

# Cyclic Amp-Elevating Drugs As Adjuvants - 2014-084

Tech ID: 25178 / UC Case 2011-208-0

## BACKGROUND

Effective adjuvants enhance antigen immunogenicity and/or modulate the type of immunity (e.g., humoral vs. cellular immune response), and, in theory, an optimal antigen-adjuvant combination should activate the both arms of the immune system (innate and adaptive immunity). Different adjuvants work via different mechanisms and, ultimately, the best adjuvant for any specific vaccine will be chosen on the basis of compatibility with the delivery route (e.g., systemic vs. mucosal), ability to provoke the desired immune response (e.g., humoral vs. cellular immunity), and relevance to a particular stage of the required anti-microbial protection (e.g., preventive vs. therapeutic immunity). One way to achieve these diverse goals is to use a combination of complementary, synergistic adjuvants and this is one current practice. However, an adjuvant that could trigger the immunomodulatory cascade upstream of current options could simplify the design of safe and effective vaccines and revolutionize modern day vaccinations.

## TECHNOLOGY DESCRIPTION

In foundational studies, UC researchers observed that cAMP production in a critical subpopulation of cells (i.e., dendritic cells) selectively activated cAMP/PKA pathway. This work has now been applied to the design and testing of a "universal vaccine" formulation, comprising an antigen of interest with a class of Th17 adjuvants and a carrier or additional adjuvant such as alum. The ability to target to the critical cell type enables a powerful adjuvant with improved toxicity profiles. Additionally, the focus on small (<1,000 Da MW), drug-like and non-immunogenic molecules should eliminate immunogenicity problems associated with bacterial polypeptides and biologic agents that raise cAMP levels via an irreversible mechanism.

## APPLICATIONS

This formulation of antigen-adjuvant-carrier is envisioned for use in vaccines that are:

- ▶ Delivered systemically or mucosally
- ▶ Therapeutic or prophylactic.

## ADVANTAGES

Where current adjuvants act by one or several of the following mechanisms, the Th17-class of adjuvants mediate all of the following:

- ▶ Increase antigen transport and uptake (phagocytosis) by antigen-presenting cells
- ▶ Provide a long-lasting depot effect, i.e., antigenic reservoir for slow release
- ▶ Trigger efficient antigen processing and presentation
- ▶ Induce co-stimulatory molecules and cytokine release by dendritic cells (necessary for the activation of naïve T cells)
- ▶ Provoke additional activation pathways (e.g., pattern-recognition receptors such as Toll-like receptors and the unfolded protein response pathway)

These features combine with the simplicity of small molecules and the design of here-to-fore dissimilar vaccines for diverse applications.

## STATE OF DEVELOPMENT

Mice have been immunized and then early indicators of immune response assessed (IL-17 response and titer of Ab vs. immunogen (Anti-OVA IgG)).

## INTELLECTUAL PROPERTY INFO

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## OTHER INFORMATION

### KEYWORDS

Cyclic AMP, cAMP, adjuvant, immune, immunity, vaccine, vaccinations, therapeutic vaccine, prophylactic vaccine

### CATEGORIZED AS

- ▶ **Biotechnology**
- ▶ Health
- ▶ **Medical**
- ▶ Vaccines

### RELATED CASES

2011-208-0, 2013-334-0, 2013-282-0

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## RELATED MATERIALS

- ▶ E. Raz (2013) A Novel Approach to Explore Th2-Biased Immunity: Implications for Asthma and Allergic Diseases, Manuscript in preparation (available under confidentiality)
- ▶ Lee J, et al., Cyclic AMP concentrations in dendritic cells induce and regulate Th2 immunity and allergic asthma, Proc Natl Acad Sci U S A. 2015, 3;112(5):1529-34.
- ▶ González-Navajas JM, et al., The immediate protective response to microbial challenge, Eur J Immunol. 2014, 44(9):2536-49. Review.
- ▶ Li, X., et al., Divergent requirement for Gas and cAMP in the differentiation and inflammatory profile of distinct mouse Th subsets, J Clin Invest., 2012, 122(3):963-73.
- ▶ Pulendran B, et al., Programming dendritic cells to induce T(H)2 and tolerogenic responses. Nat Immunol, 2010, 11: 647-55
- ▶ Datta SK, et al., Mucosal adjuvant activity of cholera toxin requires Th17 cells and protects against inhalation anthrax. Proc Natl Acad Sci U S A, 2010, 107: 10638-43

## PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Published Application	2014059147	04/17/2014	2011-208

## RELATED TECHNOLOGIES

- ▶ Novel Murine Model of Asthma Identifies Methods to Antagonize Th2 Response, Asthma and Allergic Disease
- ▶ Finding the Balance: Modulating cAMP Levels to Treat Th2/Th17-mediated Immunopathologies - 2013-282

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