

References

References

1. Snow RW, Guerra CA, Noor AM, Myint HY & Hay SI. The global distribution of clinical episodes of *Plasmodium falciparum* malaria. *Nature* **434**, 214-217 (2005).
2. Hastings IM, Bray PG & Ward SA. Parasitology. A requiem for chloroquine. *Science* **298**, 74-75 (2002).
3. Wootton JC, Feng X, Ferdig MT, Cooper RA, Mu J *et al.* Genetic diversity and chloroquine selective sweeps in *Plasmodium falciparum*. *Nature* **418**, 320-323 (2002).
4. Sidhu AB, Verdier-Pinard D & Fidock DA. Chloroquine resistance in *Plasmodium falciparum* malaria parasites conferred by *pfcr* mutations. *Science* **298**, 210-213 (2002).
5. Hemingway J, Field L & Vontas J. An overview of insecticide resistance. *Science* **298**, 96-97 (2002).
6. Hartl DL. The origin of malaria: mixed messages from genetic diversity. *Nat. Rev. Microbiol.* **2**, 15-22 (2004).
7. Hay SI, Guerra CA, Tatem AJ, Atkinson PM & Snow RW. Urbanization, malaria transmission and disease burden in Africa. *Nat. Rev. Microbiol.* **3**, 81-90 (2005).
8. Gallup JL & Sachs JD. The economic burden of malaria. *Am. J. Trop. Med. Hyg.* **64**, 85-96 (2001).
9. Jomaa H, Wiesner J, Sanderbrand S, Altincicek B, Weidemeyer C *et al.* Inhibitors of the nonmevalonate pathway of isoprenoid biosynthesis as antimalarial drugs. *Science* **285**, 1573-1576 (1999).
10. Surolia N & Surolia A. Triclosan offers protection against blood stages of malaria by inhibiting enoyl-ACP reductase of *Plasmodium falciparum*. *Nat. Med.* **7**, 167-173 (2001).
11. Florens L, Washburn MP, Raine JD, Anthony RM, Grainger M *et al.* A proteomic view of the *Plasmodium falciparum* life cycle. *Nature* **419**, 520-526 (2002).
12. Lasonder E, Ishihama Y, Andersen JS, Vermunt AM, Pain A *et al.* Analysis of the *Plasmodium falciparum* proteome by high-accuracy mass spectrometry. *Nature* **419**, 537-542 (2002).
13. Doolittle RF. The grand assault. *Nature* **419**, 493-494 (2002).
14. Rich SM & Ayala FJ. Progress in malaria research: the case for phylogenetics. *Adv. Parasitol.* **54**, 255-280 (2003).
15. Lou J, Lucas R & Grau GE. Pathogenesis of cerebral malaria: recent experimental data and possible applications for humans. *Clin. Microbiol. Rev.* **14**, 810-20, table (2001).
16. Rae C, McQuillan JA, Parekh SB, Bubb WA, Weiser S *et al.* Brain gene expression, metabolism, and bioenergetics: interrelationships in murine models of cerebral and noncerebral malaria. *FASEB J.* **18**, 499-510 (2004).
17. de Roode JC, Pansini R, Cheesman SJ, Helinski ME, Huijben S *et al.* Virulence and competitive ability in genetically diverse malaria infections. *Proc. Natl. Acad. Sci. U. S. A* **102**, 7624-7628 (2005).
18. Ellis J, Ozaki LS, Gwadz RW, Cochrane AH, Nussenzweig V *et al.* Cloning and expression in *E. coli* of the malarial sporozoite surface antigen gene from *Plasmodium knowlesi*. *Nature* **302**, 536-538 (1983).
19. Dame JB, Williams JL, McCutchan TF, Weber JL, Wirtz RA *et al.* Structure of the gene encoding the immunodominant surface antigen on the sporozoite of the human malaria parasite *Plasmodium falciparum*. *Science* **225**, 593-599 (1984).
20. Dame JB, Arnot DE, Bourke PF, Chakrabarti D, Christodoulou Z *et al.* Current status of the *Plasmodium falciparum* genome project. *Mol. Biochem. Parasitol.* **79**, 1-12 (1996).
21. Goffeau A, Barrell BG, Bussey H, Davis RW, Dujon B *et al.* Life with 6000 genes. *Science* **274**, 546, 563-546, 567 (1996).
22. Foote SJ & Kemp DJ. Chromosomes of malaria parasites. *Trends Genet.* **5**, 337-342 (1989).
23. Janse CJ. Chromosome size polymorphisms and DNA rearrangements in *Plasmodium*. *Parasitol. Today* **9**, 19-22 (1993).
24. Scherf A, Figueiredo LM & Freitas-Junior LH. *Plasmodium* telomeres: a pathogen's perspective. *Curr. Opin. Microbiol.* **4**, 409-414 (2001).
25. Carlton JM, Vinkenoog R, Waters AP & Walliker D. Gene synteny in species of *Plasmodium*. *Mol. Biochem. Parasitol.* **93**, 285-294 (1998).
26. Janse CJ, Carlton JM, Walliker D & Waters AP. Conserved location of genes on polymorphic chromosomes of four species of malaria parasites. *Mol. Biochem. Parasitol.* **68**, 285-296 (1994).

27. Waller RF & McFadden GI. The apicoplast. **In:** Malaria parasites, genomes and molecular biology - p289-338. Waters AP & Janse CJ (eds.) Caister Academic Press, Wymondham (2004).
28. Moorthy VS, Good MF & Hill AV. Malaria vaccine developments. *Lancet* **363**, 150-156 (2004).
29. Hoffman SL, Bancroft WH, Gottlieb M, James SL, Burroughs EC *et al.* Funding for malaria genome sequencing. *Nature* **387**, 647 (1997).
30. Lander ES, Linton LM, Birren B, Nusbaum C, Zody MC *et al.* Initial sequencing and analysis of the human genome. *Nature* **409**, 860-921 (2001).
31. Gibbs RA, Weinstock GM, Metzker ML, Muzny DM, Sodergren EJ *et al.* Genome sequence of the Brown Norway rat yields insights into mammalian evolution. *Nature* **428**, 493-521 (2004).
32. Waterston RH, Lindblad-Toh K, Birney E, Rogers J, Abril JF *et al.* Initial sequencing and comparative analysis of the mouse genome. *Nature* **420**, 520-562 (2002).
33. Aparicio S, Chapman J, Stupka E, Putnam N, Chia JM *et al.* Whole-genome shotgun assembly and analysis of the genome of *Fugu rubripes*. *Science* **297**, 1301-1310 (2002).
34. Dehal P, Satou Y, Campbell RK, Chapman J, Degnan B *et al.* The draft genome of *Ciona intestinalis*: insights into chordate and vertebrate origins. *Science* **298**, 2157-2167 (2002).
35. Adams MD, Celniker SE, Holt RA, Evans CA, Gocayne JD *et al.* The genome sequence of *Drosophila melanogaster*. *Science* **287**, 2185-2195 (2000).
36. Holt RA, Subramanian GM, Halpern A, Sutton GG, Charlab R *et al.* The genome sequence of the malaria mosquito *Anopheles gambiae*. *Science* **298**, 129-149 (2002).
37. The *C.elegans* Sequencing Consortium. Genome sequence of the nematode *C. elegans*: a platform for investigating biology. *Science* **282**, 2012-2018 (1998).
38. Stein LD, Bao Z, Blasiar D, Blumenthal T, Brent MR *et al.* The Genome Sequence of *Caenorhabditis briggsae*: A Platform for Comparative Genomics. *PLoS. Biol.* **1**, E45 (2003).
39. Goff SA, Ricke D, Lan TH, Presting G, Wang R *et al.* A draft sequence of the rice genome (*Oryza sativa* L. ssp. *japonica*). *Science* **296**, 92-100 (2002).
40. Yu J, Hu S, Wang J, Wong GK, Li S *et al.* A draft sequence of the rice genome (*Oryza sativa* L. ssp. *indica*). *Science* **296**, 79-92 (2002).
41. The Arabidopsis Genome Initiative. Analysis of the genome sequence of the flowering plant *Arabidopsis thaliana*. *Nature* **408**, 796-815 (2000).
42. Gardner MJ, Hall N, Fung E, White O, Berriman M *et al.* Genome sequence of the human malaria parasite *Plasmodium falciparum*. *Nature* **419**, 498-511 (2002).
43. Abrahamsen MS, Templeton TJ, Enomoto S, Abrahante JE, Zhu G *et al.* Complete genome sequence of the apicomplexan, *Cryptosporidium parvum*. *Science* **304**, 441-445 (2004).
44. Xu P, Widmer G, Wang Y, Ozaki LS, Alves JM *et al.* The genome of *Cryptosporidium hominis*. *Nature* **431**, 1107-1112 (2004).
45. Gardner MJ, Bishop R, Shah T, de Villiers EP, Carlton JM *et al.* Genome Sequence of *Theileria parva*, a Bovine Pathogen That Transforms Lymphocytes. *Science* **309**, 134-137 (2005).
46. Pain A, Renauld H, Berriman M, Murphy L, Yeats CA *et al.* Genome of the Host-Cell Transforming Parasite *Theileria annulata* Compared with *T. parva*. *Science* **309**, 131-133 (2005).
47. Berriman M, Ghedin E, Hertz-Fowler C, Blandin G, Renauld H *et al.* The genome of the African trypanosome *Trypanosoma brucei*. *Science* **309**, 416-422 (2005).
48. El Sayed NM, Myler PJ, Bartholomeu DC, Nilsson D, Aggarwal G *et al.* The genome sequence of *Trypanosoma cruzi*, etiologic agent of Chagas disease. *Science* **309**, 409-415 (2005).
49. Ivens AC, Peacock CS, Worthey EA, Murphy L, Aggarwal G *et al.* The genome of the kinetoplastid parasite, *Leishmania major*. *Science* **309**, 436-442 (2005).
50. Loftus B, Anderson I, Davies R, Alsmark UC, Samuelson J *et al.* The genome of the protist parasite *Entamoeba histolytica*. *Nature* **433**, 865-868 (2005).
51. Carlton JM, Angiuoli SV, Suh BB, Kooij TW, Perteira M *et al.* Genome sequence and comparative analysis of the model rodent malaria parasite *Plasmodium yoelii yoelii*. *Nature* **419**, 512-519 (2002).
52. Hall N, Karras M, Raine JD, Carlton JM, Kooij TW *et al.* A comprehensive survey of the *Plasmodium* life cycle by genomic, transcriptomic, and proteomic analyses. *Science* **307**, 82-86 (2005).
53. Wolfe KH & Shields DC. Molecular evidence for an ancient duplication of the entire yeast genome. *Nature* **387**, 708-713 (1997).



References

54. Zdobnov EM, von Mering C, Letunic I, Torrents D, Suyama M *et al.* Comparative genome and proteome analysis of *Anopheles gambiae* and *Drosophila melanogaster*. *Science* **298**, 149-159 (2002).
55. Rubin GM, Yandell MD, Wortman JR, Gabor Miklos GL, Nelson CR *et al.* Comparative genomics of the eukaryotes. *Science* **287**, 2204-2215 (2000).
56. Kellis M, Patterson N, Endrizzi M, Birren B & Lander ES. Sequencing and comparison of yeast species to identify genes and regulatory elements. *Nature* **423**, 241-254 (2003).
57. Glaser P, Frangeul L, Buchrieser C, Rusniok C, Amend A *et al.* Comparative genomics of *Listeria* species. *Science* **294**, 849-852 (2001).
58. Ivanova N, Sorokin A, Anderson I, Galleron N, Candelon B *et al.* Genome sequence of *Bacillus cereus* and comparative analysis with *Bacillus anthracis*. *Nature* **423**, 87-91 (2003).
59. Parkhill J, Sebaihia M, Preston A, Murphy LD, Thomson N *et al.* Comparative analysis of the genome sequences of *Bordetella pertussis*, *Bordetella parapertussis* and *Bordetella bronchiseptica*. *Nat. Genet.* **35**, 32-40 (2003).
60. van Lin LH, Pace T, Janse CJ, Birago C, Ramesar J *et al.* Interspecies conservation of gene order and intron-exon structure in a genomic locus of high gene density and complexity in *Plasmodium*. *Nucleic Acids Res.* **29**, 2059-2068 (2001).
61. Chiaromonte F, Yang S, Elnitski L, Yap VB, Miller W *et al.* Association between divergence and interspersed repeats in mammalian noncoding genomic DNA. *Proc. Natl. Acad. Sci. U. S. A* **98**, 14503-14508 (2001).
62. Freitas-Junior LH, Bottius E, Pirrit LA, Deitsch KW, Scheidig C *et al.* Frequent ectopic recombination of virulence factor genes in telomeric chromosome clusters of *P. falciparum*. *Nature* **407**, 1018-1022 (2000).
63. Dehal P, Predki P, Olsen AS, Kobayashi A, Folta P *et al.* Human chromosome 19 and related regions in mouse: conservative and lineage-specific evolution. *Science* **293**, 104-111 (2001).
64. Eichler EE. Recent duplication, domain accretion and the dynamic mutation of the human genome. *Trends Genet.* **17**, 661-669 (2001).
65. Stankiewicz P & Lupski JR. Genome architecture, rearrangements and genomic disorders. *Trends Genet.* **18**, 74-82 (2002).
66. Coghlan A & Wolfe KH. Fourfold faster rate of genome rearrangement in nematodes than in *Drosophila*. *Genome Res.* **12**, 857-867 (2002).
67. Pevzner P & Tesler G. Genome rearrangements in mammalian evolution: lessons from human and mouse genomes. *Genome Res.* **13**, 37-45 (2003).
68. Pevzner P & Tesler G. Human and mouse genomic sequences reveal extensive breakpoint reuse in mammalian evolution. *Proc. Natl. Acad. Sci. U. S. A* **100**, 7672-7677 (2003).
69. van Lin LH, Janse CJ & Waters AP. The conserved genome organisation of non-falciparum malaria species: the need to know more. *Int. J. Parasitol.* **30**, 357-370 (2000).
70. Eichler EE & Sankoff D. Structural dynamics of eukaryotic chromosome evolution. *Science* **301**, 793-797 (2003).
71. Liti G & Louis EJ. Yeast Evolution and Comparative Genomics. *Annu. Rev. Microbiol.* (2004).
72. van Lin LH, Pace T, Janse CJ, Scotti R & Ponzi M. A long range restriction map of chromosome 5 of *Plasmodium berghei* demonstrates a chromosome specific symmetrical subtelomeric organisation. *Mol. Biochem. Parasitol.* **86**, 111-115 (1997).
73. Wirth DF. Biological revelations. *Nature* **419**, 495-496 (2002).
74. Gardner MJ, Tettelin H, Carucci DJ, Cummings LM, Aravind L *et al.* Chromosome 2 sequence of the human malaria parasite *Plasmodium falciparum*. *Science* **282**, 1126-1132 (1998).
75. Bowman S, Lawson D, Basham D, Brown D, Chillingworth T *et al.* The complete nucleotide sequence of chromosome 3 of *Plasmodium falciparum*. *Nature* **400**, 532-538 (1999).
76. Foth BJ, Ralph SA, Tonkin CJ, Struck NS, Fraunholz M *et al.* Dissecting apicoplast targeting in the malaria parasite *Plasmodium falciparum*. *Science* **299**, 705-708 (2003).
77. Zuegge J, Ralph S, Schmuker M, McFadden GI & Schneider G. Deciphering apicoplast targeting signals--feature extraction from nuclear-encoded precursors of *Plasmodium falciparum* apicoplast proteins. *Gene* **280**, 19-26 (2001).
78. Foth BJ & McFadden GI. The apicoplast: a plastid in *Plasmodium falciparum* and other Apicomplexan parasites. *Int. Rev. Cytol.* **224**, 57-110 (2003).

79. Ralph SA, van Dooren GG, Waller RF, Crawford MJ, Fraunholz MJ *et al.* Tropical infectious diseases: Metabolic maps and functions of the Plasmodium falciparum apicoplast. *Nat. Rev. Microbiol.* **2**, 203-216 (2004).
80. Baruch DI, Pasloske BL, Singh HB, Bi X, Ma XC *et al.* Cloning the P. falciparum gene encoding PfEMP1, a malarial variant antigen and adherence receptor on the surface of parasitized human erythrocytes. *Cell* **82**, 77-87 (1995).
81. Smith JD, Chitnis CE, Craig AG, Roberts DJ, Hudson-Taylor DE *et al.* Switches in expression of Plasmodium falciparum var genes correlate with changes in antigenic and cytoadherent phenotypes of infected erythrocytes. *Cell* **82**, 101-110 (1995).
82. Su XZ, Heatwole VM, Wertheimer SP, Guinet F, Herrfeldt JA *et al.* The large diverse gene family var encodes proteins involved in cytoadherence and antigenic variation of Plasmodium falciparum-infected erythrocytes. *Cell* **82**, 89-100 (1995).
83. Cheng Q, Cloonan N, Fischer K, Thompson J, Waime G *et al.* stevor and rif are Plasmodium falciparum multicopy gene families which potentially encode variant antigens. *Mol. Biochem. Parasitol.* **97**, 161-176 (1998).
84. Kyes SA, Rowe JA, Kriek N & Newbold CI. Rifins: a second family of clonally variant proteins expressed on the surface of red cells infected with Plasmodium falciparum. *Proc. Natl. Acad. Sci. U. S. A* **96**, 9333-9338 (1999).
85. Figueiredo LM, Freitas-Junior LH, Bottius E, Olivo-Marin JC & Scherf A. A central role for Plasmodium falciparum subtelomeric regions in spatial positioning and telomere length regulation. *EMBO J.* **21**, 815-824 (2002).
86. Scherf A, Hernandez-Rivas R, Buffet P, Bottius E, Benatar C *et al.* Antigenic variation in malaria: in situ switching, relaxed and mutually exclusive transcription of var genes during intra-erythrocytic development in Plasmodium falciparum. *EMBO J.* **17**, 5418-5426 (1998).
87. Kooij TW, Carlton JM, Bidwell SL, Hall N, Ramesar J *et al.* A Plasmodium Whole-Genome Synteny Map: Indels and Synteny Breakpoints as Foci for Species-Specific Genes. *PLoS Pathog.* **1**, e44 (2005).
88. Thompson J, Janse CJ & Waters AP. Comparative genomics in Plasmodium: a tool for the identification of genes and functional analysis. *Mol. Biochem. Parasitol.* **118**, 147-154 (2001).
89. Hayward RE, Derisi JL, Alfadhli S, Kaslow DC, Brown PO *et al.* Shotgun DNA microarrays and stage-specific gene expression in Plasmodium falciparum malaria. *Mol. Microbiol.* **35**, 6-14 (2000).
90. Mamoun CB, Gluzman IY, Hott C, MacMillan SK, Amarakone AS *et al.* Co-ordinated programme of gene expression during asexual intraerythrocytic development of the human malaria parasite Plasmodium falciparum revealed by microarray analysis. *Mol. Microbiol.* **39**, 26-36 (2001).
91. Le Roch KG, Zhou Y, Blair PL, Grainger M, Moch JK *et al.* Discovery of gene function by expression profiling of the malaria parasite life cycle. *Science* **301**, 1503-1508 (2003).
92. Bozdech Z, Llinas M, Pulliam BL, Wong ED, Zhu J *et al.* The Transcriptome of the Intraerythrocytic Developmental Cycle of Plasmodium falciparum. *PLoS Biol.* **1**, E5 (2003).
93. Li L, Brunk BP, Kissinger JC, Pape D, Tang K *et al.* Gene discovery in the apicomplexa as revealed by EST sequencing and assembly of a comparative gene database. *Genome Res.* **13**, 443-454 (2003).
94. Li L, Crabtree J, Fischer S, Pinney D, Stoeckert CJ, Jr. *et al.* ApiEST-DB: analyzing clustered EST data of the apicomplexan parasites. *Nucleic Acids Res.* **32 Database issue**, D326-D328 (2004).
95. Watanabe J, Sasaki M, Suzuki Y & Sugano S. Analysis of transcriptomes of human malaria parasite Plasmodium falciparum using full-length enriched library: identification of novel genes and diverse transcription start sites of messenger RNAs. *Gene* **291**, 105-113 (2002).
96. Watanabe J, Suzuki Y, Sasaki M & Sugano S. Full-malaria 2004: an enlarged database for comparative studies of full-length cDNAs of malaria parasites, Plasmodium species. *Nucleic Acids Res.* **32 Database issue**, D334-D338 (2004).
97. Cui L, Rzomp KA, Fan Q, Martin SK & Williams J. Plasmodium falciparum: Differential Display Analysis of Gene Expression during Gametocytogenesis. *Exp. Parasitol.* **99**, 244-254 (2001).
98. Fidock DA, Nguyen TV, Ribeiro JM, Valenzuela JG & James AA. Plasmodium falciparum: generation of a cDNA library enriched in sporozoite-specific transcripts by directional tag subtractive hybridization. *Exp. Parasitol.* **95**, 220-225 (2000).



References

99. Munasinghe A, Patankar S, Cook BP, Madden SL, Martin RK *et al.* Serial analysis of gene expression (SAGE) in *Plasmodium falciparum*: application of the technique to A-T rich genomes. *Mol. Biochem. Parasitol.* **113**, 23-34 (2001).
100. Patankar S, Munasinghe A, Shoaibi A, Cummings LM & Wirth DF. Serial analysis of gene expression in *Plasmodium falciparum* reveals the global expression profile of erythrocytic stages and the presence of anti-sense transcripts in the malarial parasite. *Mol. Biol. Cell* **12**, 3114-3125 (2001).
101. Le Roch KG, Johnson JR, Florens L, Zhou Y, Santrosyan A *et al.* Global analysis of transcript and protein levels across the *Plasmodium falciparum* life cycle. *Genome Res.* **14**, 2308-2318 (2004).
102. Bozdech Z & Ginsburg H. Antioxidant defense in *Plasmodium falciparum*--data mining of the transcriptome. *Malar. J.* **3**, 23 (2004).
103. Bozdech Z & Ginsburg H. Data mining of the transcriptome of *Plasmodium falciparum*: the pentose phosphate pathway and ancillary processes. *Malar. J.* **4**, 17 (2005).
104. Ralph SA, Bischoff E, Mattei D, Sismeiro O, Dillies MA *et al.* Transcriptome analysis of antigenic variation in *Plasmodium falciparum*--var silencing is not dependent on antisense RNA. *Genome Biol.* **6**, R93 (2005).
105. Gissot M, Refour P, Briquet S, Boschet C, Coupe S *et al.* Transcriptome of 3D7 and its gametocyte-less derivative F12 *Plasmodium falciparum* clones during erythrocytic development using a gene-specific microarray assigned to gene regulation, cell cycle and transcription factors. *Gene* **341**, 267-277 (2004).
106. Silvestrini F, Bozdech Z, Lanfrancotti A, Di Giulio E, Bultrini E *et al.* Genome-wide identification of genes upregulated at the onset of gametocytogenesis in *Plasmodium falciparum*. *Mol. Biochem. Parasitol.* **143**, 100-110 (2005).
107. Young JA, Fivelman QL, Blair PL, De L, V, Le Roch KG *et al.* The *Plasmodium falciparum* sexual development transcriptome: a microarray analysis using ontology-based pattern identification. *Mol. Biochem. Parasitol.* **143**, 67-79 (2005).
108. Dessens JT, Margos G, Rodriguez MC & Sinden RE. Identification of differentially regulated genes of *Plasmodium* by suppression subtractive hybridization. *Parasitol. Today* **16**, 354-356 (2000).
109. Pradel G, Hayton K, Aravind L, Iyer LM, Abrahamsen MS *et al.* A Multidomain Adhesion Protein Family Expressed in *Plasmodium falciparum* Is Essential for Transmission to the Mosquito. *J. Exp. Med.* **199**, 1533-1544 (2004).
110. Vincensini L, Richert S, Blisnick T, Van Dorsselaer A, Leize-Wagner E *et al.* Proteomic analysis identifies novel proteins of the Maurer's clefts, a secretory compartment delivering *Plasmodium falciparum* proteins to the surface of its host cell. *Mol. Cell Proteomics.* (2005).
111. Florens L, Liu X, Wang Y, Yang S, Schwartz O *et al.* Proteomics approach reveals novel proteins on the surface of malaria-infected erythrocytes. *Mol. Biochem. Parasitol.* **135**, 1-11 (2004).
112. Przyborski JM, Wickert H, Krohne G & Lanzer M. Maurer's clefts--a novel secretory organelle? *Mol. Biochem. Parasitol.* **132**, 17-26 (2003).
113. Sanders PR, Gilson PR, Cantin GT, Greenbaum DC, Nebl T *et al.* Distinct protein classes including novel merozoite surface antigens in raft-like membranes of *Plasmodium falciparum*. *J. Biol. Chem.* (2005).
114. LaCount DJ, Vignali M, Chettier R, Phansalkar A, Bell R *et al.* A protein interaction network of the malaria parasite *Plasmodium falciparum*. *Nature* **438**, 103-107 (2005).
115. Suthram S, Sittler T & Ideker T. The *Plasmodium* protein network diverges from those of other eukaryotes. *Nature* **438**, 108-112 (2005).
116. Marti M, Good RT, Rug M, Knuepfer E & Cowman AF. Targeting malaria virulence and remodeling proteins to the host erythrocyte. *Science* **306**, 1930-1933 (2004).
117. Hiller NL, Bhattacharjee S, van Ooij C, Liolios K, Harrison T *et al.* A host-targeting signal in virulence proteins reveals a secretome in malarial infection. *Science* **306**, 1934-1937 (2004).
118. Martin RE, Henry RI, Abbey JL, Clements JD & Kirk K. The 'permeome' of the malaria parasite: an overview of the membrane transport proteins of *Plasmodium falciparum*. *Genome Biol.* **6**, R26 (2005).

119. Anderson TJ, Su XZ, Roddam A & Day KP. Complex mutations in a high proportion of microsatellite loci from the protozoan parasite *Plasmodium falciparum*. *Mol. Ecol.* **9**, 1599-1608 (2000).
120. Fidock DA, Nomura T, Talley AK, Cooper RA, Dzekunov SM *et al.* Mutations in the *P. falciparum* digestive vacuole transmembrane protein PfCRT and evidence for their role in chloroquine resistance. *Mol. Cell* **6**, 861-871 (2000).
121. Su X, Kirkman LA, Fujioka H & Wellems TE. Complex polymorphisms in an approximately 330 kDa protein are linked to chloroquine-resistant *P. falciparum* in Southeast Asia and Africa. *Cell* **91**, 593-603 (1997).
122. Mu J, Ferdig MT, Feng X, Joy DA, Duan J *et al.* Multiple transporters associated with malaria parasite responses to chloroquine and quinine. *Mol. Microbiol.* **49**, 977-989 (2003).
123. Mu J, Awadalla P, Duan J, McGee KM, Joy DA *et al.* Recombination hotspots and population structure in *Plasmodium falciparum*. *PLoS Biol.* **3**, e335 (2005).
124. McConkey GA, Pinney JW, Westhead DR, Plueckhahn K, Fitzpatrick TB *et al.* Annotating the *Plasmodium* genome and the enigma of the shikimate pathway. *Trends Parasitol.* **20**, 60-65 (2004).
125. Waters AP, Higgins DG & McCutchan TF. *Plasmodium falciparum* appears to have arisen as a result of lateral transfer between avian and human hosts. *Proc. Natl. Acad. Sci. U. S. A* **88**, 3140-3144 (1991).
126. Escalante AA & Ayala FJ. Phylogeny of the malarial genus *Plasmodium*, derived from rRNA gene sequences. *Proc. Natl. Acad. Sci. U. S. A* **91**, 11373-11377 (1994).
127. Carlton J. The *Plasmodium vivax* genome sequencing project. *Trends Parasitol.* **19**, 227-231 (2003).
128. Templeton TJ, Iyer LM, Anantharaman V, Enomoto S, Abraham JE *et al.* Comparative analysis of apicomplexa and genomic diversity in eukaryotes. *Genome Res.* **14**, 1686-1695 (2004).
129. Balaji S, Babu MM, Iyer LM & Aravind L. Discovery of the principal specific transcription factors of Apicomplexa and their implication for the evolution of the AP2-integrase DNA binding domains. *Nucleic Acids Res.* **33**, 3994-4006 (2005).
130. Carlton JM, Galinski MR, Barnwell JW & Dame JB. Karyotype and synteny among the chromosomes of all four species of human malaria parasite. *Mol. Biochem. Parasitol.* **101**, 23-32 (1999).
131. Tchavtchitch M, Fischer K, Huestis R & Saul A. The sequence of a 200 kb portion of a *Plasmodium vivax* chromosome reveals a high degree of conservation with *Plasmodium falciparum* chromosome 3. *Mol. Biochem. Parasitol.* **118**, 211-222 (2001).
132. van Dijk MR, Janse CJ, Thompson J, Waters AP, Braks JA *et al.* A central role for P48/45 in malaria parasite male gamete fertility. *Cell* **104**, 153-164 (2001).
133. Menard R. Gliding motility and cell invasion by Apicomplexa: insights from the *Plasmodium* sporozoite. *Cell Microbiol.* **3**, 63-73 (2001).
134. Yoshida N, Nussenzweig RS, Potocnjak P, Nussenzweig V & Aikawa M. Hybridoma produces protective antibodies directed against the sporozoite stage of malaria parasite. *Science* **207**, 71-73 (1980).
135. Robson KJ, Hall JR, Jennings MW, Harris TJ, Marsh K *et al.* A highly conserved amino-acid sequence in thrombospondin, properdin and in proteins from sporozoites and blood stages of a human malaria parasite. *Nature* **335**, 79-82 (1988).
136. Guerin-Marchand C, Druilhe P, Galey B, Londono A, Patarapotikul J *et al.* A liver-stage-specific antigen of *Plasmodium falciparum* characterized by gene cloning. *Nature* **329**, 164-167 (1987).
137. Hall R, Hyde JE, Goman M, Simmons DL, Hope IA *et al.* Major surface antigen gene of a human malaria parasite cloned and expressed in bacteria. *Nature* **311**, 379-382 (1984).
138. Peterson MG, Marshall VM, Smythe JA, Crewther PE, Lew A *et al.* Integral membrane protein located in the apical complex of *Plasmodium falciparum*. *Mol. Cell Biol.* **9**, 3151-3154 (1989).
139. Smythe JA, Coppel RL, Brown GV, Ramasamy R, Kemp DJ *et al.* Identification of two integral membrane proteins of *Plasmodium falciparum*. *Proc. Natl. Acad. Sci. U. S. A* **85**, 5195-5199 (1988).
140. Quakyi IA, Carter R, Renner J, Kumar N, Good MF *et al.* The 230-kDa gamete surface protein of *Plasmodium falciparum* is also a target for transmission-blocking antibodies. *J. Immunol.* **139**, 4213-4217 (1987).



References

141. Hisaeda H, Stowers AW, Tsuboi T, Collins WE, Sattabongkot JS *et al.* Antibodies to malaria vaccine candidates Pvs25 and Pvs28 completely block the ability of *Plasmodium vivax* to infect mosquitoes. *Infect. Immun.* **68**, 6618-6623 (2000).
142. del Carmen RM, Gerold P, Dessens J, Kurtenbach K, Schwartz RT *et al.* Characterisation and expression of pbs25, a sexual and sporogonic stage specific protein of *Plasmodium berghei*. *Mol. Biochem. Parasitol.* **110**, 147-159 (2000).
143. Siden-Kiamos I, Vlachou D, Margos G, Beetsma A, Waters AP *et al.* Distinct roles for pbs21 and pbs25 in the in vitro ookinete to oocyst transformation of *Plasmodium berghei*. *J. Cell Sci.* **113 Pt 19**, 3419-3426 (2000).
144. del Portillo HA, Fernandez-Becerra C, Bowman S, Oliver K, Preuss M *et al.* A superfamily of variant genes encoded in the subtelomeric region of *Plasmodium vivax*. *Nature* **410**, 839-842 (2001).
145. Janssen CS, Phillips RS, Turner CM & Barrett MP. *Plasmodium* interspersed repeats: the major multigene superfamily of malaria parasites. *Nucleic Acids Res.* **32**, 5712-5720 (2004).
146. Sam-Yellowe TY, Florens L, Johnson JR, Wang T, Drazba JA *et al.* A *Plasmodium* Gene Family Encoding Maurer's Cleft Membrane Proteins: Structural Properties and Expression Profiling. *Genome Res.* **14**, 1052-1059 (2004).
147. Merino EF, Fernandez-Becerra C, Madeira AM, Machado AL, Durham A *et al.* Pilot survey of expressed sequence tags (ESTs) from the asexual blood stages of *Plasmodium vivax* in human patients. *Malar. J.* **2**, 21 (2003).
148. Kappe SH, Gardner MJ, Brown SM, Ross J, Matuschewski K *et al.* Exploring the transcriptome of the malaria sporozoite stage. *Proc. Natl. Acad. Sci. U. S. A* **98**, 9895-9900 (2001).
149. Kaiser K, Matuschewski K, Camargo N, Ross J & Kappe SH. Differential transcriptome profiling identifies *Plasmodium* genes encoding pre-erythrocytic stage-specific proteins. *Mol. Microbiol.* **51**, 1221-1232 (2004).
150. Abraham EG, Islam S, Srinivasan P, Ghosh AK, Valenzuela JG *et al.* Analysis of the *Plasmodium* and *Anopheles* transcriptional repertoire during ookinete development and midgut invasion. *J. Biol. Chem.* **279**, 5573-5580 (2004).
151. Srinivasan P, Abraham EG, Ghosh AK, Valenzuela J, Ribeiro JM *et al.* Analysis of the *Plasmodium* and *Anopheles* transcriptomes during oocyst differentiation. *J. Biol. Chem.* **279**, 5581-5587 (2004).
152. Matuschewski K, Ross J, Brown SM, Kaiser K, Nussenzweig V *et al.* Infectivity-associated changes in the transcriptional repertoire of the malaria parasite sporozoite stage. *J. Biol. Chem.* **277**, 41948-41953 (2002).
153. Hayward RE. *Plasmodium falciparum* phosphoenolpyruvate carboxykinase is developmentally regulated in gametocytes. *Mol. Biochem. Parasitol.* **107**, 227-240 (2000).
154. Khan SM, Franke-Fayard B, Mair GR, Lasonder E, Janse CJ *et al.* Proteome analysis of separated male and female gametocytes reveals novel sex-specific *Plasmodium* biology. *Cell* **121**, 675-687 (2005).
155. Kimura M. Preponderance of synonymous changes as evidence for the neutral theory of molecular evolution. *Nature* **267**, 275-276 (1977).
156. Kafatos FC, Efstratiadis A, Forget BG & Weissman SM. Molecular evolution of human and rabbit beta-globin mRNAs. *Proc. Natl. Acad. Sci. U. S. A* **74**, 5618-5622 (1977).
157. Plotkin JB, Dushoff J & Fraser HB. Detecting selection using a single genome sequence of *M. tuberculosis* and *P. falciparum*. *Nature* **428**, 942-945 (2004).
158. Friedman R & Hughes AL. Codon volatility as an indicator of positive selection: data from eukaryotic genome comparisons. *Mol. Biol. Evol.* **22**, 542-546 (2005).
159. Sharp PM. Gene "volatility" is most unlikely to reveal adaptation. *Mol. Biol. Evol.* **22**, 807-809 (2005).
160. Peixoto L, Fernandez V & Musto H. The effect of expression levels on codon usage in *Plasmodium falciparum*. *Parasitology* **128**, 245-251 (2004).
161. Doolan DL, Southwood S, Freilich DA, Sidney J, Graber NL *et al.* Identification of *Plasmodium falciparum* antigens by antigenic analysis of genomic and proteomic data. *Proc. Natl. Acad. Sci. U. S. A* **100**, 9952-9957 (2003).

162. Martinelli A, Cheesman S, Hunt P, Culleton R, Raza A *et al.* A genetic approach to the de novo identification of targets of strain-specific immunity in malaria parasites. *Proc. Natl. Acad. Sci. U. S. A* (2005).
163. Haddad D, Bilcikova E, Witney AA, Carlton JM, White CE *et al.* Novel antigen identification method for discovery of protective malaria antigens by rapid testing of DNA vaccines encoding exons from the parasite genome. *Infect. Immun.* **72**, 1594-1602 (2004).
164. Coulson RM, Hall N & Ouzounis CA. Comparative genomics of transcriptional control in the human malaria parasite *Plasmodium falciparum*. *Genome Res.* **14**, 1548-1554 (2004).
165. Bahl A, Brunk B, Crabtree J, Fraunholz MJ, Gajria B *et al.* PlasmoDB: the *Plasmodium* genome resource. A database integrating experimental and computational data. *Nucleic Acids Res.* **31**, 212-215 (2003).
166. Kissinger JC, Brunk BP, Crabtree J, Fraunholz MJ, Gajria B *et al.* The *Plasmodium* genome database. *Nature* **419**, 490-492 (2002).
167. Paton MG, Barker GC, Matsuoka H, Ramesar J, Janse CJ *et al.* Structure and expression of a post-transcriptionally regulated malaria gene encoding a surface protein from the sexual stages of *Plasmodium berghei*. *Mol. Biochem. Parasitol.* **59**, 263-275 (1993).
168. Cui L, Fan Q & Li J. The malaria parasite *Plasmodium falciparum* encodes members of the Puf RNA-binding protein family with conserved RNA binding activity. *Nucleic Acids Res.* **30**, 4607-4617 (2002).
169. Vervenne RA, Dirks RW, Ramesar J, Waters AP & Janse CJ. Differential expression in blood stages of the gene coding for the 21-kilodalton surface protein of ookinetes of *Plasmodium berghei* as detected by RNA in situ hybridisation. *Mol. Biochem. Parasitol.* **68**, 259-266 (1994).
170. Kooij TW, Franke-Fayard B, Renz J, Kroeze H, van Dooren MW *et al.* *Plasmodium berghei* alpha-tubulin II: a role in both male gamete formation and asexual blood stages. *Mol. Biochem. Parasitol.* **144**, 16-26 (2005).
171. Waters AP, van Spaendonk RM, Ramesar J, Vervenne RA, Dirks RW *et al.* Species-specific regulation and switching of transcription between stage-specific ribosomal RNA genes in *Plasmodium berghei*. *J. Biol. Chem.* **272**, 3583-3589 (1997).
172. Janse CJ, Ramesar J, van den Berg FM & Mons B. *Plasmodium berghei*: in vivo generation and selection of karyotype mutants and non-gametocyte producer mutants. *Exp. Parasitol.* **74**, 1-10 (1992).
173. Su XZ, Wu Y, Sifri CD & Wellems TE. Reduced extension temperatures required for PCR amplification of extremely A+T-rich DNA. *Nucleic Acids Res.* **24**, 1574-1575 (1996).
174. Carter R & Diggs CL. In: *Parasitic Protozoa* - p359-465. Academic Press, New York/San Francisco/London (1977).
175. van Dijk MR, Waters AP & Janse CJ. Stable transfection of malaria parasite blood stages. *Science* **268**, 1358-1362 (1995).
176. Carlton JM & Carucci DJ. Rodent models of malaria in the genomics era. *Trends Parasitol.* **18**, 100-102 (2002).
177. Weinbaum FI, Evans CB & Tigelaar RE. An in vitro assay for T cell immunity to malaria in mice. *J. Immunol.* **116**, 1280-1283 (1976).
178. Landau I & Chabaud AG. [Natural infection by 2 plasmodia of the rodent *Thamnomys rutilans* in the Central African Republic]. *C. R. Acad. Sci. Hebd. Seances Acad. Sci. D.* **261**, 230-232 (1965).
179. Sutton GG, White OR, Adams MD & Kerlavage AR. TIGR Assembler: A new tool for assembling large shotgun sequencing projects. *Genome Science & Technology* **1**, 9-19 (1995).
180. Mural RJ, Adams MD, Myers EW, Smith HO, Miklos GL *et al.* A comparison of whole-genome shotgun-derived mouse chromosome 16 and the human genome. *Science* **296**, 1661-1671 (2002).
181. Beetsma AL, van de Wiel TJ, Sauerwein RW & Eling WM. *Plasmodium berghei* ANKA: purification of large numbers of infectious gametocytes. *Exp. Parasitol.* **88**, 69-72 (1998).
182. Gardner MJ, Shallom SJ, Carlton JM, Salzberg SL, Nene V *et al.* Sequence of *Plasmodium falciparum* chromosomes 2, 10, 11 and 14. *Nature* **419**, 531-534 (2002).
183. Bateman A, Birney E, Cerruti L, Durbin R, Etwiller L *et al.* The Pfam protein families database. *Nucleic Acids Res.* **30**, 276-280 (2002).



References

184. Haft DH, Loftus BJ, Richardson DL, Yang F, Eisen JA *et al.* TIGRFAMs: a protein family resource for the functional identification of proteins. *Nucleic Acids Res.* **29**, 41-43 (2001).
185. Eddy SR. Profile hidden Markov models. *Bioinformatics.* **14**, 755-763 (1998).
186. Delcher AL, Phillippy A, Carlton J & Salzberg SL. Fast algorithms for large-scale genome alignment and comparison. *Nucleic Acids Res.* **30**, 2478-2483 (2002).
187. Benson G. Tandem repeats finder: a program to analyze DNA sequences. *Nucleic Acids Res.* **27**, 573-580 (1999).
188. Ogurtsov AY, Roytberg MA, Shabalina SA & Kondrashov AS. OWEN: aligning long collinear regions of genomes. *Bioinformatics.* **18**, 1703-1704 (2002).
189. Thompson JD, Higgins DG & Gibson TJ. CLUSTAL W: improving the sensitivity of progressive multiple sequence alignment through sequence weighting, position-specific gap penalties and weight matrix choice. *Nucleic Acids Res.* **22**, 4673-4680 (1994).
190. Nei M & Gojobori T. Simple methods for estimating the numbers of synonymous and nonsynonymous nucleotide substitutions. *Mol. Biol. Evol.* **3**, 418-426 (1986).
191. Myers EW, Sutton GG, Delcher AL, Dew IM, Fasulo DP *et al.* A whole-genome assembly of *Drosophila*. *Science* **287**, 2196-2204 (2000).
192. Lander ES & Waterman MS. Genomic mapping by fingerprinting random clones: a mathematical analysis. *Genomics* **2**, 231-239 (1988).
193. McCutchan TF, Dame JB, Miller LH & Barnwell J. Evolutionary relatedness of *Plasmodium* species as determined by the structure of DNA. *Science* **225**, 808-811 (1984).
194. Daly TM, Long CA & Bergman LW. Interaction between two domains of the *P. yoelii* MSP-1 protein detected using the yeast two-hybrid system. *Mol. Biochem. Parasitol.* **117**, 27-35 (2001).
195. Quackenbush J, Cho J, Lee D, Liang F, Holt I *et al.* The TIGR Gene Indices: analysis of gene transcript sequences in highly sampled eukaryotic species. *Nucleic Acids Res.* **29**, 159-164 (2001).
196. Cawley SE, Wirth AI & Speed TP. Phat-a gene finding program for *Plasmodium falciparum*. *Mol. Biochem. Parasitol.* **118**, 167-174 (2001).
197. Salzberg SL, Pertea M, Delcher AL, Gardner MJ & Tettelin H. Interpolated Markov models for eukaryotic gene finding. *Genomics* **59**, 24-31 (1999).
198. Ohkanda J, Lockman JW, Yokoyama K, Gelb MH, Croft SL *et al.* Peptidomimetic inhibitors of protein farnesyltransferase show potent antimalarial activity. *Bioorg. Med. Chem. Lett.* **11**, 761-764 (2001).
199. The GO Consortium. Creating the gene ontology resource: design and implementation. *Genome Res.* **11**, 1425-1433 (2001).
200. Black CG, Wang L, Hibbs AR, Werner E & Coppel RL. Identification of the *Plasmodium chabaudi* homologue of merozoite surface proteins 4 and 5 of *Plasmodium falciparum*. *Infect. Immun.* **67**, 2075-2081 (1999).
201. Cooke BM, Mohandas N & Coppel RL. The malaria-infected red blood cell: structural and functional changes. *Adv. Parasitol.* **50**, 1-86 (2001).
202. Janssen CS, Barrett MP, Turner CM & Phillips RS. A large gene family for putative variant antigens shared by human and rodent malaria parasites. *Proc. R. Soc. Lond B Biol. Sci.* **269**, 431-436 (2002).
203. Cunningham DA, Jarra W, Koernig S, Fonager J, Fernandez-Reyes D *et al.* Host immunity modulates transcriptional changes in a multigene family (*yir*) of rodent malaria. *Mol. Microbiol.* **58**, 636-647 (2005).
204. Strimmer K & von Haeseler A. Quartet puzzling: a quartet maximum likelihood method for reconstructing tree topologies. *Molecular Biological Evolution* **13**, 964-969 (1996).
205. Preiser PR, Jarra W, Capiod T & Snounou G. A rho-trypanin-associated mechanism of clonal phenotypic variation in rodent malaria. *Nature* **398**, 618-622 (1999).
206. Galinski MR, Xu M & Barnwell JW. *Plasmodium vivax* reticulocyte binding protein-2 (PvRBP-2) shares structural features with PvRBP-1 and the *Plasmodium yoelii* 235 kDa rho-trypanin protein family. *Mol. Biochem. Parasitol.* **108**, 257-262 (2000).
207. Rayner JC, Galinski MR, Ingravalleo P & Barnwell JW. Two *Plasmodium falciparum* genes express merozoite proteins that are related to *Plasmodium vivax* and *Plasmodium yoelii* adhesive proteins involved in host cell selection and invasion. *Proc. Natl. Acad. Sci. U. S. A* **97**, 9648-9653 (2000).

208. Wiser MF, Giraldo LE, Schmitt-Wrede HP & Wunderlich F. Plasmodium chabaudi: immunogenicity of a highly antigenic glutamate-rich protein. *Exp. Parasitol.* **85**, 43-54 (1997).
209. Spielmann T & Beck HP. Analysis of stage-specific transcription in plasmodium falciparum reveals a set of genes exclusively transcribed in ring stage parasites. *Mol. Biochem. Parasitol.* **111**, 453-458 (2000).
210. Favaloro JM, Culvenor JG, Anders RF & Kemp DJ. A Plasmodium chabaudi antigen located in the parasitophorous vacuole membrane. *Mol. Biochem. Parasitol.* **62**, 263-270 (1993).
211. Mu J, Duan J, Makova KD, Joy DA, Huynh CQ *et al.* Chromosome-wide SNPs reveal an ancient origin for Plasmodium falciparum. *Nature* **418**, 323-326 (2002).
212. Garnham PCC. *Malaria Parasites and Other Haemosporidia*. Blackwell Scientific, Oxford (1966).
213. Liu SL & Sanderson KE. Rearrangements in the genome of the bacterium Salmonella typhi. *Proc. Natl. Acad. Sci. U. S. A* **92**, 1018-1022 (1995).
214. Ashburner M, Ball CA, Blake JA, Botstein D, Butler H *et al.* Gene ontology: tool for the unification of biology. The Gene Ontology Consortium. *Nat. Genet.* **25**, 25-29 (2000).
215. Dame JB & McCutchan TF. The four ribosomal DNA units of the malaria parasite Plasmodium berghei. Identification, restriction map, and copy number analysis. *J. Biol. Chem.* **258**, 6984-6990 (1983).
216. Jareborg N, Birney E & Durbin R. Comparative analysis of noncoding regions of 77 orthologous mouse and human gene pairs. *Genome Res.* **9**, 815-824 (1999).
217. Shabalina SA, Ogurtsov AY, Kondrashov VA & Kondrashov AS. Selective constraint in intergenic regions of human and mouse genomes. *Trends Genet.* **17**, 373-376 (2001).
218. Makalowski W & Boguski MS. Evolutionary parameters of the transcribed mammalian genome: an analysis of 2,820 orthologous rodent and human sequences. *Proc. Natl. Acad. Sci. U. S. A* **95**, 9407-9412 (1998).
219. Carlton JM, Fidock DA, Djimde A, Plowe CV & Wellems TE. Conservation of a novel vacuolar transporter in Plasmodium species and its central role in chloroquine resistance of P. falciparum. *Curr. Opin. Microbiol.* **4**, 415-420 (2001).
220. Sinden RE. In: *Rodent Malaria* - p85-168. Killick-Kendrick R & Peters W (eds.) Academic Press, London (1978).
221. Janse CJ & Waters AP. Plasmodium berghei: The application of cultivation and purification techniques to molecular studies of malaria parasites. *Parasitol. Today* **11**, 138-143 (1995).
222. Hall N, Pain A, Berriman M, Churcher C, Harris B *et al.* Sequence of Plasmodium falciparum chromosomes 1, 3-9 and 13. *Nature* **419**, 527-531 (2002).
223. Mullikin JC & Ning Z. The phusion assembler. *Genome Res.* **13**, 81-90 (2003).
224. Birney E & Durbin R. Using GeneWise in the Drosophila annotation experiment. *Genome Res.* **10**, 547-548 (2000).
225. Enright AJ, Van Dongen S & Ouzounis CA. An efficient algorithm for large-scale detection of protein families. *Nucleic Acids Res.* **30**, 1575-1584 (2002).
226. Rice P, Longden I & Bleasby A. EMBOSS: the European Molecular Biology Open Software Suite. *Trends Genet.* **16**, 276-277 (2000).
227. Yang Z. PAML: a program package for phylogenetic analysis by maximum likelihood. *Comput. Appl. Biosci.* **13**, 555-556 (1997).
228. Janse CJ, Boorsma EG, Ramesar J, van Vianen P, van der MR *et al.* Plasmodium berghei: gametocyte production, DNA content, and chromosome-size polymorphisms during asexual multiplication in vivo. *Exp. Parasitol.* **68**, 274-282 (1989).
229. Dimopoulos G, Christophides GK, Meister S, Schultz J, White KP *et al.* Genome expression analysis of Anopheles gambiae: responses to injury, bacterial challenge, and malaria infection. *Proc. Natl. Acad. Sci. U. S. A* **99**, 8814-8819 (2002).
230. Eisen MB, Spellman PT, Brown PO & Botstein D. Cluster analysis and display of genome-wide expression patterns. *Proc. Natl. Acad. Sci. U. S. A* **95**, 14863-14868 (1998).
231. Sinden RE, Butcher GA & Beetsma AL. Maintenance of the Plasmodium berghei life cycle. *Methods Mol. Med.* **72**, 25-40 (2002).
232. Wu CC, MacCoss MJ, Howell KE & Yates JR, III. A method for the comprehensive proteomic analysis of membrane proteins. *Nat. Biotechnol.* **21**, 532-538 (2003).
233. Eng JK, McCormack AL & Yates JR, III. *Journal of the American Society of Mass Spectrometry* **5**, 976 (1994).



References

234. Sadygov RG & Yates JR, III. A hypergeometric probability model for protein identification and validation using tandem mass spectral data and protein sequence databases. *Anal. Chem.* **75**, 3792-3798 (2003).
235. Fischer K, Chavchich M, Huestis R, Wilson DW, Kemp DJ *et al.* Ten families of variant genes encoded in subtelomeric regions of multiple chromosomes of *Plasmodium chabaudi*, a malaria species that undergoes antigenic variation in the laboratory mouse. *Mol. Microbiol.* **48**, 1209-1223 (2003).
236. Endo T, Ikeo K & Gojobori T. Large-scale search for genes on which positive selection may operate. *Mol. Biol. Evol.* **13**, 685-690 (1996).
237. Han YS, Thompson J, Kafatos FC & Barillas-Mury C. Molecular interactions between *Anopheles stephensi* midgut cells and *Plasmodium berghei*: the time bomb theory of ookinete invasion of mosquitoes. *EMBO J.* **19**, 6030-6040 (2000).
238. Washburn MP, Wolters D & Yates JR, III. Large-scale analysis of the yeast proteome by multidimensional protein identification technology. *Nat. Biotechnol.* **19**, 242-247 (2001).
239. Vickerman K. Polymorphism and mitochondrial activity in sleeping sickness trypanosomes. *Nature* **208**, 762-766 (1965).
240. Krungkrai J, Prapunwattana P & Krungkrai SR. Ultrastructure and function of mitochondria in gametocytic stage of *Plasmodium falciparum*. *Parasite* **7**, 19-26 (2000).
241. Kaiser K, Camargo N, Coppens I, Morrisey JM, Vaidya AB *et al.* A member of a conserved Plasmodium protein family with membrane-attack complex/perforin (MACPF)-like domains localizes to the micronemes of sporozoites. *Mol. Biochem. Parasitol.* **133**, 15-26 (2004).
242. Mota MM, Hafalla JC & Rodriguez A. Migration through host cells activates *Plasmodium* sporozoites for infection. *Nat. Med.* **8**, 1318-1322 (2002).
243. Crooks GE, Hon G, Chandonia JM & Brenner SE. WebLogo: a sequence logo generator. *Genome Res.* **14**, 1188-1190 (2004).
244. Waters AP. Parasitology. Guilty until proven otherwise. *Science* **301**, 1487-1488 (2003).
245. Bailey TL & Gribskov M. Methods and statistics for combining motif match scores. *J. Comput. Biol.* **5**, 211-221 (1998).
246. Hillier LW, Miller W, Birney E, Warren W, Hardison RC *et al.* Sequence and comparative analysis of the chicken genome provide unique perspectives on vertebrate evolution. *Nature* **432**, 695-716 (2004).
247. Murphy WJ, Larkin DM, Everts-van der Wind A, Bourque G, Tesler G *et al.* Dynamics of mammalian chromosome evolution inferred from multispecies comparative maps. *Science* **309**, 613-617 (2005).
248. Severson DW, DeBruyn B, Lovin DD, Brown SE, Knudson DL *et al.* Comparative genome analysis of the yellow fever mosquito *Aedes aegypti* with *Drosophila melanogaster* and the malaria vector mosquito *Anopheles gambiae*. *J. Hered.* **95**, 103-113 (2004).
249. Sharakhov IV, Serazin AC, Grushko OG, Dana A, Lobo N *et al.* Inversions and gene order shuffling in *Anopheles gambiae* and *A. funestus*. *Science* **298**, 182-185 (2002).
250. El Sayed NM, Myler PJ, Blandin G, Berriman M, Crabtree J *et al.* Comparative genomics of trypanosomatid parasitic protozoa. *Science* **309**, 404-409 (2005).
251. Kyes S, Horrocks P & Newbold C. Antigenic variation at the infected red cell surface in malaria. *Annu. Rev. Microbiol.* **55**, 673-707 (2001).
252. Barry JD, Ginger ML, Burton P & McCulloch R. Why are parasite contingency genes often associated with telomeres? *Int. J. Parasitol.* **33**, 29-45 (2003).
253. Bailey TL & Elkan C. Fitting a mixture model by expectation maximization to discover motifs in biopolymers. *Proc. Int. Conf. Intell. Syst. Mol. Biol.* **2**, 28-36 (1994).
254. Schultz J, Milpetz F, Bork P & Ponting CP. SMART, a simple modular architecture research tool: identification of signaling domains. *Proc. Natl. Acad. Sci. U. S. A* **95**, 5857-5864 (1998).
255. Felsenstein J. Inferring phylogenies from protein sequences by parsimony, distance, and likelihood methods. *Methods Enzymol.* **266**, 418-427 (1996).
256. Felsenstein J. Confidence limits on phylogenies: an approach using the bootstrap. *Evolution* **39**, 783-791 (1985).
257. Day WH & McMorris FR. A consensus program for molecular sequences. *Comput. Appl. Biosci.* **9**, 653-656 (1993).

258. Perkins ME. Surface proteins of *Plasmodium falciparum* merozoites binding to the erythrocyte receptor, glycophorin. *J. Exp. Med.* **160**, 788-798 (1984).
259. Spielmann T, Ferguson DJ & Beck HP. etramps, a new *Plasmodium falciparum* gene family coding for developmentally regulated and highly charged membrane proteins located at the parasite-host cell interface. *Mol. Biol. Cell* **14**, 1529-1544 (2003).
260. Pearce JA, Mills K, Triglia T, Cowman AF & Anders RF. Characterisation of two novel proteins from the asexual stage of *Plasmodium falciparum*, H101 and H103. *Mol. Biochem. Parasitol.* **139**, 141-151 (2005).
261. Anamika, Srinivasan N & Krupa A. A genomic perspective of protein kinases in *Plasmodium falciparum*. *Proteins* **58**, 180-189 (2005).
262. Schneider AG & Mercereau-Pujalon O. A new Apicomplexa-specific protein kinase family : multiple members in *Plasmodium falciparum*, all with an export signature. *BMC. Genomics* **6**, 30 (2005).
263. Ward P, Equinet L, Packer J & Doerig C. Protein kinases of the human malaria parasite *Plasmodium falciparum*: the kinome of a divergent eukaryote. *BMC. Genomics* **5**, 79 (2004).
264. Nadeau JH & Sankoff D. Landmarks in the Rosetta Stone of mammalian comparative maps. *Nat. Genet.* **15**, 6-7 (1997).
265. Escalante AA, Barrio E & Ayala FJ. Evolutionary origin of human and primate malarial parasites: evidence from the circumsporozoite protein gene. *Mol. Biol. Evol.* **12**, 616-626 (1995).
266. McCutchan TF, Kissinger JC, Touray MG, Rogers MJ, Li J *et al.* Comparison of circumsporozoite proteins from avian and mammalian malarial parasites: biological and phylogenetic implications. *Proc. Natl. Acad. Sci. U. S. A* **93**, 11889-11894 (1996).
267. Rathore D, Wahl AM, Sullivan M & McCutchan TF. A phylogenetic comparison of gene trees constructed from plastid, mitochondrial and genomic DNA of *Plasmodium* species. *Mol. Biochem. Parasitol.* **114**, 89-94 (2001).
268. Kissinger JC, Souza PC, Soarest CO, Paul R, Wahl AM *et al.* Molecular phylogenetic analysis of the avian malarial parasite *Plasmodium (Novyella) juxtannucleare*. *J. Parasitol.* **88**, 769-773 (2002).
269. Carlton JM. Gene synteny across *Plasmodium* spp: could 'operon-like' structures exist? *Parasitol. Today* **15**, 178-179 (1999).
270. Bailey JA, Baertsch R, Kent WJ, Haussler D & Eichler EE. Hotspots of mammalian chromosomal evolution. *Genome Biol.* **5**, R23 (2004).
271. Armengol L, Pujana MA, Cheung J, Scherer SW & Estivill X. Enrichment of segmental duplications in regions of breaks of synteny between the human and mouse genomes suggest their involvement in evolutionary rearrangements. *Hum. Mol. Genet.* **12**, 2201-2208 (2003).
272. Kraemer SM & Smith JD. Evidence for the importance of genetic structuring to the structural and functional specialization of the *Plasmodium falciparum* var gene family. *Mol. Microbiol.* **50**, 1527-1538 (2003).
273. Hyams JS & Lloyd CW. Microtubules. Wiley-Liss, New York (1994).
274. Luduena RF. Multiple forms of tubulin: different gene products and covalent modifications. *Int. Rev. Cytol.* **178**, 207-275 (1998).
275. Little M & Seehaus T. Comparative analysis of tubulin sequences. *Comp Biochem. Physiol B* **90**, 655-670 (1988).
276. van Belkum A, Janse C & Mons B. Nucleotide sequence variation in the beta-tubulin genes from *Plasmodium berghei* and *Plasmodium falciparum*. *Mol. Biochem. Parasitol.* **47**, 251-254 (1991).
277. Holloway SP, Gerousis M, Delves CJ, Sims PF, Scaife JG *et al.* The tubulin genes of the human malaria parasite *Plasmodium falciparum*, their chromosomal location and sequence analysis of the alpha-tubulin II gene. *Mol. Biochem. Parasitol.* **43**, 257-270 (1990).
278. Sen K & Godson GN. Isolation of alpha- and beta-tubulin genes of *Plasmodium falciparum* using a single oligonucleotide probe. *Mol. Biochem. Parasitol.* **39**, 173-182 (1990).
279. Holloway SP, Sims PF, Delves CJ, Scaife JG & Hyde JE. Isolation of alpha-tubulin genes from the human malaria parasite, *Plasmodium falciparum*: sequence analysis of alpha-tubulin. *Mol. Microbiol.* **3**, 1501-1510 (1989).
280. Wesseling JG, Dirks R, Smits MA & Schoenmakers JG. Nucleotide sequence and expression of a beta-tubulin gene from *Plasmodium falciparum*, a malarial parasite of man. *Gene* **83**, 301-309 (1989).



References

281. Delves CJ, Ridley RG, Goman M, Holloway SP, Hyde JE *et al.* Cloning of a beta-tubulin gene from *Plasmodium falciparum*. *Mol. Microbiol.* **3**, 1511-1519 (1989).
282. Akella R, Arasu P & Vaidya AB. Molecular clones of alpha-tubulin genes of *Plasmodium yoelii* reveal an unusual feature of the carboxy terminus. *Mol. Biochem. Parasitol.* **30**, 165-174 (1988).
283. Rawlings DJ, Fujioka H, Fried M, Keister DB, Aikawa M *et al.* Alpha-tubulin II is a male-specific protein in *Plasmodium falciparum*. *Mol. Biochem. Parasitol.* **56**, 239-250 (1992).
284. Delves CJ, Alano P, Ridley RG, Goman M, Holloway SP *et al.* Expression of alpha and beta tubulin genes during the asexual and sexual blood stages of *Plasmodium falciparum*. *Mol. Biochem. Parasitol.* **43**, 271-278 (1990).
285. Kappe SH, Buscaglia CA, Bergman LW, Coppens I & Nussenzweig V. Apicomplexan gliding motility and host cell invasion: overhauling the motor model. *Trends Parasitol.* **20**, 13-16 (2004).
286. Aikawa M, Carter R, Ito Y & Nijhout MM. New observations on gametogenesis, fertilization, and zygote transformation in *Plasmodium gallinaceum*. *J. Protozool.* **31**, 403-413 (1984).
287. Sinden RE, Canning EU & Spain B. Gametogenesis and fertilization in *Plasmodium yoelii nigeriensis*: a transmission electron microscope study. *Proc. R. Soc. Lond B Biol. Sci.* **193**, 55-76 (1976).
288. Inaba K. Molecular architecture of the sperm flagella: molecules for motility and signaling. *Zool. Sci.* **20**, 1043-1056 (2003).
289. Dearsly AL, Sinden RE & Self IA. Sexual development in malarial parasites: gametocyte production, fertility and infectivity to the mosquito vector. *Parasitology* **100 Pt 3**, 359-368 (1990).
290. Vinkenoog R, Veldhuisen B, Speranca MA, del Portillo HA, Janse C *et al.* Comparison of introns in a *cdc2*-homologous gene within a number of *Plasmodium* species. *Mol. Biochem. Parasitol.* **71**, 233-241 (1995).
291. Ponzi M, Janse CJ, Dore E, Scotti R, Pace T *et al.* Generation of chromosome size polymorphism during in vivo mitotic multiplication of *Plasmodium berghei* involves both loss and addition of subtelomeric repeat sequences. *Mol. Biochem. Parasitol.* **41**, 73-82 (1990).
292. Franke-Fayard B, Trueman H, Ramesar J, Mendoza J, van der KM *et al.* A *Plasmodium berghei* reference line that constitutively expresses GFP at a high level throughout the complete life cycle. *Mol. Biochem. Parasitol.* **137**, 23-33 (2004).
293. van der Wel AM, Tomas AM, Kocken CH, Malhotra P, Janse CJ *et al.* Transfection of the primate malaria parasite *Plasmodium knowlesi* using entirely heterologous constructs. *J. Exp. Med.* **185**, 1499-1503 (1997).
294. Rigaut G, Shevchenko A, Rutz B, Wilm M, Mann M *et al.* A generic protein purification method for protein complex characterization and proteome exploration. *Nat. Biotechnol.* **17**, 1030-1032 (1999).
295. Koning-Ward TF, Janse CJ & Waters AP. The development of genetic tools for dissecting the biology of malaria parasites. *Annu. Rev. Microbiol.* **54**, 157-185 (2000).
296. Janse CJ, Mons B, Rouwenhorst RJ, van der Klooster PF, Overdulve JP *et al.* In vitro formation of ookinetes and functional maturity of *Plasmodium berghei* gametocytes. *Parasitology* **91 (Pt 1)**, 19-29 (1985).
297. Janse CJ, Rouwenhorst RJ, van der Klooster PF, van der Kaay HJ & Overdulve JP. Development of *Plasmodium berghei* ookinetes in the midgut of *Anopheles atroparvus* mosquitoes and in vitro. *Parasitology* **91 (Pt 2)**, 219-225 (1985).
298. Pace T, Birago C, Janse CJ, Picci L & Ponzi M. Developmental regulation of a *Plasmodium* gene involves the generation of stage-specific 5' untranslated sequences. *Mol. Biochem. Parasitol.* **97**, 45-53 (1998).
299. Watanabe J, Sasaki M, Suzuki Y & Sugano S. FULL-malaria: a database for a full-length enriched cDNA library from human malaria parasite, *Plasmodium falciparum*. *Nucleic Acids Res.* **29**, 70-71 (2001).
300. Rusan NM, Fagerstrom CJ, Yvon AM & Wadsworth P. Cell cycle-dependent changes in microtubule dynamics in living cells expressing green fluorescent protein-alpha tubulin. *Mol. Biol. Cell* **12**, 971-980 (2001).
301. Straight AF, Marshall WF, Sedat JW & Murray AW. Mitosis in living budding yeast: anaphase A but no metaphase plate. *Science* **277**, 574-578 (1997).
302. Jarvik JW & Telmer CA. Epitope tagging. *Annu. Rev. Genet.* **32**, 601-618 (1998).

303. Corcoran LM, Thompson JK, Walliker D & Kemp DJ. Homologous recombination within subtelomeric repeat sequences generates chromosome size polymorphisms in *P. falciparum*. *Cell* **53**, 807-813 (1988).
304. Dore E, Pace T, Ponzi M, Picci L & Frontali C. Organization of subtelomeric repeats in *Plasmodium berghei*. *Mol. Cell Biol.* **10**, 2423-2427 (1990).
305. Pace T, Ponzi M, Dore E, Janse C, Mons B *et al.* Long insertions within telomeres contribute to chromosome size polymorphism in *Plasmodium berghei*. *Mol. Cell Biol.* **10**, 6759-6764 (1990).
306. Janse CJ & Mons B. Deletion, insertion and translocation of DNA sequences contribute to chromosome size polymorphism in *Plasmodium berghei*. *Mem. Inst. Oswaldo Cruz* **87 Suppl 3**, 95-100 (1992).
307. del Portillo HA, Lanzer M, Rodriguez-Malaga S, Zavala F & Fernandez-Becerra C. Variant genes and the spleen in *Plasmodium vivax* malaria. *Int. J. Parasitol.* **34**, 1547-1554 (2004).
308. Romero D, Martinez-Salazar J, Ortiz E, Rodriguez C & Valencia-Morales E. Repeated sequences in bacterial chromosomes and plasmids: a glimpse from sequenced genomes. *Res. Microbiol.* **150**, 735-743 (1999).
309. Fischer G, James SA, Roberts IN, Oliver SG & Louis EJ. Chromosomal evolution in *Saccharomyces*. *Nature* **405**, 451-454 (2000).
310. Zhang J & Peterson T. Genome rearrangements by nonlinear transposons in maize. *Genetics* **153**, 1403-1410 (1999).
311. Caceres M, Ranz JM, Barbadilla A, Long M & Ruiz A. Generation of a widespread *Drosophila* inversion by a transposable element. *Science* **285**, 415-418 (1999).
312. Kaminker JS, Bergman CM, Kronmiller B, Carlson J, Svirskas R *et al.* The transposable elements of the *Drosophila melanogaster* euchromatin: a genomics perspective. *Genome Biol.* **3**, RESEARCH0084 (2002).
313. Hoskins RA, Smith CD, Carlson JW, Carvalho AB, Halpern A *et al.* Heterochromatic sequences in a *Drosophila* whole-genome shotgun assembly. *Genome Biol.* **3**, RESEARCH0085 (2002).
314. Glockner G, Szafranski K, Winckler T, Dingermann T, Quail MA *et al.* The complex repeats of *Dictyostelium discoideum*. *Genome Res.* **11**, 585-594 (2001).
315. Glockner G, Eichinger L, Szafranski K, Pachebat JA, Bankier AT *et al.* Sequence and analysis of chromosome 2 of *Dictyostelium discoideum*. *Nature* **418**, 79-85 (2002).
316. Ventura M, Archidiacono N & Rocchi M. Centromere emergence in evolution. *Genome Res.* **11**, 595-599 (2001).
317. Amor DJ & Choo KH. Neocentromeres: role in human disease, evolution, and centromere study. *Am. J. Hum. Genet.* **71**, 695-714 (2002).
318. Dujon B, Sherman D, Fischer G, Durrrens P, Casaregola S *et al.* Genome evolution in yeasts. *Nature* **430**, 35-44 (2004).
319. Henikoff S, Ahmad K & Malik HS. The centromere paradox: stable inheritance with rapidly evolving DNA. *Science* **293**, 1098-1102 (2001).
320. Talbert PB, Bryson TD & Henikoff S. Adaptive evolution of centromere proteins in plants and animals. *J. Biol.* **3**, 18 (2004).
321. Trenholme KR, Gardiner DL, Holt DC, Thomas EA, Cowman AF *et al.* clag9: A cytoadherence gene in *Plasmodium falciparum* essential for binding of parasitized erythrocytes to CD36. *Proc. Natl. Acad. Sci. U. S. A* **97**, 4029-4033 (2000).
322. Barnwell JW, Howard RJ, Coon HG & Miller LH. Splenic requirement for antigenic variation and expression of the variant antigen on the erythrocyte membrane in cloned *Plasmodium knowlesi* malaria. *Infect. Immun.* **40**, 985-994 (1983).
323. Brown KN. Antibody induced variation in malaria parasites. *Nature* **242**, 49-50 (1973).
324. Bonnefoy S, Guillotte M, Langsley G & Mercereau-Puijalon O. *Plasmodium falciparum*: characterization of gene R45 encoding a trophozoite antigen containing a central block of six amino acid repeats. *Exp. Parasitol.* **74**, 441-451 (1992).
325. Massague J. TGF-beta signal transduction. *Annu. Rev. Biochem.* **67**, 753-791 (1998).
326. Josso N & di Clemente N. Serine/threonine kinase receptors and ligands. *Curr. Opin. Genet. Dev.* **7**, 371-377 (1997).
327. Harrison T, Samuel BU, Akompong T, Hamm H, Mohandas N *et al.* Erythrocyte G protein-coupled receptor signaling in malarial infection. *Science* **301**, 1734-1736 (2003).



References

328. Omer FM & Riley EM. Transforming growth factor beta production is inversely correlated with severity of murine malaria infection. *J. Exp. Med.* **188**, 39-48 (1998).
329. Omer FM, Kurtzhals JA & Riley EM. Maintaining the immunological balance in parasitic infections: a role for TGF-beta? *Parasitol. Today* **16**, 18-23 (2000).
330. Wang T, Li BY, Danielson PD, Shah PC, Rockwell S *et al.* The immunophilin FKBP12 functions as a common inhibitor of the TGF beta family type I receptors. *Cell* **86**, 435-444 (1996).
331. Sokol JP & Schiemann WP. Cystatin C antagonizes transforming growth factor beta signaling in normal and cancer cells. *Mol. Cancer Res.* **2**, 183-195 (2004).
332. Inman GJ, Nicolas FJ, Callahan JF, Harling JD, Gaster LM *et al.* SB-431542 is a potent and specific inhibitor of transforming growth factor-beta superfamily type I activin receptor-like kinase (ALK) receptors ALK4, ALK5, and ALK7. *Mol. Pharmacol.* **62**, 65-74 (2002).
333. Laping NJ, Grygielko E, Mathur A, Butter S, Bomberger J *et al.* Inhibition of transforming growth factor (TGF)-beta1-induced extracellular matrix with a novel inhibitor of the TGF-beta type I receptor kinase activity: SB-431542. *Mol. Pharmacol.* **62**, 58-64 (2002).
334. Bottinger EP, Factor VM, Tsang ML, Weatherbee JA, Kopp JB *et al.* The recombinant proregion of transforming growth factor beta1 (latency-associated peptide) inhibits active transforming growth factor beta1 in transgenic mice. *Proc. Natl. Acad. Sci. U. S. A* **93**, 5877-5882 (1996).
335. Carter R. Transmission blocking malaria vaccines. *Vaccine* **19**, 2309-2314 (2001).
336. Nolte D, Hundt E, Langsley G & Knapp B. A Plasmodium falciparum blood stage antigen highly homologous to the glycophorin binding protein GBP. *Mol. Biochem. Parasitol.* **49**, 253-264 (1991).
337. Rudolph B, Nolte D & Knapp B. Isolation of a third member of the Plasmodium falciparum glycophorin-binding protein gene family. *Mol. Biochem. Parasitol.* **68**, 173-176 (1994).
338. Cowman AF, Baldi DL, Healer J, Mills KE, O'Donnell RA *et al.* Functional analysis of proteins involved in Plasmodium falciparum merozoite invasion of red blood cells. *FEBS Lett.* **476**, 84-88 (2000).
339. Bourgon R, Delorenzi M, Sargeant T, Hodder AN, Crabb BS *et al.* The serine repeat antigen (SERA) gene family phylogeny in Plasmodium: the impact of GC content and reconciliation of gene and species trees. *Mol. Biol. Evol.* **21**, 2161-2171 (2004).
340. Holt DC, Gardiner DL, Thomas EA, Mayo M, Bourke PF *et al.* The cytoadherence linked asexual gene family of Plasmodium falciparum: are there roles other than cytoadherence? *Int. J. Parasitol.* **29**, 939-944 (1999).
341. Adams JH, Sim BK, Dolan SA, Fang X, Kaslow DC *et al.* A family of erythrocyte binding proteins of malaria parasites. *Proc. Natl. Acad. Sci. U. S. A* **89**, 7085-7089 (1992).