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Malaria Vaccines: TBV Antigens as Conjugates with Alternate Carriers

Project Number	Contact PI/Project Leader	Awardee Organization
1ZIAAI001008-14	DUFFY, PATRICK	NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Description

Abstract Text











In FY2020, LMIV scientists contributed to 1 publication on conjugate or particle vaccines, and we describe progress reported in those manuscripts here: 1. In published work, we observed that alternate carriers increase antibody titers of Pfs25 & Pfs230 above benchmark EPA carrier; TBV antigens conjugated to TT and CRM197 induce highest functional activity; liposomal GLA-LSQ adjuvant further enhances titers and Th1 isotype switching. Scaria PV, et al. **Vaccine**. 2020;38(34):5480-5489.) Based on the enhanced immune response observed in these studies, we selected an E. Coli produced CRM197 (EcoCRM from FinaBiosolutions) as an alternate carrier for Pfs230. Currently working on establishing a collaborative agreement with FinaBiosolutions for the use of EcoCRM, process development for scaled up synthesis of Pfs230-EcoCRM conjugate, evaluation of the conjugate in NHP studies and product development activities that enable its clinical testing. In unpublished work, we report below our progress on other ongoing projects: Further evaluation of OMPC as a delivery platform for Transmission Blocking **Vaccine** antigens: In FY2020, we continued the evaluation of OMPC as a delivery platform for TBV antigens. In our previous report, we described a qualitatively different, Th1-biased immune response was observed for OMPC conjugates as opposed to a Th2 response of EPA conjugates. Based on these findings, we have initiated evaluation of OMPC conjugates of Pfs25 and Pfs230 in nonhuman primates to determine their efficacy in this model and to evaluate the duration of immune response. In these studies, Pfs230 conjugates showed superior transmission blocking activity compared to Pfs25 conjugates. In addition, Pfs230 - OMPC conjugates in Alum adjuvant showed a durable immune response with high antibody titer and functional activity, equivalent to EPA conjugate of Pfs230 formulated in a potent liposomal adjuvant. Evaluation of **mRNA** technology for malaria antigens: In FY2020, we continued the collaboration with CureVac, Germany to test the immunogenicity of LMIVs malaria antigens in CureVacs RNaive technology platform. Antigen delivery using **mRNA** has generated considerable excitement in the **vaccine** field as a technology that can rapidly generate **vaccine** candidates for clinical testing. This technology is now being tested in a number of clinical trials by CureVac and Moderna Therapeutics; both have their proprietary technologies for designing and manufacturing potent mRNAs for **vaccine**. We worked with CureVac to construct **mRNA** for our TBV and PMV antigens. In FY2019, CureVac generated a series of **mRNA** constructs for LMIVs TBV and pregnancy malaria antigens and tested their expression in mammalian cells. As part of this continuing collaboration, mouse immunogenicity studies have been initiated at LMIV to test the immunogenicity and functional activity of these **mRNA** constructs. Needle-free **vaccine** delivery: In FY2020, we completed the collaboration established with Takeda Pharmaceuticals, Japan to evaluate their proprietary Microneedle Patch delivery technology for delivery of our conjugate immunogens for transmission blocking **vaccine**. Takedas dissolving microneedle is a technology for **vaccine** delivery that has a number of attractive features useful for malaria vaccines. Administration of microneedle patches do not require a skilled medical professional or can be self-administered. It avoids needle use by eliminating accidental needle injuries and pain associated with needle delivery. It also does not require cold-chain transport and storage, thereby reducing the cost of mass immunization campaigns. These patches were evaluated in mouse immunogenicity studies at LMIV and showed a poor performance based on antibody responses. Based on these results, Takeda is considering manufacturing issues that may have contributed to poor immunogenicity.

Public Health Relevance Statement

Data not available.

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1ZIAAI001008-14		DUFFY, PATRICK			NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES		
Project Terms							
Adjuvant	Agreement	Aluminum	Antibody Response				
Antibody titer measurement		Antigens	Area	Benchmarking		Clinical Trials	
Cold Chains	Collaborations	Development		Escherichia coli		Evaluation	
Formulation	Germany	Goals	Immune response				
Immunoglobulin Class Switching		Injury	Japan	Liposomes		Malaria	
Malaria Vaccines	Mammalian Cell		Manuscripts		Mass Immunization		Medical
Membrane Proteins		Messenger RNA		Modeling	Mus	Needles	
Neisseria meningitidis		Pain	Parasites	Performance			
Read More							

Details

Contact PI/ Project Leader		Other PIs	Program Official
Name		Not Applicable	Name
DUFFY, PATRICK 			Contact
Title			Email not available
Contact			
Email not available			
Organization			
Name		Department Type	State Code
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES		Unavailable	Congressional District
City		Organization Type	
Country		Unavailable	
Other Information			
FOA		Administering Institutes or Centers	Project Start Date
Study Section		NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES	Project End Date
Fiscal Year	Award Notice Date	DUNS Number CFDA Code	Budget Start Date
2020			Budget End Date
Project Funding Information for 2020			
Total Funding		Direct Costs	Indirect Costs
\$3,037,907		\$0	
Thank you for your feedback!			

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Funding ID		PI Total Cost by IC	Category
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES		\$3,037,907	Biotechnology; Emerging Infectious Diseases; Immunization; Infectious Diseases; Malaria; Malaria Vaccine; Orphan Drug; Prevention; Rare Diseases; Vaccine Related; Vector-Borne Diseases;

Sub Projects

No Sub Projects information available for 1ZIAAI001008-14

Publications

No Publications available for 1ZIAAI001008-14

Patents

No Patents information available for 1ZIAAI001008-14

Outcomes

The Project Outcomes shown here are displayed verbatim as submitted by the Principal Investigator (PI) for this award. Any opinions, findings, and conclusions or recommendations expressed are those of the PI and do not necessarily reflect the views of the National Institutes of Health. NIH has not endorsed the content below.











No Outcomes available for 1ZIAAI001008-14

Clinical Studies

No Clinical Studies information available for 1ZIAAI001008-14

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1ZIAAI001008-14	DUFFY, PATRICK	NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

History

No Historical information available for 1ZIAAI001008-14

Similar Projects

No Similar Projects information available for 1ZIAAI001008-14

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