

BIOGRAPHICAL SKETCH

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NAME Kyle, Dennis E.	POSITION TITLE Professor		
eRA COMMONS USER NAME dekyle			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
University of Tennessee at Chattanooga	BA	1979	Biology
Clemson University	PhD	1984	Zoology/Parasitology
University of Georgia (postdoc)		1984-5	Parasitology

A. Positions and Honors.**Positions and Employment**

- 1984-1985 Postdoctoral Research Associate, Department of Poultry Science, University of Georgia
 1986-1990 Chief, Malaria Research Laboratory, WRAIR, Washington, DC
 1991-1992 Chief, Parasitology Section, Armed Forces Research Institute of the Medical Sciences (AFRIMS), Bangkok, Thailand
 1992-1994 Chief, Department of Parasitology and Immunology, AFRIMS, Bangkok, Thailand
 1994-1996 Chief, Antiparasitic Drug Discovery, Walter Reed Army Institute of research (WRAIR), Washington, DC
 1996-1999 Chief, Department of Parasitology, WRAIR, Washington, DC
 1999-2001 Deputy Director (Antimalarial Drug Discovery), Division of Experimental Therapeutics, WRAIR, Washington, DC
 1999-2001 Assistant Research Coordinator, Drug Discovery and Development, Military Infectious Diseases Research Program, Frederick, MD
 2000 Technology Staff Officer, Office of the Deputy for Medical Systems, Assistant Secretary of the Army (Acquisition, Logistics, and Technology, Arlington, VA)
 2002- 2004 Senior Scientist, Australian Army Malaria Institute, Brisbane, Queensland, Australia
 2004- 2006 Deputy Director, Division of Experimental Therapeutics, WRAIR; Chair, Antimalarial Drug Lead Optimization Program, Military Infectious Diseases program
 2006- Professor, Global Health, College of Public Health, University of South Florida, Tampa, FL

Honors and Awards

- 1984 E.E. Byrd Award, Southeastern Society of Parasitologists
 1987 Edward L. Buescher Young Investigator Award, WRAIR Association
 '88/ '94/'01 Department of the Army Research and Development Technical Achievement Award
 1995 Outstanding Research and Development Scientist Award, Society of Armed Forces Medical Laboratory Sciences
 1996 US Army Surgeon General "A" Proficiency Designator (highest level of scientific proficiency)
 2000 Distinguished Alumni Award, College of Agriculture, Forestry, and Life Sciences, Clemson University
 2001 Order of Military Medical Merit
 2005-2006 NIAID "Drug Discovery and Mechanisms of Antimicrobial Resistance" Study Section NIAID
 2005 Chair, "Biology of Plasmodium and Trypanosome Vectors" Special Emphasis Review Panel, NIAID
 2006 Scientist of the Year, Malaria Foundation International

B. Selected peer-reviewed publications (in chronological order).

(Publications selected from 130 peer-reviewed publications)

1. **Kyle, D.E.**, and G.P. Noblet. 1985. Vertical distribution of potentially pathogenic free-living amoebae in freshwater lakes. *J. Protozool.* 32: 99-105.

2. Krogstad, D.J., I.Y. Gluzman, **D.E. Kyle**, A.M.J. Oduola, S.K. Martin, W.K. Milhous and P.H. Schlesinger. 1987. Efflux of chloroquine from *Plasmodium falciparum*: Mechanism of chloroquine resistance. *Science* 238: 1283-1285.
3. Bitonti, A.J., A. Sjoerdsma, P.P. McCann, **D.E. Kyle**, A.M.J. Oduola, R.N. Rossan, W.K. Milhous, and D.E. Davidson, Jr. 1988. Reversal of chloroquine resistance in malaria parasite *Plasmodium falciparum* by desipramine. *Science* 242: 1301-1303.
4. **Kyle, D.E.**, A.M.J. Oduola, S.K. Martin, and W.K. Milhous. 1990. *Plasmodium falciparum*: Modulation by calcium antagonists of resistance to chloroquine, desethyl-chloroquine, quinine, and quinidine *in vitro*. *Trans. Royal Soc. Trop. Med. Hyg.* 84: 474-478.
5. Foote, S.J., **D.E. Kyle**, R.K. Martin, A.M.J. Oduola, K. Forsyth, D.J. Kemp, and A.F. Cowman. 1990. Several alleles of the multidrug-resistance gene are closely linked to chloroquine resistance in *Plasmodium falciparum*. *Nature* 345: 255-258.
6. Wilson, C.M., S.K. Volkman, S. Thaithong, R.K. Martin, **D.E. Kyle**, W.K. Milhous, and D.F. Wirth. 1993. Amplification of *pfmdr1* associated with mefloquine and halofantrine resistance in *Plasmodium falciparum* from Thailand. *Mol. Biochem. Parasitol.* 57: 151-160.
7. **Kyle, D.E.**, W.K. Milhous, and R.N. Rossan. 1993. Reversal of *Plasmodium falciparum* resistance to chloroquine in Panamanian *Aotus* monkeys. *Am. J. Trop. Med. Hyg.* 48: 126-133.
8. Nosten, F., F.O. ter Kuile, C. Luxemburger, C. Woodrow, **D.E. Kyle**, T. Chongsuphajaisiddhi, and N.J. White. 1993. Cardiac effects of antimalarial treatment with halofantrine. *Lancet* 341: 1054-1056.
9. Looareesuwan, S., C. Viravan, H.K. Webster, **D.E. Kyle**, D.B. Hutchinson, and C.J. Canfield. 1996. Clinical studies of atovaquone, alone or in combination with other antimalarial drugs, for the treatment of acute uncomplicated malaria in Thailand. *Am. J. Trop. Med. Hyg.* 54: 62-66.
10. Nosten, F., C. Luxemburger, **D.E. Kyle**, W.R. Ballou, J. Wittes, E. Wah, T. Chongsuphajaisiddhi, D.M. Gordon, N.J. White, J.C. Sadoff, D.G. Heppner & The Shoklo SPf66 Malaria Vaccine Trial Group. 1996. SPf66 vaccine fails to protect against falciparum malaria in a randomized double-blind controlled trial in children in northwestern Thailand. *Lancet* 348: 701-707.
11. Petras, J.M., **D.E. Kyle**, M. Ngampochjana, G.D. Young, R.A. Bauman, H.K. Webster, K.D. Corcoran, J.O. Peggins, M.A. Vane, and T.G. Brewer. 1997. Arteether: Risks of chronic administration in *Macaca mulatta*. *Am. J. Trop. Med. Hyg.* 56: 390-396.
12. Teja-Isavadharm, P., F. Nosten, **D.E. Kyle**, C. Luxemburger, F. ter Kuile, J.O. Peggins, T.G. Brewer, and N.J. White. 1996. Comparative bioavailability of oral, rectal, and intramuscular artemether in healthy subjects: use of simultaneous measurement by high performance liquid chromatography and bioassay. *Br. J. Clin. Pharmacol.* 42: 599-604.
13. Lin, A.J., A.B. Zikry, and **D.E. Kyle**. 1997. Antimalarial activity of new dihydroartemisinin derivatives. 7. 4-(p-substituted phenyl)-4-(R or S)[10-(α or β) dihydroartemisininoxy] butyric acids. *J. Med. Chem.* 40: 1396-1400.
14. Roberts, F., C.C. Roberts, J.J. Johnson, **D.E. Kyle**, T. Krell, J.R. Coggins, G.H. Coombs, W.K. Milhous, S. Tzipori, D.J.P. Ferguson, D. Chakrabarti, and R. McLeod. 1998. Evidence for the shikimate pathway in apicomplexan parasites. *Nature* 393: 801-805.
15. Milhous, W.K., and **D.E. Kyle**. 1998. Introduction to the modes of action and mechanisms of resistance to antimalarials. In: *Malaria: Parasite Biology, Pathogenesis, and Protection*. Ed.: I.W. Sherman, ASM Press, Washington, DC, pp. 303-316.
16. Aldous, W.K., R.K. Martin, and **D.E. Kyle**. 1998. Stage specific detection and inhibition studies of *Plasmodium falciparum* telomerase. *Mol. Biochem. Parasitol.* 95: 281-285.
17. **Kyle, D.E.**, P. Teja-Isavadharm, Q. Li, and K.U. Leo. 1998. Pharmacokinetics and pharmacodynamics of qinghaosu derivatives: How do they impact on the choice of drug and the dosage regimens? *Med Tropicales* 58: 38-44.
18. Nau, M.E., L. Emerson, R.K. Martin, **D.E. Kyle**, D.F. Wirth, N.L. Michael, D.L. Birx, and M. Vahey. 2000. Technical assessment of the Affymetrix yeast expression GeneChip YE6100 platform in a heterologous model of genes that confer resistance to antimalarial drugs in yeast. *J. Clin. Microbiol.* 38: 1901-1908.
19. Mehlotra, R. V., H. Fujioka, P.D. Roepe, O. Janneh, L.M.B. Ursos, V. Jacobs-Lorena, D.T. McNamara, M. J. Bockarie, J.W. Kazura, **D.E. Kyle**, D.A. Fidock, and P.A. Zimmerman. Evolution of New *Plasmodium falciparum* chloroquine resistance phenotype in association with *pfcr1* polymorphism in Papua New Guinea and South America. *PNAS* 98:12689-12694.
20. Jiang, S., S.T. Prigge, L. Wei, Y. Gao, T.H. Hudson, L. Gerena, J.B. Dame, and **D.E. Kyle**. 2001. A new class of small non-peptidyl compounds blocks *Plasmodium falciparum* development *in vitro* by inhibiting plasmepsins. *Antimicrob. Agents Chemother.* 45(9): 2577-2584.

21. Guan, J, **D.E. Kyle**, L. Gerena, Q. Zhang, W.K. Milhous, and A.J. Lin. 2002. Design, synthesis and evaluation of new chemosensitizers in multi-drug resistant *Plasmodium falciparum*. *J. Med. Chem.* 45: 2741-2748.
22. Chen, N., **Kyle, D.E.**, Pasay, C.M. Fowler, E.V., Peters, J. M. and Cheng, Q. (2003) Pfcr1 allelic types with novel amino acid mutations in chloroquine resistant *Plasmodium falciparum* from the Philippines. *Antimicrobial Agents and Chemotherapy* 47(11):3500-3505.

C. Research Support.

1. NIAID, R01AI058973 (Kyle, PI) 2005-2008
Artemisinin-Induced Dormancy and Malaria Treatment Failure
This project aims to investigate the rate at which dormant parasites develop and recover following treatment with various artemisinin derivatives in vitro. In addition the duration of dormancy will be estimated and the role of dormancy in vivo will be investigated in an animal model. Physiological, cellular and molecular characterization of the dormant parasites will be performed to identify determinants/markers for dormancy and establish the mechanism(s) by which dormancy occurs. The results of this project will provide valuable information regarding the mechanisms of treatment failure for artemisinin drugs.
2. NIH, 2 RO1, AI047500-04A2 (Cheng, PI) 2005-2008
"Evolution of drug resistance in *Plasmodium falciparum*."
The project investigates the process and switch rates involved in PfEMP1 antigenic variation and the role of antigenic variation in the emergence and spread of drug resistance in *Plasmodium falciparum*.
Role: CI
3. Medicine for Malaria Venture (Kozar, PI) 2006-2007
"Lead Optimization of Liver Stage Antimalarial Drugs"
Medicines for Malaria Venture 2006-2008
The project involves optimizing the bioavailability and radical curative/causal prophylactic activity of novel imidazolidinediones.
Role: CI (PI prior to moving to USF)
4. Medicines for Malaria Venture (Tidwell, PI) 2006-2007
"Discovery of Dicationic Compounds for the Treatment of Malaria"
The project focused on optimizing oral bioavailability and selective efficacy of diamidine prodrugs for the treatment of acute, uncomplicated malaria.
Role: CI
5. Bill and Melinda Gates Foundation (Tidwell, PI) 2006-2011
"Development of New Drugs to Treat Leishmaniasis and Late Stage Human African Trypanosomiasis"
The goal of the proposed studies is to find new orally active therapeutic agents to treat late stage Human African Trypanosomiasis and visceral leishmaniasis. USF (Kyle Lab) will conduct in vitro and in vivo (hamster) evaluation of new drug candidates for the treatment of leishmaniasis.
Role: CI
6. Fogarty International Center, NIH (Gerwick, PI) 2007
"International Cooperative Biodiversity Group – Panama"
Building on a previous five-year ICBG award, the consortium are using ecological insight to build a sustainable bioprospecting program in Panama for discovery of both pharmaceutical and agricultural products from plants and marine algae in collaboration with Oregon State University, Panama's National Secretariat for Science, Technology and Innovation, the Nature Foundation of Panama, the University of Panama, Novartis Oncology, and Dow Agrosiences.
Role: PI, Associate Program 2