Fwd: JGEN: Your manuscript entitled Genetic characterisation of the Erythrocyte Binding Protein (PkβII) of Plasmodium knowlesi isolates from Malaysia Running Headline: Genetic characterisation of PkβII

1 message

CHEONG FEI WEN <fwcheong18@um.edu.my>

Thu, Mar 7, 2019 at 7:30 PM

To: FONG MUN YIK <fongmy@um.edu.my>, YEE LING LAU I UM <lauyeeling@um.edu.my>

Dear Prof,

Pk beta paper finally been accepted by journal of genetics. :)

FW

---------- Forwarded message ----------
From: Journal of Genetics Editorial Office <em@editorialmanager.com>
Date: Thursday, March 7, 2019
Subject: JGEN: Your manuscript entitled Genetic characterisation of the Erythrocyte Binding Protein (PkβII) of Plasmodium knowlesi isolates from Malaysia Running Headline: Genetic characterisation of PkβII
To: Fei Wen Cheong <fwcheong18@um.edu.my>

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Genetic characterisation of the Erythrocyte Binding Protein (PkβII) of Plasmodium knowlesi isolates from Malaysia Running Headline: Genetic characterisation of PkβII
Journal of Genetics

Dear Dr. Cheong,

I am pleased to tell you that your work has now been accepted for publication in Journal of Genetics.

Thank you for submitting your work to this journal.

With kind regards

Hassan Annegowda Ranganath
Editor in Chief
%EIC_ROLE%
Journal of Genetics

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Genetic characterisation of the Erythrocyte Binding Protein (PkβII) of Plasmodium knowlesi isolates from Malaysia

Running Headline: Genetic characterisation of PkβII

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Abstract. Plasmodium knowlesi contributes to majority of human malaria incidences in Malaysia. Its uncontrollable passage among the natural monkey hosts can potentially lead to zoonotic outbreaks. The merozoite of this parasite invades host erythrocytes via interaction between its erythrocyte binding proteins (EBPs) and their respective receptor on the erythrocytes. The region II of P. knowlesi EBP, P. knowlesi beta (PkβII) protein is found to be mediating merozoite invasion into monkey erythrocytes by interacting with sialic acid receptors. Hence, the objective of this study is to investigate the genetic diversity, natural selection and haplotype grouping of PkβII of P. knowlesi
isolates in Malaysia. PCR amplifications of PkβII were performed on archived blood samples from Malaysia and 64 PkβII sequences were obtained. Sequence analysis revealed length polymorphism, and its amino acids at critical residues indicate the ability of PkβII to mediate *P. knowlesi* invasion into monkey erythrocytes. Low genetic diversity (π = 0.007) was observed in the PkβII of Malaysia Borneo compared to Peninsular Malaysia (π = 0.015). The PkβII was found to be under strong purifying selection to retain infectivity in monkeys and it plays a limited role in the zoonotic potential of *P. knowlesi*. Its haplotypes could be clustered into Peninsular Malaysia and Malaysia Borneo groups, indicating the existence of two distinct *P. knowlesi* parasites in Malaysia as reported in an earlier study.

**Key words.** beta protein, genetic diversity, haplotypes, natural selection, *Plasmodium knowlesi*

**Introduction**

*Plasmodium knowlesi*, a simian malaria parasite of long-tailed (*Macaca fascicularis*) and pig-tailed (*M. nemestrina*) monkeys, is now causing emerging zoonotic malaria in Southeast Asians and responsible for over 69% of human malaria cases in Malaysia (WHO, 2017), particularly in Malaysia Borneo (Singh *et al.*, 2004). Its 24-hour rapid asexual life cycle can lead to hyperparasitaemia and fatal complications in patients. Furthermore, the parasite’s passage among its natural monkey hosts may lead to zoonotic outbreaks, impeding the Malaysian government’s aim for malaria elimination.

Invasion of *Plasmodium* spp. merozoite into host erythrocytes regulates the infection pathogenesis and it involves interaction between the parasite’s erythrocyte binding proteins (EBPs) and their respective receptor on the erythrocytes. Erythrocyte binding proteins region II is the ligand for interaction with erythrocyte receptors (Chitnis and Miller, 1994). Region II of *P. knowlesi* EBP, *P. knowlesi* beta (PkβII) protein plays a role to mediate merozoite invasion into monkey erythrocytes by binding to sialic acid receptors on the erythrocytes (Dankwa *et al.*, 2016).