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

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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-a but not IFN-g 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.

Biography

Talha Bin Emran has been working as an assistant professor in the department of Pharmacy at the BGC Trust University Bangladesh. He has had his BSc honors and MS 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 develoments 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.

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