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ALTERATIONS OF THE ERYTHROCYTE MEMBRANE IN MALARIA INFECTION*

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Abstract

The membrane of malaria-infected erythrocytes undergoes various alterations, with important implications on parasite survival and multiplication. We have found alterations in the membrane proteins of infected erythrocytes, in membrane transport of ions, and in bulk properties of the membrane including its capacity to undergo fusion, and its mechanical properties. Degradation of spectrin, an important component of the membrane skeleton, was found in infection by many species. A structural alteration, namely membrane protein phosphorylation, is highly correlated with alterations in mechanical properties. Enhanced Ca^{2+} uptake by infected erythrocytes was observed, and is probably linked with regulation of membrane alterations. An understanding of the nature of these alterations should contribute to the explanation of some aspects of malaria pathophysiology, and of the mechanism of action of some antimalarials.

Introduction

Recent advances in the study of structure and function of biological membranes have contributed significantly to the understanding of pathological systems. The erythrocyte membrane, because of its availability and ease of isolation, has been intensively studied as a model membrane. Detailed knowledge has been accumulated on the structure of the erythrocyte membrane and the relationship with its function. Since the erythrocyte plays an important role in the blood system, this knowledge also has implications for

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physiology as well as biochemistry. Furthermore, many changes are found in the erythrocyte membrane in many blood and other disorders. The study of these changes therefore contributes to the understanding of the pathology of these diseases.

Malaria has long been one of the most important tropical diseases, inflicting great human suffering and heavy economic loss in many tropical developing countries, including Thailand. The proclamation of 18 August as the National Science Day has in fact an ironical link with malaria in history: King Mongkut, the Father of Thai Science, died of malaria after a journey to the South to observe a solar eclipse on 18 August 1868. After the Second World War, the use of synthetic antimalarials and large-scale DDT spraying gave a false optimism that the disease would soon be eradicated. However, since over twenty years ago, when chloroquine resistance of *falciparum* malaria parasites was first noted in Thailand by Prof. Harinasuta's group[1] and in other endemic regions of the world, the malaria problem became increasingly more serious. The problem is further complicated by the emergence of insecticide-resistant mosquitoes and mosquitoes which evade sprayed areas, human migration and resettlement in endemic zones, and weak public health organizational structure. New approaches therefore need to be undertaken to tackle this problem, the scientific component of which should play a prominent role.

Since infection of the erythrocyte is an important part of the life cycle of the malaria parasite, and since many events in this infection, comprising invasion, intracellular parasite development and multiplication, and eventual erythrocyte rupture involve the interaction of the parasite with the erythrocyte membrane and membrane modification as the result of infection, a study of the role of the erythrocyte membrane in malaria infection should yield information of interest to the effort to tackle the malaria problem.

Malaria infection in man and other vertebrate hosts begins with inoculation of spindle-shaped sporozoites from the salivary glands of infected anopheline mosquitoes during blood meal. The sporozoites enter the blood stream and soon invade liver parenchyma cells in man, where they develop and multiply asexually to produce merozoites. The merozoites are liberated and invade erythrocytes. After development and multiplication, the erythrocytic merozoites are released, to begin a new round of invasion, development and multiplication. The malaria-infected erythrocyte presents a challenging complex system for biochemical studies. A complex biochemical relationship exists between the parasite and the host, since the parasite develops and multiply in the intracellular environment of the host erythrocyte. The erythrocyte membrane is the medium through which exogenous nutrients can pass for use by the parasite, and through which waste products can be released. It furthermore provides the shelter for the parasite to escape from host immune mechanisms. Therefore, the erythrocyte membrane is an important host component used by the parasite for its own survival and multiplication. It is very likely that some alterations in the host membrane are generated by the parasite

for its own purpose. In turn, it is also likely that a number of these alterations can be detected by the host immune system. Furthermore, the mechanisms of action of some antimalarials may depend on transport through the altered membrane, or binding with the altered membrane components. Study of the membrane of malaria-infected erythrocytes should therefore be important for the understanding of pathophysiology and drug action at the molecular level.

Molecular Pathology of the Erythrocyte Membrane in Malaria Infection

The role of the erythrocyte membrane in malaria infection gives a striking example of the importance of molecular pathology in the studies of infectious diseases. In order to understand this role, it is necessary to build on previous knowledge on the structure and function of biomembranes in general. Our research group has long been interested in basic aspects of biomembranes, and therefore considered the membrane of malaria-infected erythrocytes as a natural target on which to focus our attention. Fortunately, a few strong research groups in our university, eg. those in the Haematology Unit, Siriraj Hospital, and in the Faculty of Tropical Medicine, have complementary research interests and could help us with the clinical aspects of the work. Experience gained from leading researchers outside Thailand, including Prof. William Trager who conducted two international workshops on *in vitro* culture of *Plasmodium falciparum* at our Department in 1978, also contributed substantially to our initial stock of expertise. The initial infrastructure, combined with relatively simple experimental approaches[2], enabled us to carry out competitive research in spite of the many usual drawbacks of a less developed country.

The proteins of the erythrocyte membrane have been well studied on dodecylsulphate polyacrylamide gel electrophoresis. In 1973, it was reported that the membrane of malaria-infected mouse erythrocytes has alterations in the proteins revealed by this technique[3]. Further studies may reveal the relationship between such molecular changes and other previously known alterations of the erythrocytes as shown by microscopy, eg. the membrane surface deformations and the alterations in cell shape. Furthermore, some pathological complications, such as obstruction in capillary blood flow in human organs, and enhanced intravascular haemolysis, may be due to molecular changes of the erythrocyte membrane components. Alterations of the membrane proteins and other components also have immunological implications: they may constitute targets of immune defense mechanisms, or on the contrary may lead to immunological complications of advantage to parasite survival or of detrimental effects to the host.

Another set of research problems originated many decades ago, leading to the discovery that erythrocytes have greater influx of sodium and greater efflux of potassium during malarial infection[4]. Other studies showed greatly enhanced membrane transport of glucose, amino acids and other nutrients[5]. It is pertinent, in the light of existing knowledge on the structure and function of the erythrocyte membrane, to investigate

the molecular mechanism of the increase in membrane transport activities. This investigation will be relevant to the understanding not only of parasite-host physiological interactions, but also of the mechanism of action of some antimalarial drugs. For example, malaria-infected erythrocytes have greatly enhanced chloroquine transport for susceptible strains, but only slightly enhanced transport for resistant strains[6]. Understanding of the mechanisms of these increased transport activities may therefore provide important clues to the fight against malaria.

Erythrocyte Membrane Proteins in Malaria Infection

Our group was first interested in alterations of erythrocyte membrane proteins in rodent and human malaria infection. It was relatively more easy to study the rodent model, since substantial quantities of experimental materials could be obtained through simple procedures. Through the courtesy of Prof. Geoffrey Beale, we obtained clonal isolates of a number of rodent malaria species for examination. Our results[7] showed that for many, but not all, species of parasites, infection of the erythrocytes lead to reduction of spectrin and appearance of a new protein band of an apparent molecular weight of 165,000, similar to a previous report for *P. berghei* infection[3]. Further studies (P. Wilairat, S. Chaicharoen and Y. Yuthavong, unpublished observation) led to the conclusion that this new band is derived from the degradation of one or both of spectrin bands. In many malaria infections, spectrin is apparently degraded by increased proteolytic activity, either through the release of parasite-specific protease or activation of the host enzyme. Recently, a cathepsin D-like protease obtained from *P. lophurae* parasites was shown to be capable of cleaving duckling erythrocyte membrane proteins, including spectrin, and of producing new bands of lower molecular weight[8].

Alterations of a different nature were found in the membrane proteins of infected erythrocytes. Membrane from *P. berghei*-infected mouse erythrocytes was found to have different patterns of protein phosphorylation from normal erythrocyte membrane[9-11]. Difference could be shown both in phosphorylation of isolated membranes with γ-^{32}P-ATP and of intact cells with $^{32}P_i$. The most dominant feature of the difference is the phosphorylation of a protein with apparent molecular weight of 42,000. Approximately 0.1-0.5 mole of phosphate is bound per mole of this normally non-phosphorylated protein, and the phosphorylation is associated only with infected cells, but not with uninfected cells. Extractability properties and peptide maps of this protein suggest that it is phosphorylated actin. The alteration in phosphorylation pattern of infected erythrocytes has been confirmed recently[12], although there was a difference in the interpretation of the results concerning the origin of the major phosphorylated protein. The level of phosphorylation of this and other proteins varies with the stage of infection, increasing to a maximum at the mature trophozoite stage and declining thereafter[13, 14]. There is furthermore a heterogeneity in the level of phosphorylation of infected cells at the same stage of infection. Interestingly, a relationship was observed between the level

of phosphorylation and osmotic fragility and filterability of infected cells: cells with a higher level of phosphorylation display a lower osmotic fragility and greater filterability than those with lower level of phosphorylation. Apparently the level of phosphorylation is associated with maintenance of the mechanical properties of the infected erythrocytes. Malaria-infected cells are known to have increased osmotic fragility[15], and lower filterability[16, 17] than normal cells. However, in order for the parasite to survive, the infected cells must maintain some resistance to premature lysis, and maintain enough deformability to enable them to escape host splenic clearance. Phosphorylation of some membrane components may be associated with maintenance of the mechanical integrity of infected cells in the presence of other degradative changes. It remains to be seen whether a causal relationship exists between phosphorylation change and modulation of the mechanical properties of the cells.

Many studies[5, 8, 19] have shown other changes in the membrane of malaria-infected erythrocytes not discussed here, including appearance of parasite-specific proteins, changes in lipids and carbohydrates. Fig. 1 shows in summary the general host membrane changes in rodent and other types of malaria.

Calcium Transport Through Malaria-Infected Erythrocyte Membrane

The increased influx of sodium and increased efflux of potassium in erythrocytes in malaria infection[4] are conditions similar to those induced by increased intracellular calcium. It is therefore possible that the infection is associated with abnormal calcium transport, leading to subsequent alterations in sodium and potassium transport. The erythrocyte membrane is normally little permeable to extracellular calcium, and has furthermore an effective mechanism for pumping out calcium until the intracellular concentration is very small (of the order of 10^{-7} M). However, calcium probably has an important role in regulating the activity of many intracellular enzymes, and it is quite possible that the developing parasite within the erythrocyte has requirements for calcium in its metabolism. In order to test these possibilities, we compared the uptake of $^{45}Ca^{2+}$ by erythrocytes from normal and *P. berghei*-infected mouse blood. In the presence of glucose, a greatly enhanced calcium uptake was found for infected cells, the level of enhancement being higher with maturation of the parasites[20-22]. Other groups[23-25] also reported similar results for various types of malaria-infected erythrocytes. It was furthermore shown that calcium was mostly accumulated within the parasite[23, 24]. At the schizont stage, the enhanced calcium uptake was accompanied by greatly enhanced lysis[20-22], raising the possibility that calcium may have a role in the regulation of merozoite release. The alteration in the calcium status was also detected[26] though the use of a specific ionophore A23187. In the presence of this ionophore there is far less calcium uptake by cells from infected blood than those from normal blood. All cells, both infected and uninfected, from infected blood show the alteration in calcium status as revealed by the ionophore. The alterations in the calcium status may therefore be due

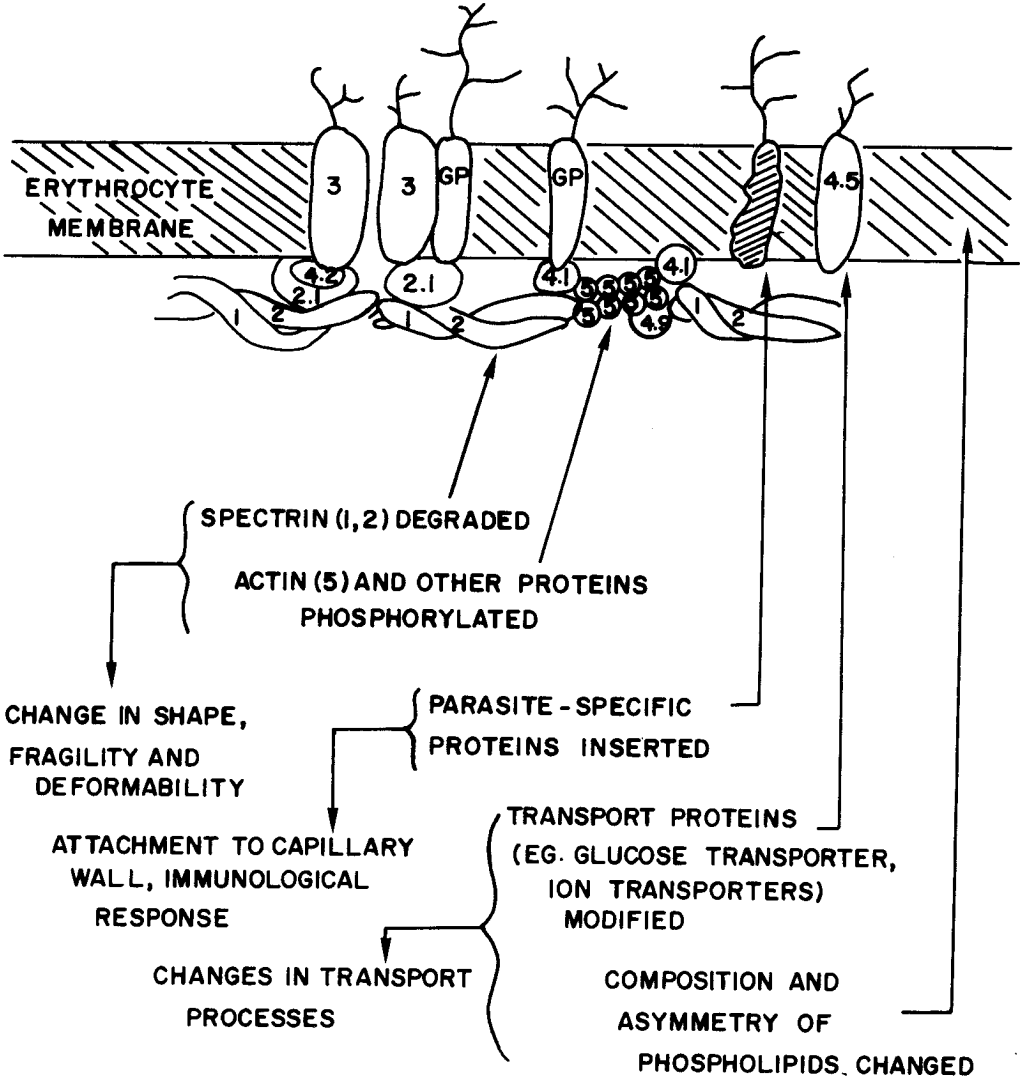

Fig. 1 Some alterations of the erythrocyte membrane during malaria infection and possible relationship with pathological states. GP = glycophorin; numbers indicate the membrane protein components as assigned in the Steck system.

not only to the direct infection of the erythrocytes, but also to secondary factors produced in host-parasite interaction.

What are the main contributing factors to the changes in calcium transport observed in infected erythrocytes? While much further classification is required, the diagram in Fig. 2 depicts the main events concerning calcium transport of the host-parasite complex. Enhanced host membrane permeability to calcium, probably combined with reduced efficiency of the Ca^{2+}-ATPase-driven calcium pump, lead to an increase in intracellular calcium. The parasite furthermore may have a mechanism for accumulation of calcium through the use of H^+-ATPase[23]. Calcium transport is therefore probably closely linked with the energy status, and transport of H^+, nutrients and metabolites. This vast and important field in the study of parasite biochemistry still remains to be investigated in detail. For example, the role of parasite mitochondria, long presumed to be of minor importance in its metabolism, in the accumulation and transport of calcium should be carefully assessed, since antimalarials like tetracycline may act by interfering with these mechanisms.

What are the main consequences of the increase in transport and intracellular calcium in infected cells? Fig. 3 shows some of the possible effects on the erythrocyte membrane worthy of further investigation. In the rodent model, calcium inhibits membrane protein phosphorylation (ref. 13 and D. Wititsuwannakul, personal communication), hence possibly exerting an effect on the mechanical properties of the erythrocytes. Calcium can activate protease and phospholipases which digest membrane components. The calcium-induced changes may combine with other degradative changes on the host membrane in preparing for erythrocyte lysis and merozoite release.

The change in calcium transport of malaria-infected cells can account for our previous observation[27] that these cells have significantly higher capacity to undergo membrane fusion than normal cells. The work of Prof. Jack Lucy's group, among others, has shown that calcium transport is an important process in membrane fusion[28]. In agreement with this general conclusion, we found that the increased fusion capacity of infected cells is related with the increased uptake of calcium[29]. The increased fusion capacity may have implications for malaria chemotherapy, since it may be possible to encapsulate antimalarials in liposomes which will preferentially fuse with, and deliver the drugs to, the infected cells.

The Role of the Erythrocyte Membrane in the Action of Chloroquine

Information about the erythrocyte membrane is useful in the investigation of the mechanism of action of some antimalarial agents, such as chloroquine. Chloroquine is a 4-aminoquinoline derivative which showed high activity against both *falciparum* and *vivax* malaria, but has been increasingly less effective for the former. Chloroquine resistance is a complex problem, owing substantially to the fact that its mechanism of action is still unclear at present. An important aspect of the action mechanism is the

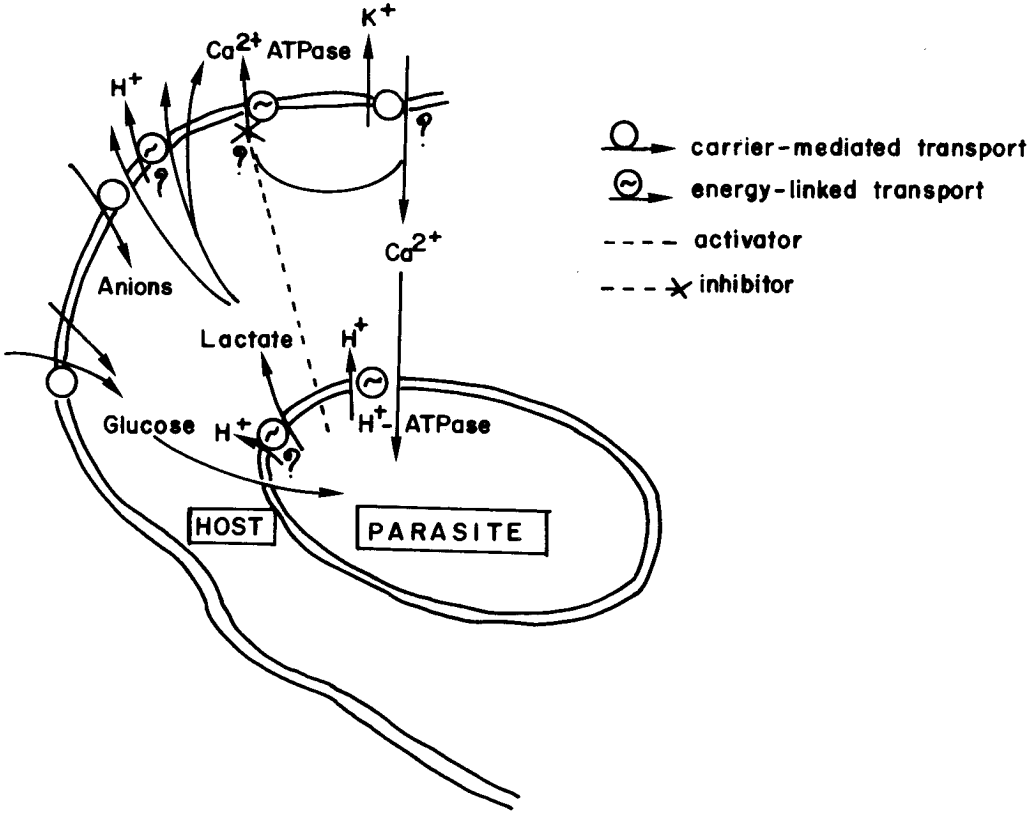

Fig. 2 Mechanisms of calcium transport processes of the infected erythrocytes, and relationship with other transport processes.

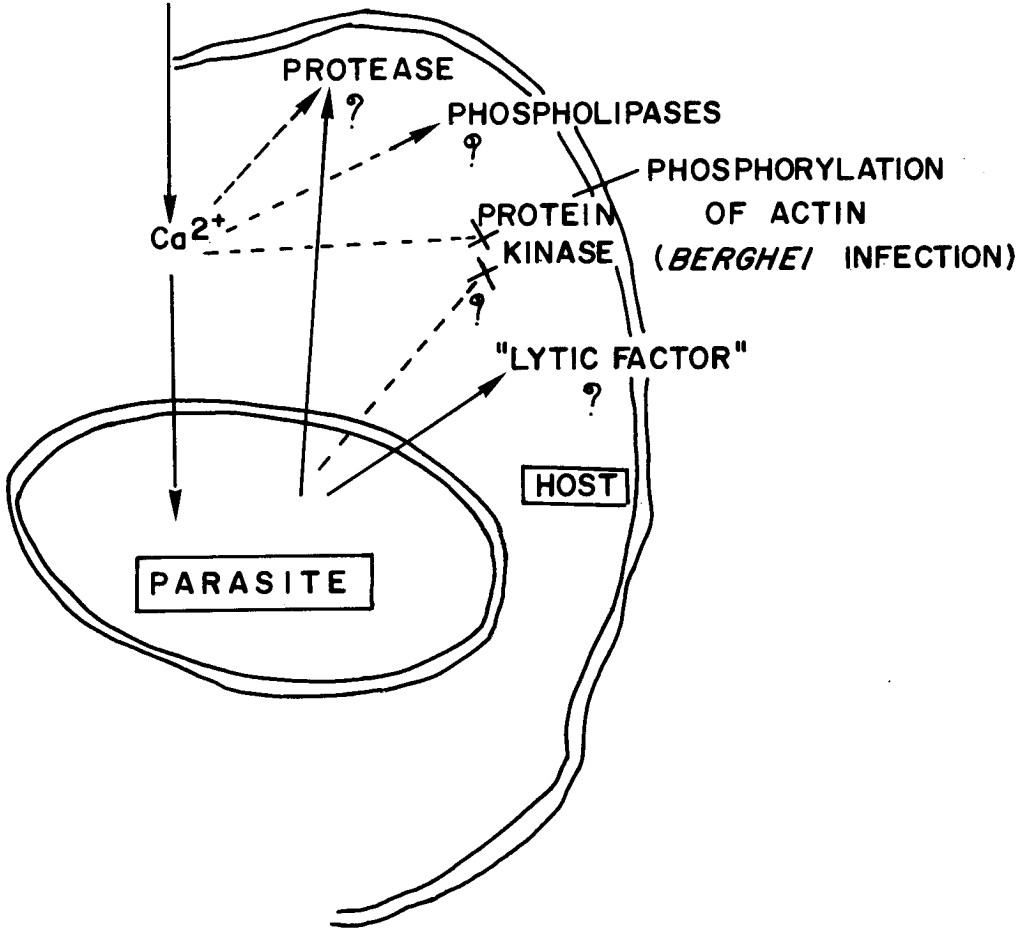

Fig. 3 Possible roles of calcium in regulation of changes on the membrane of infected erythrocytes.

rapid and high accumulation of chloroquine by infected erythrocytes[6]. It was at first thought that the erythrocyte membrane has latent receptors for chloroquine, since protease treatment of normal erythrocytes confer upon them a similar capability to accumulate chloroquine[30]. However, the distribution of chloroquine in the membrane and lysate fractions are different for protease-treated and malaria-infected erythrocytes: the membrane of the former is the preferential site for chloroquine binding, while the membrane of the latter can acquire a similar characteristic only through similar protease treatment[31]. Subsequent detailed investigation[32, 33] showed that only infected cells from infected blood have the chloroquine-accumulation capability, which is enhanced with maturation of the parasites. The distribution of chloroquine within the host-parasite complex depends on external drug concentration. At therapeutic external concentration (approx. 10^{-6}M) most of the drug is located in the parasite, while minor but significant fractions are found with the host membrane and host cytosol. Another line of study by Dr. Bhinyo Panijpan's group[21] indicated that chloroquine binds tightly with haemin and haemozoin, which constitute the residue left from haemoglobin digestion by the parasite. This conclusion is similar to that of Prof. C.D. Fitch's group[35] derived from different experimental approaches. The complexes formed from such binding may be the mediator of the drug action. Recent work[36] has shown that the erythrocyte membrane may be a target for the damaging action of the chloroquine-haemozoin and chloroquine-haemin complexes.

Conclusion

We have studied some general changes in the structure and function of the erythrocyte membrane in malaria infection. The information gained from such studies should be complementary to that obtained from most previous studies by other investigators, which have concentrated mainly on such specific changes as appearance of parasite-specific antigens on the host erythrocyte. Our studies with focus on the cellular and molecular aspects, should furthermore be relevant to the mechanisms of pathophysiology in malaria at the level of the whole organism. It is hoped that the attempts to answer some basic questions on the changes of the erythrocyte membrane in malaria infection will demonstrate the possible contributions of basic science, done within a developing country, to the alleviation of an important problem of the developing countries.

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References

1. Harinasuta, T., Migasen, S. and Bunnag, D. (1962) Chloroquine Resistance in *Plasmodium falciparum* in Thailand. UNESCO 1st Regional Symposium on Scientific Knowledge of Tropical Parasites, Singapore, pp. 148-153.
2. Yuthavong, Y. and Wilairat, P. (1981) The Biochemistry of Malaria. *Biochem. Ed.* **9**, 122-127.
3. Weidekamm, E., Wallach, D.F.H., Lin, P.S. and Hendricks, J. (1973) Erythrocyte Membrane Alterations Due to Infection with *Plasmodium berghei*. *Biochim. Biophys. Acta* **323**, 539-546.
4. Dunn, M.J. (1969) Alterations of Red Blood Cell Sodium Transport During Malarial Infection. *J. Clin. Invest.* **48**, 674-685.
5. Sherman, I.W. (1979) Biochemistry of *Plasmodium* (Malarial Parasites). *Microbiol. Rev.* **43**, 453-495.
6. Fitch, C.D. (1969) Chloroquine Resistance in Malaria: A Deficiency of Chloroquine Binding. *Proc. Nat. Acad. Sci. USA.* **64**, 1181-1187.
7. Yuthavong, Y., Wilairat, P. Panijpan, B., Potiwan, C. and Beale, G.H. (1979) Alterations in Membrane Proteins of Mouse Erythrocytes Infected with Different Species and Strains of Malaria Parasites. *Comp. Biochem. Physiol.* **63B**, 83-85.
8. Sherman, I. W. and Tanigoshi, L. (1983) Purification of *Plasmodium lophurae* Cathepsin D and Its Effects on Erythrocyte Membrane Proteins. *Mol. Biochem. Parasitol.* **8**, 207-226.
9. Chaimanee, P. and Yuthavong, Y. (1979) Phosphorylation of Membrane Proteins from *Plasmodium berghei*-Infected Red Cells. *Biochem. Biophys. Res. Commun.* **87**, 953-959.
10. Chaimanee, P. (1982) Erythrocyte Membrane Phosphorylation in *Plasmodium berghei*-Infected Mice. Ph.D. Thesis, Mahidol University.
11. Chaimanee, P. and Yuthavong, Y. (1985) Characteristics of Membrane Protein Phosphorylation in *Plasmodium berghei*-Infected Mouse Erythrocytes. In preparation.
12. Wiser, M.F., Wood, P.A., Eaton, J.W. and Sheppard, J.R. (1983) Membrane-associated Phosphoproteins in *Plasmodium berghei*-Murine Erythrocytes. *J. Cell Biol.* **97**, 196-201.
13. Limpaiboon, T. (1983) Relationship of Phosphorylation of Membrane Proteins with Membrane Properties of Malaria-Infected Erythrocytes. M.Sc. Thesis, Mahidol University.
14. Yuthavong, Y. and Limpaiboon, T. (1985) Relationship of Phosphorylation of Membrane Proteins with Osmotic Fragility and Deformability of *Plasmodium berghei*-Infected Mouse Erythrocytes. In preparation.
15. Seed, T.M., Brindley, D., Aikawa, M. and Rabbege, I.R. (1976) *Plasmodium berghei:* Osmotic Fragility of Malaria Parasites and Mouse Host Erythrocytes. *Exp. Parasitol.* **40**, 380-390.
16. Miller, L.H., Shien, S. and Usami S. (1972) Decreased Deformability of *Plasmodium coatneyi* Infected Red Cells and Its Possible Relation to Cerebral Malaria. *Am. J. Trop. Med. Hyg.* **21**, 133-137.
17. Pattanakitsakul, S. and Yuthavong, Y. (1982) Heterogeneity in Filterability of Erythrocytes from Malaria *(Plasmodium berghei)*-Infected Blood. *Experientia* **38**, 626-628.
18. Howard, R.J. (1982) Alterations in the Surface Membrane of Red Blood Cells During Malaria. *Immunol. Rev.* **61**, 67-107.

19. Newbold, C.I. (1984) Intraerythrocytic Development and Antigenicity of Asexual Malaria Parasites. *Mol. Biochem. Parasitol.* **11**, 1-22.

20. Krungkrai, J. (1981) Alterations of Erythrocyte Ca^{2+} Status in Malaria *(Plasmodium berghei)*-Infection. M.Sc. Thesis, Mahidol University.

21. Yuthavong, Y. and Krungkrai, J. (1982) Ca^{2+} Uptake of Erythrocytes in Malarial Infection. From *Application of Biochemical Micromethods for the Investigation of Tropical Disease Pathogens* Ed. F. Michal, TDR, WHO.

22. Krungkrai, J. and Yuthavong, Y. (1983) Enhanced Ca^{2+} Uptake by Mouse Erythrocytes in Malarial *(Plasmodium berhei)*-Infection. *Mol. Biochem. Parasitol.* **7**, 227-235.

23. Tanabe, K., Mikkelsen, R.B., and Wallach, D.F.H. (1982) Calcium Transport of *Plasmodium chabaudi*-Infected Erythrocytes. *J. Cell Biol.* **93**, 680-684.

24. Leida, M.N., Mahoney, J.R. and Eaton, J.W. (1981) Intraerythrocytic Plasmodium Calcium Metabolism. *Biochem. Biophys. Res. Commun.* **103**, 402-406.

25. Bookchin, R.M. Raventos, C., Nagel, R.L. and Lew, V.L. (1981) Abnormal K and Ca Transport and Ca Accumulation in Red Cells Infected *In Vitro* with *Plasmodium falciparum*. *Clin. Res.* **29**, 516A.

26. Krungkrai, J. and Yuthavong, Y. (1983) Reduction of Ca^{2+} Uptake Induced by Ionophore A23187 of Red Cells from Malaria *(Plasmodium berghei)*-Infected Mice. *Cell Biol. Int. Rep.* **7**, 237-244.

27. Nakornchai, S., Satarug, S., Potiwan, C. and Yuthavong, Y. (1980) Enhanced Fusion Capacity of Malaria *(Plasmodium berghei)*-Infected Mouse Red Cells. *Cell Biol. Int. Rep.* **4**, 933-940.

28. Ahkong, Q.F. Fisher, D., Tampion, W. and Lucy, J.A. (1975) Mechanisms of Cell Fusion. *Nature (Lond.)* **253**, 194-195.

29. Nakornchai, S., Sathitudsahakorn, C., Chongchirasiri, S. and Yuthavong, Y. (1983) Mechanism of Enhanced Fusion Capacity of Mouse Red Cells Infected with *Plasmodium berghei*. *J. Cell Sci.* **63**, 147-154.

30. Fitch, C.D., Chevli, R. and Gonzalez, Y. (1974) Chloroquine Accumulation by Erythrocytes: A Latent Capability. *Life Sci.* **14**, 2441-2446.

31. Yuthavong, Y. (1980) Distribution of Chloroquine in Normal, Pronase-Treated and Malaria-Infected Red Cells. *Life Sci.* **26**, 1899-1903.

32. Sirawaraporn, W. (1980) Distribution of Chloroquine in *P. berghei*-Infected Red Cells. M.Sc. Thesis, Mahidol University.

33. Sirawaraporn, W., Panijpan, B. and Yuthavong, Y. (1982) *Plasmodium berghei:* Uptake and Distribution of Chloroquine in Infected Mouse Erythrocytes. *Exp. Parasitol.* **54**, 260-270.

34. Jearnpipatkul, A., Govitrapong, P., Yuthavong, Y., Wilairat, P. and Panijpan, B. (1980) Binding of Antimalarial Drugs to Hemozoin from *Plasmodium berghei*. *Experientia* **36**, 1063-1064.

35. Chou, A.C., Chevli, R. and Fitch, C.D. (1980) Ferriprotoporphyrin IX Fulfills the Criteria for Identification as the Chloroquine Receptor of Malaria Parasites. *Biochemistry* **19**, 1543-1549.

36. Balasubramanian, D., Rao, C.M. and Panijpan, B. (1984) The Malaria Parasite Monitored by Photoacoustic Spectroscopy. *Science* **223**, 828-830.

บทคัดย่อ

เม็ดเลือดแดงที่ติดเชื้อมาลาเรียมีการเปลี่ยนแปลงหลายอย่างที่เยื่อหุ้ม อันส่งผลสะท้อนต่อการอยู่รอดและการขยายจำนวนของเชื้อ งานวิจัยนี้ได้ตรวจพบการเปลี่ยนแปลงหลายประการในโปรตีนที่เป็นส่วนประกอบของเยื่อหุ้มเม็ดเลือดแดงที่ติดเชื้อมาลาเรีย พบการเปลี่ยนแปลงของการลำเลียงไอออนส์ (คัลเซียม) ผ่านเยื่อนี้ และการเปลี่ยนแปลงในคุณสมบัติอื่น ๆ เช่น ความสามารถในการหลอม (fusion) และคุณสมบัติทางกล ได้พบว่าการเปลี่ยนแปลงด้านโครงสร้างบางอย่าง กล่าวคือ ฟอสฟอริเลชัน (phosphorylation) ของโปรตีน มีความสัมพันธ์กับการเปลี่ยนแปลงของคุณสมบัติทางกลของเยื่อหุ้มนี้ ความเข้าใจเรื่องการเปลี่ยนแปลงเหล่านี้ ช่วยทำให้สามารถอธิบายพยาธิสภาพบางประการของโรคมาลาเรีย และอธิบายกลไกการทำงานของยาต่อต้านมาลาเรียบางตัวได้