Erythrocyte membrane phosphorylation in

*Plasmodium berghei*-infected mice

During the maturation of the malarial parasite within the host erythrocyte, various changes in structural and biochemical properties of erythrocyte is observed. These include (1) changes in erythrocyte shape and deformability, (2) abnormalities in membrane transport properties and (3) abnormalities in membrane proteins. It has been suggested that the shape of erythrocyte is maintained by cytoskeleton framework, including spectrin-actin complex, beneath the erythrocyte membrane. Most studies, however, implicate the spectrin phosphorylation directly in the regulation of the cytoskeleton framework of the erythrocyte. It has been shown that spectrin of the *P. berghei*, *P. chabaudi* and *P. knowlesi*-infected erythrocyte is degraded during intraerythrocytic growth of the parasite. These alterations in cytoskeleton component could indirectly account for the change observed in infected erythrocytes. However, alteration in phosphorylation of cytoskeletal components mediated through protein kinase has not been investigated before.

The aim of the studies reported in this thesis is to determine the change in membrane phosphorylation of *P. berghei*-infected erythrocytes, identify these phosphorylated components and suggest the possible role of these phosphorylated components in the organization of the erythrocyte cytoskeleton during parasite growth.
Endogenous protein phosphorylation in *P. berghei*-infected erythrocyte membrane was examined by both incubating intact infected erythrocyte with \(^{32}\text{P}\)orthophosphate and infected erythrocyte membrane with \(\gamma^{32}\text{P}\)ATP. Individual phosphorylated proteins were detected by autoradiography after one- and two-dimensional separation (isoelectric focusing followed by SDS-polyacrylamide gel electrophoresis). In addition to phosphorylated protein found in membrane from normal erythrocytes, a protein of about 43,000 (band 5) was phosphorylated in infected erythrocytes. The molar ratio of phosphate to protein of band 5 was 0.1-0.5. This 43,000 species was shown to be similar to muscle actin by isoelectric focusing-SDS polyacrylamide gel electrophoresis, peptide mapping, ability to be extracted with low ionic strength buffer but not with Triton X-100, and ability to inhibit DNase I. DNase I inhibition was reduced with increasing degree of phosphorylation. It is suggested that the 43,000 species is erythrocyte actin which undergoes endogenous phosphorylation specifically in *P. berghei*-infected erythrocytes. However, spectrin phosphorylation observed in infected erythrocyte was not changed although there is evidence for degradation of spectrin by proteolysis. In low-ionic strength buffer, dissociation of cytoskeletal proteins (spectrin-band 4.1-actin) from infected erythrocytes was significantly lower than from normal membrane and phospho-actin was found to be less prone to extraction from infected erythrocyte membrane than non-phosphorylated actin. These results suggest that a possible role of phosphoactin in infected erythrocyte may be to regulate the stability of infected erythrocyte membrane during maturation.
BIOGRAPHY

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