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**Recombinant Buffalo Antibodies as a Resource for  
Diagnostics and Therapeutics: Proof-of-Concept and  
Applications in Schistosomiasis**

**GRANTEE:** University of the Philippines Los Baños (UPLBFI)

**PRINCIPAL INVESTIGATOR:** Dr. Rina B. Opulencia

**US UNIVERSITY PARTNER:** University of Illinois, Chicago (UIC)

**GRANT PERIOD:** September 1, 2015, to December 15, 2016

**CONTRACT AMOUNT:** Php 4,699,951 (approximately USD100,000)

**Researchers aid in developing a vaccine**

*Schistosomiasis*, or snail fever, is the second-most devastating of all human diseases caused by parasites, surpassed only by Malaria. It is caused by parasitic flatworms (*Schistosoma*) and acquired when people come into contact with fresh water infested with the larval forms of the parasitic blood flukes. It is prevalent in tropical and subtropical areas, in poor communities without potable water and adequate sanitation. Signs and symptoms of the disease include abdominal pain and bloody stool or urine. If infected for a long time, liver damage, kidney failure, infertility, or bladder cancer may occur; in children, it may cause poor growth and learning difficulty.



**Dr. Amado Angeles, UPLBFI, undergoes training on Sample loading for SDS-PAGE at the University of Illinois at Chicago**

The only effective mechanism to combat schistosomiasis is the drug praziquantel. However, mass treatment does not prevent re-infection due to sporadic resistance developed by the parasite. Therefore, alternative treatment strategies are needed. Many vaccines against schistosomiasis have been explored but none has been successfully developed. Likewise, diagnostic tests were generally unsatisfactory due to low sensitivity and specificity of detecting schistosomiasis infection.

In the absence of biological therapeutics and diagnostics of schistosomiasis in the Philippines, UPLB, with support from USAID STRIDE, researched development of technology aimed at significantly reducing costs of research reagents via local production through the isolation of specific antibodies against *Schistosoma* antigens found in infected water buffalo. Water buffalo are a natural host and reservoir for the propagation

of *Schistosoma*, though they do not succumb to the disease, suggesting that they have a robust immune repertoire. The isolated specific antibody from the water buffalo antibody library can be fused to other functional properties, which can lead to better diagnostic reagents for schistosomiasis. In turn, the antigen can be used as a surrogate reagent in the development of future vaccines to prevent further transmission of the disease.

A major challenge encountered was the insolubility of the recombinant antigen proteins. However, this was resolved when the extraction of a recombinant form of Cut1A-like protein was fused with a maltose-binding protein in *Escherichia coli*. The recombinant protein produced is now being used to select *Schistosoma*-specific antibodies from the water buffalo antibody library.



*The research team undergoes training on Sample loading for SDS-PAGE at the University of Illinois at Chicago*

## Milestones

Significant accomplishments include the following:

- Successful identification of good candidates of six antigens, representing various *Schistosoma* life-stages, to be utilized for vaccine and diagnostic purposes through the assistance of Monash University, Australia;
- Engagement of practicing researchers and future scientists in the phage display and other relevant recombinant antibody techniques to establish a strong research and development team capable of steering the biotherapeutics and diagnostics industry in the Philippines;
- Transformation of plasmids harboring any of the six antigen genes identified as good candidates for vaccine and for diagnostic purposes into *E. coli* DH5a at Monash University;
- Establishment of the process to select antibodies to antigens found in the adult stage of the parasite;
- Optimization of the protocol for selecting schistosome-specific antibodies from the enriched scFv phage antibodies; and
- Cloning of other antigen genes in the vector; fusing them with maltose-binding protein in *E. coli* to increase solubility.

In this study, a single-chain variable fragment of an antibody specific to CutA1-like recombinant protein was isolated from scFv phage library generated from *Schistosoma japonicum*-infected water buffalo. The antibody may be designed for improved diagnostic reagents for schistosomiasis. The Antigen CutA1-like protein may be explored in the development of vaccines to prevent the spread of schistosomiasis.