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NONGLUK SRIWILAIJAREON : STUDIES ON TELOMERASE OF THE HUMAN MALARIA PARASITE *PLASMODIUM FALCIPARUM*. THESIS ADVISORS : PRAPON WILAIRAT, Ph.D., MATHUROSE PONGIKITMONGKOL, Ph.D. 141 p. ISBN 974-662-510-1

Of the four species of *Plasmodium* that cause human malaria, *Plasmodium falciparum* causes the most widespread and severe disease. It has become resistant to almost all of the available antimalarial drugs. There is a need to find new targets for malaria chemotherapy.

Telomeres are repeating sequences of base pairs at the ends of linear eukaryotic chromosomes that preserve genome stability and cell viability by preventing aberrant recombination and degradation of DNA. Telomeric repeats are progressively shortened after each cycle of DNA replication due to the inability of DNA polymerase to replace the RNA primer located at the $5'$-end (end-replication problem). This causes a limit to the number of cell divisions. However germline and immortalized cells can overcome this problem by expression of telomerase, a ribonucleoprotein enzyme that synthesizes the telomeric DNA at chromosome ends using a segment of its RNA component as a template.

P. falciparum has been maintained in culture for more than 20 years without any sign of cessation of parasite cell division. This indicates that *P. falciparum* must have a capacity to repair telomere ends present in its 14 chromosomes. *P. falciparum* telomerase activity was detected using TRAP assay. The activity was sensitive to RNase A and was detectable at all stages of the parasite erythrocytic cycle, with an increase in activity in trophozoite and schizont extracts compared with ring, suggesting that there is a relationship between telomerase activity and erythrocytic cycle regulation. In addition, among the four ddNTPs, ddGTP was the most potent telomerase inhibitor. Berberine, extracted from *Arcangelisia flava* (L.) Merr. could also inhibit parasite telomerase. These data suggest that *P. falciparum* telomerase may be a novel target for future malaria chemotherapy.