of adverse effects in babies born to mothers who were inadvertently vaccinated with the live-attenuated vaccine [2–4]. We have to take into account that live attenuated vaccines containing replicating virus have the risk of reverting back to their virulent form and cause the disease [5]. Vaccination of adult women has been associated with chronic arthritis which is thought to be due to persistence of the vaccine virus [4,6]. The rate of vaccine-associated chronic arthritis appears to be extremely low [7–9], however chronic arthritis following rubella vaccination is included in the National Vaccine Injury Compensation Program [10]. Furthermore another complications of vaccination may occur such as post-infections encephalopathy, Guillain–Barré syndrome, haematological complications: transient thrombocytopenia, purpuric rash, haemolytic anemia [4,11–13]. Additionally, AIDS children and children with other immunodeficiencies also cannot be vaccinated with the current attenuated rubella virus vaccine, and can suffer severely from rubella infection [14]. The availability of a nonreplicating vaccine would offer an alternative that potentially should not be associated with different complications and limitations including the drawbacks of human cell line-derived vaccines such as adverse and allergic reactions and also strict storage conditions. Therefore, the development of a new generation of safe vaccines is needed.

During viral infection, antibodies specific to three structural proteins of the rubella virus (capsid protein (C protein), and glycoproteins E1 and E2) develop. Capsid protein is an internal protein not normally exposed to the immune system in its native form. In the natural infection the protective immune response is predominantly directed toward the glycoproteins [15], mainly against the glycoprotein E1. However, antibodies to glycoprotein E1 persist within the infected person for decades, and progressively increase their affinity [16]. For a period of a month, antibodies to

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