

## CURRICULUM VITAE

NAME Takafumi Tsuboi	POSITION TITLE Professor and Director		
EDUCATION			
INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
Ehime University School of Medicine	MD	03/80	Medicine
Ehime University Graduate School of Medicine	PhD	03/86	Parasitology

### A. Personal Statement

Proteo-Science Center, Ehime University has been established the eukaryotic wheat germ cell-free system (WGCFS) for translational research especially on development of medical application. My laboratory is a pioneer to use this system for production of malaria proteins that can be vaccine candidates. Recent advance on bioinformatics and genome database of malaria parasites has increased the usefulness of using WGCFS to screen for many parasite proteins in short time comparing with the other systems. We can produce 1800~ malaria proteins. Our system successfully produces correct conformation of the malaria proteins which are difficult to be done in some other systems. Our major research interests are as follows: 1) Genome-wide discovery of novel malaria vaccine candidates, 2) Malaria transmission-blocking vaccine research, 3) Molecular mechanism of malaria parasite invasion into host cell.

### B. Positions and Honors

#### EMPLOYMENT RECORD

1980-1982	Resident in Internal Medicine, Ehime University
1986-1997	Instructor, Department of Parasitology, Ehime University School of Medicine
1997-2003	Associate Professor, Department of Molecular Parasitology, Ehime University School of Medicine
2003-2013	Professor, Division of Proteomedical Sciences, Cell-free Science and Technology Research Center, Ehime University
2006-2012	Director, Venture Business Laboratory, Ehime University
2012-2013	Director, Cell-free Science and Technology Research Center, Ehime University
2003-present	Professor, Division of Malaria Research, Proteo-Science Center, Ehime University
2013-present	Director, Proteo-Science Center, Ehime University

#### HONORS

1985	32nd Award of The Japanese Society Of Nutrition And Dietetics
1993	1st Award of The Ehime Medical Society
2006	53rd Award of The Japanese Society of Parasitology (Koizumi Award)
2014	President, 83 <sup>rd</sup> Annual Meeting of the Japanese Society of Parasitology

#### SOCIETIES

The Japanese Society of Parasitology, director; The Japanese Society of Tropical Medicine, councilor; The Molecular Biology Society of Japan; The Japanese Biochemical Society; American Society of Tropical Medicine and Hygiene; American Society for Microbiology

### C. Editorial Board Members

PLoS ONE (Editor 2013-); Infection and Immunity (2013-18); Parasitology International (2010-); Korean Journal of Parasitology (2009-); Vaccine (2013-); npj Vaccines (2016-)

### D. Peer-Reviewed Publications (selected from 169 publications)

1. **Tsuboi T**, Cao Y-M, Kaslow DC, Shiwaku K, Torii M. Primary structure of a novel ookinete surface protein from *Plasmodium berghei*. **Mol Biochem Parasitol.** 1997, 85(1):131-134.
2. **Tsuboi T**, Kaslow DC, Cao Y-M, Shiwaku K, Torii M. Comparison of *Plasmodium yoelii* ookinete surface antigens with human and avian malaria parasite homologues reveals two highly conserved regions. **Mol Biochem Parasitol.** 1997, 87:107-111.
3. **Tsuboi T**, Cao Y-M, Hitsumoto Y, Yanagi T, Kanbara H, Torii M. Two antigens on zygotes and ookinetes of *Plasmodium yoelii* and *Plasmodium berghei* that are distinct targets of transmission-blocking immunity. **Infect Immun.** 1997, 65 (6):2260-2264.
4. **Tsuboi T**, Kaslow DC, Gozar MMG, Tachibana M, Cao YM, Torii M. Sequence polymorphism in two novel *Plasmodium vivax* ookinete surface proteins, Pvs25 and Pvs28, that are malaria transmission-blocking vaccine candidates. **Mol Med.** 1998, 4(12):772-782.
5. Hisaeda H, Stowers AW, **Tsuboi T**, Collins WE, Sattabongkot J, Suwanabun N, Torii M, Kaslow DC. Antibodies to malaria vaccine candidates Pvs25 and Pvs28 completely block the ability of *Plasmodium vivax* to infect mosquitoes. **Infect Immun.** 2000, 68:6618-6623.
6. **Tsuboi T**, Tachibana M, Kaneko O, Torii M. Transmission-blocking vaccine of vivax malaria. **Parasitol Int.** 2003, 52:1-11.
7. Arakawa T, **Tsuboi T**, Kishimoto A, Sattabongkot J, Suwanabun N, T Rungruang, Matsumoto Y, Tsuji N, Hisaeda H, Stowers A, Shimabukuro I, Sato Y, Torii M. Serum antibodies induced by intranasal immunization of mice with *Plasmodium vivax* Pvs25 co-administered with cholera toxin completely block parasite transmission to mosquitoes. **Vaccine** 2003, 21:3143-3148.
8. Sattabongkot J, **Tsuboi T**, Hisaeda H, Tachibana M, Suwanabun N, Rungruang T, Cao Y-M, Stowers A, Sirichaisinthop J, Coleman RE, Torii M. Blocking of transmission to mosquitoes by antibody to *Plasmodium vivax* malaria vaccine candidates Pvs25 and Pvs28 despite antigenic polymorphism in field isolates. **Am J Trop Med Hyg.** 2003, 69:536-541.
9. Sattabongkot J, **Tsuboi T**, Zollner GE, Sirichaisinthop J, Cui L. *Plasmodium vivax* transmission: chances for control? **Trends Parasitol.** 2004, 20:192-198.

10. Li F, Templeton TJ, Popov VL, Comer JE, **Tsuboi T**, Torii M, Vinetz JM. *Plasmodium* ookinete-secreted proteins secreted through a common micronemal pathway are targets of blocking malaria transmission. **J Biol Chem.** 2004, 279:26635-26644.
11. Arakawa T, Komesu A, Otsuki H, Sattabongkot J, Udomsangpetch R, Matsumoto Y, Tsuji N, Wu Y, Torii M, **Tsuboi T**. Nasal immunization with a malaria transmission-blocking vaccine candidate, Pfs25, induces complete protective immunity in mice against field isolates of *Plasmodium falciparum*. **Infect Immun.** 2005, 73:7375-7380.
12. **Tsuboi T**, Takeo S, Iriko H, Jin L, Tsuchimochi M, Matsuda S, Han ET, Otsuki H, Kaneko O, Sattabongkot J, Udomsangpetch R, Sawasaki T, Torii M, Endo Y. Wheat germ cell-free system-based production of malaria proteins for discovery of novel vaccine candidates. **Infect Immun.** 2008, 76:1702-1708.
13. Otsuki H, Kaneko O, Thongkukiattkul A, Tachibana M, Iriko H, Takeo S, **Tsuboi T**, Torii M. Single amino acid substitution in *Plasmodium yoelii* erythrocyte ligand determines its localization and controls parasite virulence. **Proc Natl Acad Sci USA.** 2009, 106:7167-7172.
14. VanBuskirk KM, O'Neill MT, De La Vega P, Maier AG, Krzych U, Williams J, Dowler MG, Sacci, Jr. JB, Kangwanransan N, **Tsuboi T**, Kneteman NM, Heppner, Jr. DG, Murdock BA, Mikolajczak SA, Aly ASI, Cowman AF Kappe SHI. Preerythrocytic, live-attenuated *Plasmodium falciparum* vaccine candidates by design. **Proc Natl Acad Sci USA.** 2009, 106:13004-13009.
15. Takeo S, Arumugam TU, Torii M, **Tsuboi T**. Wheat germ cell-free technology for accelerating the malaria vaccine research. **Expert Opin Drug Discov.** 2009, 4:1191-1199.
16. Arakawa T, Tachibana M, Miyata T, Harakuni T, Kohama H, Matsumoto Y, Tsuji N, Hisaeda H, Stowers A, Torii M, **Tsuboi T**. Malaria ookinete surface protein-based vaccination via the intranasal route completely blocks parasite transmission in both passive and active vaccination regimens in a rodent model of malaria infection. **Infect Immun.** 2009, 77: 5496-5500.
17. **Tsuboi T**, Takeo S, Sawasaki T, Torii M, Endo Y. An efficient approach to the production of vaccines against the malaria parasite. **Methods Mol Biol.** 2010, 607:73-83.
18. **Tsuboi T**, Takeo S, Arumugam TU, Otsuki H, Torii M. The wheat germ cell-free protein synthesis system: a key tool for novel malaria vaccine candidate discovery. **Acta Trop.** 2010, 114:171-176.
19. Miyata T, Harakuni T, **Tsuboi T**, Sattabongkot J, Kohama H, Tachibana M, Matsuzaki G, Torii M, Arakawa T. *Plasmodium vivax* ookinete surface protein, Pvs25, linked to cholera toxin B subunit induces potent transmission-blocking immunity by intranasal as well as subcutaneous immunization. **Infect Immun.** 2010, 78:3773-3782.
20. Chen JH, Jung JW, Wang Y, Ha KS, Lu F, Lim CS, Takeo S, **Tsuboi T**, Han ET. Immunoproteomics profiling of blood stage *Plasmodium vivax* infection by high-throughput screening assays. **J Proteome Res.** 2010, 9:6479-6489.
21. Tachibana M, Wu Y, Iriko H, Muratova O, Macdonald NJ, Sattabongkot J, Takeo S, Otsuki H, Torii M, **Tsuboi T**. N-terminal pro-domain of Pfs230 synthesized using cell-free system is sufficient to induce the complement dependent malaria transmission-blocking activity. **Clin Vaccine Immunol.** 2011, 18:1343-1350.
22. Farrance CE, Rhee A, Jones RM, Musychuk K, Shamloul M, Sharma S, Mett V, Chichester JA, Streatfield SJ, Roeffen W, van de Vegte-Bolmer M, Sauerwein RW, **Tsuboi T**, Muratova OV, Wu Y, Yusibov V. A Plant-Produced Pfs230 Vaccine Candidate Blocks Transmission of *Plasmodium falciparum*. **Clin Vaccine Immunol.** 2011, 18:1351-1357.
23. Rui E, Fernandez-Becerra C, Takeo S, Sanz S, Lacerda MV, **Tsuboi T**, Del Portillo HA. *Plasmodium vivax*: comparison of immunogenicity among proteins expressed in the cell-free systems of *Escherichia coli* and wheat germ by suspension array assays. **Malar J.** 2011, 10:192.
24. Arumugam TU, Takeo S, Yamasaki T, Thonkukiattkul A, Miura K, Otsuki H, Zhou H, Long CA, Sattabongkot J, Thompson J, Wilson DW, Beeson JG, Healer J, Crabb BS, Cowman AF, Torii M, **Tsuboi T**. Discovery of GAMA, a *Plasmodium falciparum* merozoite micronemal protein, as a novel blood-stage vaccine candidate antigen. **Infect Immun.** 2011, 79:4523-4532.
25. Volz JC, Bártfai R, Petter M, Langer C, Josling GA, **Tsuboi T**, Schwach F, Baum J, Rayner JC, Stunnenberg HG, Duffy MF, Cowman AF. PfSET10, a *Plasmodium falciparum* methyltransferase, maintains the active var gene in a poised state during parasite division. **Cell Host Microbe.** 2012, 11(1):7-18.
26. Tachibana M, Sato C, Otsuki H, Sattabongkot J, Kaneko O, Torii M, **Tsuboi T**. *Plasmodium vivax* gametocyte protein Pvs230 is a transmission-blocking vaccine candidate. **Vaccine.** 2012, 30:1807-1812.
27. Fowkes FJ, McGready R, Cross NJ, Hommel M, Simpson JA, Elliott SR, Richards JS, Lackovic K, Viladpai-Nguen J, Narum D, **Tsuboi T**, Anders RF, Nosten F, Beeson JG. New insights into acquisition, boosting and longevity of immunity to malaria in pregnant women. **J Infect Dis.** 2012, 206(10):1612-21.
28. Mueller I, Galinski MR, **Tsuboi T**, Arevalo-Herrera M, Collins WE, King CL. Natural Acquisition of Immunity to *Plasmodium vivax*: Epidemiological Observations and Potential Targets. in: Rollinson D, (Ed.), *The Epidemiology of Plasmodium vivax: History, Hiatus and Hubris*, Part B, Academic Press, **Adv Parasitol.** 2013, 81:77-131.
29. Cheng Y, Wang Y, Ito D, Kong DH, Ha KS, Chen JH, Lu F, Li J, Wang B, Takashima E, Sattabongkot J, **Tsuboi T**, Han ET. PvMSP1P, merozoite surface protein 1 paralog, is a novel erythrocyte-binding ligand of *Plasmodium vivax*. **Infect Immun.** 2013, 81(5):1585-1595.
30. Richards JS, Arumugam TU, Reiling L, Healer J, Hodder AN, Fowkes FJI, Cross N, Langer C, Takeo S, Uboldi AD, Thompson JK, Gilson PR, Coppel RL, Siba PM, King CL, Torii M, Chitnis CE, Narum DL, Mueller I, Crabb BS, Cowman AF, **Tsuboi T**, Beeson JG. Identification and prioritization of merozoite antigens as targets of protective human immunity to *Plasmodium falciparum* malaria for vaccine and biomarker development. **J Immunol.** 2013, 191:795-809.
31. Ito D, Hasegawa T, Miura K, Yamasaki T, Arumugam TU, Thonkukiattkul A, Takeo S, Takashima E, Sattabongkot J, Han ET, Long CA, Torii M, **Tsuboi T**. RALP1 is a rhoptry-neck erythrocyte-binding protein of *Plasmodium falciparum* merozoite and a potential blood-stage vaccine candidate antigen. **Infect Immun.** 2013, 81(11):4290-4298.
32. Miura K, Takashima E, Deng B, Tullo G, Diouf A, Moretz SE, Nikolaeva D, Diakite M, Fairhurst RM, Fay MP, Long CA, **Tsuboi T**. Functional comparison of *Plasmodium falciparum* transmission-blocking vaccine candidates by the standard membrane-feeding assay. **Infect Immun.** 2013, 81(12):4377-4382.

33. Kaneko A, Chaves L, Taleo G, Kalkoa M, Isozumi R, Wickremasinghe R, Perlmann H, Takeo S, **Tsuboi T**, Tachibana S-I, Kimura M, Björkman A, Troye-Blomberg M, Tanabe K, Drakeley C. Characteristic age distribution of *Plasmodium vivax* infections after malaria elimination on Aneityum island. **Infect Immun.** 2014, 82(1):243-252.
34. Arumugam TU, Ito D, Takashima E, Tachibana M, Ishino T, Torii M, **Tsuboi T**. Application of wheat germ cell-free protein expression system for novel malaria vaccine candidate discovery. **Expert Rev Vaccines.** 2014, 13(1):75-85.
35. Arakawa T, **Tsuboi T**, Sattabongkot J, Sakao K, Torii M, Miyata T. Tricomponent complex loaded with a mosquito-stage antigen of malaria parasite induces potent transmission-blocking immunity. **Clin Vaccine Immunol.** 2014, 21(4):561-569.
36. Sattabongkot J, **Tsuboi T**, Han ET, Bantuchai S, Buates S. Loop-mediated isothermal amplification assay for rapid diagnosis of malaria infections in an area of endemicity in Thailand. **J Clin Microbiol.** 2014, 52(5):1471-1477.
37. Lu F, Li J, Wang B, Cheng Y, Kong DH, Cui L, Ha KS, Sattabongkot J, **Tsuboi T**, Han ET. Profiling the humoral immune responses to *Plasmodium vivax* infection and identification of candidate immunogenic rhoptry-associated membrane antigen (RAMA). **J Proteomics.** 2014, 102:66-82.
38. Fujii Y, Kaneko S, Nzou SM, Mwau M, Njenga SM, Tanigawa C, Kimotho J, Mwangi AW, Kiche I, Matsumoto S, Niki M, Osada-Oka M, Ichinose Y, Inoue M, Itoh M, Tachibana H, Ishii K, **Tsuboi T**, Yoshida LM, Mondal D, Haque R, Hamano S, Changoma M, Hoshi T, Kamo K, Karama M, Miura M, Hirayama K. Serological surveillance development for tropical infectious diseases using simultaneous microsphere-based multiplex assays and finite mixture models. **PLoS Negl Trop Dis.** 2014, 8(7):e3040.
39. Otsuki H, Yokouchi Y, Iyoku N, Tachibana M, **Tsuboi T**, Torii M. Rodent malaria lactate dehydrogenase assay provides a high throughput solution for in vivo vaccine studies. **Parasitol Int.** 2015, 64:60-63.
40. Tanabe K, Zollner G, Vaughand JA, Sattabongkot J, Khuntirat B, Honma H, Mita T, **Tsuboi T**, Coleman R. *Plasmodium falciparum*: Genetic diversity and complexity of infections in an isolated village in western Thailand. **Parasitol Int.** 2015, 64:260-266.
41. Tachibana M, Suwanabun N, Kaneko O, Iriko H, Otsuki H, Sattabongkot J, Kaneko A, Herrera S, Torii M, **Tsuboi T**. *Plasmodium vivax* gametocyte proteins, Pvs48/45 and Pvs47, induce transmission-reducing antibodies by DNA immunization. **Vaccine.** 2015, 33:1901-1908.
42. Wu Y, Sinden RE, Churcher TS, **Tsuboi T**, Yusibov V. Development of malaria transmission-blocking vaccines: from concept to product. **Adv Parasitol.** 2015, 89:109-152.
43. Kapulu MC, Da DF, Miura K, Li Y, Blagborough AM, Churcher TS, Nikolaeva D, Williams AR, Goodman AL, Sangare I, Turner AV, Cottingham MG, Nicosia A, Straschil U, **Tsuboi T**, Gilbert SC, Long CA, Sinden RE, Draper SJ, Hill AVS, Cohuet A, Biswas S. Comparative assessment of transmission-blocking vaccine candidates against *Plasmodium falciparum*. **Sci Rep.** 2015, 5:11193.
44. Wang B, Lu F, Cheng Y, Chen JH, Jeon HY, Ha KS, Cao J, Nyunt MH, Han JH, Lee SK, Kyaw MP, Sattabongkot J, Takashima E, **Tsuboi T**, Han ET. Immunoprofiling of the tryptophan-rich antigen family in *Plasmodium vivax*. **Infect Immun.** 2015, 83(8):3083-3095.
45. Aguiar JC, Bolton J, Wanga J, Sacci JB, Iriko H, Mazeika JK, Han ET, Limbach K, Patterson NB, Sedegah M, Cruz AM, **Tsuboi T**, Hoffman SL, Carucci D, Hollingdale MR, Villasante ED, Richie TL. Discovery of novel *Plasmodium falciparum* pre-erythrocytic antigens for vaccine development. **PLoS One.** 2015, 10(8):e0136109.
46. **Tsuboi T**, Takashima E. Antibody titre as a surrogate of protection of the first malaria subunit vaccine, RTS,S/AS01. **Lancet Infect Dis.** 2015, 15(12):1371-2.
47. Feng H, Gupta B, Wang M, Zheng W, Zheng L, Zhu X, Yang Y, Fang Q, Luo E, Fan Q, **Tsuboi T**, Cao Y, Cui L. Genetic diversity of transmission-blocking vaccine candidate Pvs48/45 in *Plasmodium vivax* populations in China. **Parasit Vectors.** 2015, 8:615.
48. Takashima E, Morita M, **Tsuboi T**. Vaccine candidates for malaria: what's new? **Expert Rev Vaccines.** 2016, 15(1):1-3.
49. Charnaud, SC, McGready R, Herten-Crabb A, Powell R, Guy A, Langer C, Richards JS, Gilson PR, Chotivanich K, **Tsuboi T**, Narum DL, Pimanpanarak M, Simpson JA, Beeson JG, Nosten F, Fowkes FJI. Maternal-foetal transfer of *Plasmodium falciparum* and *Plasmodium vivax* antibodies in a low transmission setting. **Sci Rep.** 2016, 6:20859.
50. Lin CS, Uboldi AD, Epp C, Bujard H, **Tsuboi T**, Czabotar PE, Cowman AF. Multiple *P. falciparum* merozoite surface protein 1 complexes mediate merozoite binding to human erythrocytes. **J Biol Chem.** 2016, 291(14):7703-15.
51. Han JH, Lee SK, Wang B, Muh F, Nyunt MH, Na S, Ha KS, Hong SH, Park WS, Sattabongkot J, **Tsuboi T**, Han ET. Identification of a reticulocyte-specific binding domain of *Plasmodium vivax* reticulocyte-binding protein 1 that is homologous to the Pfrh4 erythrocyte-binding domain. **Sci Rep.** 2016, 6:26993.
52. McLean ARD, Boel ME, McGready R, Ataide R, Drew D, **Tsuboi T**, Beeson JG, Nosten F, Simpson JA, Fowkes FJI. Antibody responses to *Plasmodium falciparum* and *Plasmodium vivax* blood-stage and sporozoite antigens in the postpartum period. **Sci Rep.** 2016, 6:32159.
53. Weaver R, Reiling L, Feng G, Drew DR, Mueller I, Siba PM, **Tsuboi T**, Richards JS, Fowkes FJI, Beeson JG. The association between naturally acquired IgG subclass specific antibodies to the PfrH5 invasion complex and protection from *Plasmodium falciparum* malaria. **Sci Rep.** 2016, 6:33094.
54. Ntege EH, Arisue N, Ito D, Hasegawa T, Palacpac NMQ, Egwang TG, Horii T, Takashima E, **Tsuboi T**. Identification of *Plasmodium falciparum* reticulocyte binding protein homologue 5-interacting protein, PfRipr, as a highly conserved blood-stage malaria vaccine candidate. **Vaccine.** 2016, 34:5612-5622.
55. Bargieri DY, Thiberge S, Tay CL, Carey AF, Rantz A, Hischen F, Lorthiois A, Straschil U, Singh P, Singh S, Triglia T, **Tsuboi T**, Cowman A, Chitnis C, Alano P, Baum J, Pradel G, Lavazec C, Ménard R. *Plasmodium* merozoite TRAP family protein is essential for vacuole membrane disruption and gamete egress from erythrocytes. **Cell Host Microbe.** 2016, 20(5):618-630.