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Molecular Characterization of Immunomodulatory Factors from *Aedes aegypti* Salivary Glands and Its Possible Use as Novel Target for Developing Transmission Blocking Vaccines (TBV) against Dengue Fever

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ABSTRAK

Mosquito borne diseases are rampant in most tropical regions of the world, especially rural, forested and coastal areas such as Indonesia. Despite long-standing chemotherapeutic intercession and vector control programs, mosquito-borne diseases exact a heavy burden on human health in Indonesia. Two major public health problems transmitted by mosquito in Indonesia are Malaria and Dengue Haemorrhagic Fever (DHF), causing million clinical episodes occurring annually. Although malaria had ever been virtually eradicated from Indonesia but currently malaria is recognized as a serious re-emerging threat to public health. DHF cases were first observed in 1968; since then, the incidence has been constantly increasing and the disease is now one of the principal causes of child lethality. It has been widely observed that arthropod saliva is able to modify the outcome of infection in the context of mosquitoes and its transmitted pathogens. Furthermore, many of the salivary components are immunogenic and elicit strong immune responses, evidenced by the swelling and itching that accompany a mosquito bite. Saliva of mosquito that transmits disease contains vasomodulatory and immunomodulatory factors. The vasodilatory factors in arthropod saliva help the vector to obtain a blood meal. There are 2 hypotheses concerning the function of immunomodulatory factor in saliva of mosquitoes. Many reports showed that salivary immunomodulators could enhance pathogen infection (1). However, there is also evidence that saliva appeared to directly protect dendritic cells from infection in vitro (2). In relation with the first case, it should be possible to control pathogen transmission by vaccinating the host against the molecule (s) in saliva that potentiate the infection, thereby blocking the enhancing effects of saliva and thus preventing the pathogen from establishing infection in the host. In case of second condition, it could be used directly to protect host cells from infection of transmitted pathogens. These hypotheses lead into new field of research that examine these salivary factor especially the immunomodulatory factor to serve as target to control pathogens transmission i.e. Transmission Blocking Vaccine (TBV). However, specific component as a potential target for TBV in mosquitoes i.e. Anopheles as well as Aedes aegypti has not yet been identified so far. Our research group has been started to explore the immunomodulatory factor from Anopheles mosquitoes since 2009 (Research Grant from: RISBIN IPTEKDOK-DEPKES, Hibah Bersaing DIKTI, Hibah Strategis Nasional). L'oreal-UNESCO for woman in Science Award in category of Life Sciences has been granted to the Principle Investigator for developing this area of research in Indonesia. In collaboration with The International Vaccine Institute (IVI), an International Organization established at the initiative of the United Nations Development Programme under the Vienna Convention of 1969 with the signature so far of 40 countries and the World Health Organization (WHO), we will develop the same approach to be applied in developing TBV against DHF using Grant from RISTEK. So far, our research group is the only research group in Indonesia that tries to develop TBV against mosquitoes borne diseases by using this approach. The objectives of this research are therefore to investigate the putative immunomodulatory factors in the salivary glands of Aedes Aegypti, vector for Dengue

Viruses (1), to localize and isolate the putative immunomodulatory proteins (2), to analyze their activity and function as well as its possible use as molecular target for the development of TBV against DHF (3). Characterization of the putative immunomodulatory proteins from *Aedes aegypti* salivary gland will be done from its cDNA library which constructed from RNA of Salivary Gland Extract (SGE). In collaboration with B2P2VRP (Balai Besar Pengembangan dan Penelitian Vektor dan Reservoir Penyakit)-Salatiga, we have settled up an established insectaria in our research group in Department of Biology-FMIPA UNEJ, for rearing uninfected *Aedes aegypti*. In sum, more than 700 pairs of SG has been isolated from about 1000 mosquitoes. The methodological optimization of RNA isolation from mosquito's SG has been successfully conducted. cDNA library which is constructed from the total RNA of SG has been successfully done as target for result in the first year of Project. cDNA preparation was stored at -20°C until used. From the updated informations regarding the transcriptomes of SG salivary Gland and its putative encoded proteins, 3 candidates have been identified to be further analysed for their function as immunomodulator i.e. putative secreted 37 kD rotein, Putative DenV binding Protein (58 kD). Primers design as well as experimental arrangement to amplify full cDNA sequence encoding those protein are currently being done and will be finished by the end of this year. Using cDNA as template from the result of the first year project, full cDNA sequence encoding those 2 protein target will be generated in the 2nd year of proposed project. Overexpression as well as purification of the protein will also be conducted during this period so that the purified proteins for further functional analysis will be ready by the end of 2012. In the 3rd year, we will conduct functional analysis of the selected proteins for their immunomodulatory activities as target for TBV. Since there no adequate animal model for dengue infection so far, therefore, immune modulation function in relation with Dengue infection, could only be investigated in vitro through Human Dendritic Cell line prior to challenge with DenV serotype I-IV (lab. Isolates from the IVI) as well as from clinical isolate in Indonesia.

Key Words : ---

