Baculovirus as a new stand-alone prophylactic and therapeutic immunostimulatory agent against malaria

Talha Bin Emran*, PhD, BGC Trust University, Bangladesh
Foisal Mahmud, MBA, University of Chittagong, Bangladesh
Mitsuhiro Iyori, PhD, Kanazawa University, Japan
Shigeto Yoshida, PhD, Kanazawa University, Japan

Abstract

Introduction: Baculovirus (BV), which is an enveloped insect virus with a circular double-stranded DNA genome, possesses unique characteristics to induce strong innate immune responses in various mammalian cells and in mice. **Aim:** Here we show that the innate immune responses induced by BV not only eliminate *Plasmodium* liver-stage parasites but also elicit sterile protection against *Plasmodium* sporozoite infection through type I IFN signaling pathway. **Methodology:** Mice had infected with liver-stage parasites before 24h completely prevented blood-stage parasites following a single dose of BV intramuscular (i.m.) administration, which was much superior to primaquine, the only drug approved to eradicate liver-stage parasites. **Findings:** This BV-mediated liver-stage parasite elimination was also observed in *TLR-9*$^{-/-}$ and *iNOS*$^{-/-}$ mice. In addition to the therapeutic effect, BV i.m. administration sterilely protects mice for at least 7 days from subsequence sporozoite infection, indicating the prophylactic effect. In vivo passive transfer with sera from mice i.m. administered with BV effectively eliminated liver-stage parasites and this effect was canceled by neutralization of IFN-α but not IFN-γ in the sera, indicating a killing mechanism downstream of type I IFN signaling pathway. In fact, 6h after BV i.m. administration, both type I and II IFNs were robustly produced in sera and RNA transcripts of interferon-stimulated genes were drastically upregulated in the liver. **Conclusion & Significance:** Our results provide a great potential of BV for development of BV-based vaccine and anti-hypnozoite drug as a new stand-alone therapeutic and prophylactic immunostimulatory agent, which is applicable not only for malaria but also for other serious infectious diseases such as viral hepatitis.

Image

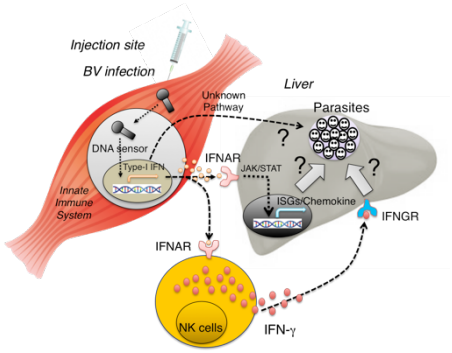


Figure 1: Schematic representation of proposed mechanism for elimination of liver-stage parasites by BV-mediated innate immune responses.

Recent Publications

1. Emran TB *et al.*, (2018) Baculovirus-induced fast-acting innate immunity kills liver-stage *Plasmodium*. J Immunol; 201(8): 2441-2451.
2. Islam A *et al.*, (2019) Anopheline antiplatelet protein from mosquito saliva regulates blood feeding behavior. Sci Rep; 9(1): 3129.
3. Amelia F *et al.*, (2019) Down-selecting circumsporozoite-protein-based malaria vaccine formulations: a comparison of malaria sporozoite challenge models. Parasite Immunol; 18:e12624.
4. Yenni Y *et al.*, (2019) Adeno-associated virus as an effective malaria booster vaccine vector following adenovirus priming. Front Immunol. doi: 10.3389/fimmu.2019.00730
5. Shahriar A *et al.*, (2019) Cold shock and thawing effect on the growth of *Escherichia coli*. EC Microbiol; 15(1): 36-43



Biography

Dr. Talha Bin Emran has been working as an assistant professor in the Department of Pharmacy at the BGC Trust University Bangladesh. Dr. Emran has had his B.Sc. honors and M.S. in Biochemistry & Molecular Biology from the University of Chittagong, PhD from Graduate School of Medical Sciences, Kanazawa University, Japan. The aim of his research is to develop novel vaccine candidates against infectious diseases such as malaria, which is outstanding among domestic pharmaceutical institutes. His researches are focusing on the biology of malaria parasites, the basic researches about infectious diseases and molecular immunology, and those clinical outputs such as vaccine developments and innovative drug developments. His long-term goal is to develop more highly effective next-generation vaccines against malaria, raising an army of "exploitation of a novel pharmaceutical research" at the laboratory of biological pharmacy.

Email: talhabmb@gmail.com or
talha-bgctub@bgctrustbd.org

Notes/Comments: I am interested in attending as a speaker in the 3rd Annual Cell Congress 2019 which will be held on June 24-25 at New York, USA.