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Cyclic-di-AMP: a promising adjuvant for neonatal vaccines

Keywords: adjuvant, cyclic di-nucleotides (CDN), cyclic di-AMP (CDA), vaccine, neonatal vaccine

INVENTION NOVELTY

Cyclic dinucleotide compounds (CDNs), specifically c-di AMP (CDA), have been identified as being especially useful as adjuvants in therapeutic or prophylactic vaccines including usage in neonates and infants. CDNs are bacterial second messengers serving as signaling molecules sensed by the immune system as a danger signal in eukaryotic organisms. Thereby, CDNs induce or promote an immune response, allowing the utilization of these molecules as potent activators of the immune system increasing reactogenicity and immunogenicity of vaccines, especially for highly vulnerable newborns.

VALUE PROPOSITION

With 5.5 million neonatal classic and opportunistic infections registered every year, the immunization of newborns remains a challenge. Since especially young infants lack previous antigen exposure the effectiveness of T-cell responses is limited, resulting in impaired responses to many stimuli. On the other hand, due to higher permeability of barriers like skin and mucosae to vaccine antigens and the underdevelopment of the associated microbiota in neonates, the neonatal period of life is a window of opportunity for immunizations and a key strategy to overcome morbidity and mortality of newborns. Few vaccines for newborns have been approved; however, these comprise aluminium salts as adjuvants mediating insufficient immunization. Thus, new adjuvants tailored for neonatal and infant vaccination are urgently needed.

Neonatal vaccination.

TECHNOLOGY DESCRIPTION

Co-administration of CDNs evoke antigen-specific immune responses superior in eliciting T helper 1 (Th1) and T follicular helper (TfH) cytokines. Moreover, the importance of the CDA-triggered type I interferon (IFN-α/β) response on B cell activation and subsequent antigen-specific IgG production was observed in newborn mice. Furthermore, neonatal priming is beneficial when CDA is used as vaccine adjuvant. Thus, CDA is a potent and versatile adjuvant, capable of promoting both humoral and cellular immunity in neonates.

COMMERCIAL OPPORTUNITY

The technology is offered for co-development or in-licensing.

DEVELOPMENT STATUS

The data were obtained with neonatal human cord blood cells and in newborn mice. CDA is in late preclinical development as adjuvant for various vaccines and will be tested in a first phase I clinical trial probably at the beginning of 2021.

PATENT SITUATION

Priority application was filed in August 2019 (EP19193982.6) followed by an international PCT-application filed 2020 (WO2021/038022). National/regional applications are pending in Europe, USA, Canada, Australia, India and China.

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FURTHER READING

Lirussi et al. 2021. Cyclic di-AMP: a promising adjuvant candidate for the development of neonatal vaccines. Pharmaceutics 2021; 13 (2):188. DOI: 10.3390/pharmaceutics13020188.

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