様式4）（Form4）

学 位 論 文 の 内 容 の 要 旨

Dissertation Abstract

ゴー タン ハー 印
NGO THANH HA

（学位論文のタイトル） Title

Blood–cerebrospinal fluid barrier: another site disrupted during experimental cerebral malaria caused by *Plasmodium berghei* ANKA

血液脳脊髄液関門：プラスモディウムベルゲイANKA株が引き起こす実験的脳マラリアにおいて破壊された別の部位

（「論文目録（様式3）」の主論文の部分を記載する。英文の場合は和訳をつける。）

For English paper, Japanese title is necessary.

（学位論文の要旨）2,000字程度、A4判 （Abstract approx.800 Words in English / A4 size）

Abstract

Cerebral malaria (CM) is one of the most severe pathologies of malaria; it induces neuro-cognitive sequela and has a high mortality rate. Although many factors involved in the development of CM have been discovered, its pathogenic mechanisms are still not completely understood. Most studies on CM have focused on the blood–brain barrier (BBB), despite the importance of the blood–cerebrospinal fluid barrier (BCSFB), which protects the brain from peripheral inflammation. Consequently, the pathological role of the BCSFB in CM is currently unknown. To examine the status of the BCSFB in CM and malaria without this pathology (non-CM), we developed a new method for evaluating the permeabilization of the BCSFB during CM in mice, using Evans blue dye and a software-assisted image analysis. Using C57BL/6J (B6) mice infected with *Plasmodium berghei* ANKA as an experimental CM model and B6 mice infected with *P. berghei* NK65 or *Plasmodium yoelii* as non-CM models, we revealed that the permeability of the BCSFB increased during experimental CM but not during non-CM. We observed hemorrhaging in the cerebral ventricles and hemozoin-like structures in the choroid plexus, which is a key component of the BCSFB, in CM mice. Taken together, this evidence indicates that the BCSFB is disrupted in experimental CM, whereas it remains intact in non-CM. We also found that *P. berghei* ANKA parasites and $CD8^+$ T cells are involved in the BCSFB disruption in experimental CM. An understanding of the mechanisms underlying CM might help in the development of effective strategies to prevent and manage CM in humans.