

References

1. World Health Organization. WHO methods and data sources for global causes of death 2000-2011. [Internet]. Geneva, Switzerland: WHO; 2013. Available: http://www.who.int/healthinfo/statistics/GlobalCOD_method.pdf
2. Reiter P. From Shakespeare to Defoe: malaria in England in the Little Ice Age. *Emerg Infect Dis.* 2000;6: 1–11. doi:10.3201/eid0601.000101
3. World Health Organization. World malaria report 2012. WHO. 2012;
4. Ansari MT, Saify ZS, Sultana N, Ahmad I, Saeed-Ul-Hassan S, Tariq I, et al. Malaria and artemisinin derivatives: an updated review. *Mini Rev Med Chem.* 2013;13: 1879–902. Available: <http://www.ncbi.nlm.nih.gov/pubmed/24070206>
5. Crawley J, Chu C, Mtobe G, Nosten F. Malaria in children. *Lancet.* Elsevier Ltd; 2010;375: 1468–81. doi:10.1016/S0140-6736(10)60447-3
6. Fernando SD, Rodrigo C, Rajapakse S. The “hidden” burden of malaria: cognitive impairment following infection. *Malar J.* 2010;9: 366. doi:10.1186/1475-2875-9-366
7. Karunaweera ND, Wijesekera SK, Wanasekera D, Mendis KN, Carter R. The paroxysm of Plasmodium vivax malaria. *Trends Parasitol.* 2003;19: 188–93. Available: <http://www.ncbi.nlm.nih.gov/pubmed/12689650>
8. Dondorp AM, Nosten F, Yi P, Das D, Phyo AP, Tarning J, et al. Artemisinin resistance in Plasmodium falciparum malaria. *N Engl J Med.* 2009;361: 455–67. doi:10.1056/NEJMoa0808859
9. Manske M, Miotto O, Campino S, Auburn S, Almagro-Garcia J, Maslen G, et al. Analysis of Plasmodium falciparum diversity in natural infections by deep sequencing. *Nature.* Nature Publishing Group; 2012;487: 375–9. doi:10.1038/nature11174
10. Wykes MN. Why haven’t we made an efficacious vaccine for malaria? *EMBO Rep.* Nature Publishing Group; 2013;14: 661. doi:10.1038/embor.2013.103
11. Goldberg DE, Siliciano RF, Jacobs WR. Outwitting evolution: fighting drug-resistant TB, malaria, and HIV. *Cell.* Elsevier Inc.; 2012;148: 1271–83. doi:10.1016/j.cell.2012.02.021
12. World Health Organization. WHO | Guidelines for the treatment of malaria. Second edition. WHO. World Health Organization; 2010; Available: <http://www.who.int/malaria/publications/atoz/9789241547925/en/>
13. Sibley LD. Intracellular parasite invasion strategies. *Science.* 2004;304: 248–53. doi:10.1126/science.1094717

14. Baumeister S, Winterberg M, Przyborski JM, Lingelbach K. The malaria parasite Plasmodium falciparum: cell biological peculiarities and nutritional consequences. *Protoplasma*. 2010;240: 3–12. doi:10.1007/s00709-009-0090-3
15. Waller RF, Ralph SA, Reed MB, Su V, Douglas JD, Minnikin DE, et al. A Type II Pathway for Fatty Acid Biosynthesis Presents Drug Targets in Plasmodium falciparum. *Antimicrob Agents Chemother*. 2003;47: 297–301. doi:10.1128/AAC.47.1.297-301.2003
16. Prudêncio M, Rodriguez A, Mota MM. The silent path to thousands of merozoites: the Plasmodium liver stage. *Nat Rev Microbiol*. 2006;4: 849–56. doi:10.1038/nrmicro1529
17. Khan SM, Waters AP. Malaria parasite transmission stages: an update. *Trends Parasitol*. 2004;20: 575–80. doi:10.1016/j.pt.2004.10.001
18. Sturm A, Amino R, van de Sand C, Regen T, Retzlaff S, Rennenberg A, et al. Manipulation of host hepatocytes by the malaria parasite for delivery into liver sinusoids. *Science*. 2006;313: 1287–90. doi:10.1126/science.1129720
19. Sanger F, Air GM, Barrell BG, Brown NL, Coulson AR, Fiddes CA, et al. Nucleotide sequence of bacteriophage phi X174 DNA. *Nature*. 1977;265: 687–95. Available: <http://www.ncbi.nlm.nih.gov/pubmed/870828>
20. Swerdlow H, Wu SL, Harke H, Dovichi NJ. Capillary gel electrophoresis for DNA sequencing. Laser-induced fluorescence detection with the sheath flow cuvette. *J Chromatogr*. 1990;516: 61–7. Available: <http://www.ncbi.nlm.nih.gov/pubmed/2286629>
21. Droege M, Hill B. The Genome Sequencer FLX System--longer reads, more applications, straight forward bioinformatics and more complete data sets. *J Biotechnol*. 2008;136: 3–10. doi:10.1016/j.jbiotec.2008.03.021
22. Bentley DR, Balasubramanian S, Swerdlow HP, Smith GP, Milton J, Brown CG, et al. Accurate whole human genome sequencing using reversible terminator chemistry. *Nature*. 2008;456: 53–9. doi:10.1038/nature07517
23. Shendure J, Porreca GJ, Reppas NB, Lin X, McCutcheon JP, Rosenbaum AM, et al. Accurate multiplex polony sequencing of an evolved bacterial genome. *Science*. 2005;309: 1728–32. doi:10.1126/science.1117389
24. Roberts RJ, Carneiro MO, Schatz MC. The advantages of SMRT sequencing. *Genome Biol*. 2013;14: 405. doi:10.1186/gb-2013-14-6-405
25. Metzker ML. Sequencing technologies - the next generation. *Nat Rev Genet*. Nature Publishing Group; 2010;11: 31–46. Available: <http://www.ncbi.nlm.nih.gov/pubmed/19997069>
26. Moorthie S, Mattocks CJ, Wright CF. Review of massively parallel DNA sequencing technologies. *Hugo J*. 2011;5: 1–12. doi:10.1007/s11568-011-9156-3

27. Quail MA, Smith M, Coupland P, Otto TD, Harris SR, Connor TR, et al. A tale of three next generation sequencing platforms: comparison of Ion Torrent, Pacific Biosciences and Illumina MiSeq sequencers. *BMC Genomics*. 2012;13: 341. doi:10.1186/1471-2164-13-341
28. Shendure J, Ji H. Next-generation DNA sequencing. *Nat Biotechnol*. 2008;26: 1135–45. doi:10.1038/nbt1486
29. Fedurco M, Romieu A, Williams S, Lawrence I, Turcatti G. BTA, a novel reagent for DNA attachment on glass and efficient generation of solid-phase amplified DNA colonies. *Nucleic Acids Res*. 2006;34: e22. doi:10.1093/nar/gnj023
30. Turcatti G, Romieu A, Fedurco M, Tairi A-P. A new class of cleavable fluorescent nucleotides: synthesis and optimization as reversible terminators for DNA sequencing by synthesis. *Nucleic Acids Res*. 2007;36: e25–e25. doi:10.1093/nar/gkn021
31. Mortazavi A, Williams BA, McCue K, Schaeffer L, Wold B. Mapping and quantifying mammalian transcriptomes by RNA-Seq. *Nat Methods*. 2008;5: 621–8. doi:10.1038/nmeth.1226
32. Gardner MJ, Hall N, Fung E, White O, Berriman M, Hyman RW, et al. Genome sequence of the human malaria parasite Plasmodium falciparum. *Nature*. 2002;419: 498–511. doi:10.1038/nature01097
33. Carlton JM, Angiuoli S V, Suh BB, Kooij TW, Pertea M, Silva JC, et al. Genome sequence and comparative analysis of the model rodent malaria parasite Plasmodium yoelii yoelii. *Nature*. 2002;419: 512–9. doi:10.1038/nature01099
34. Hall N, Karras M, Raine JD, Carlton JM, Kooij TW a, Berriman M, et al. A comprehensive survey of the Plasmodium life cycle by genomic, transcriptomic, and proteomic analyses. *Science*. 2005;307: 82–6. doi:10.1126/science.1103717
35. Kooij TW a, Carlton JM, Bidwell SL, Hall N, Ramesar J, Janse CJ, et al. A Plasmodium whole-genome synteny map: indels and synteny breakpoints as foci for species-specific genes. *PLoS Pathog*. 2005;1: e44. doi:10.1371/journal.ppat.0010044
36. Volkman SK, Neafsey DE, Schaffner SF, Park DJ, Wirth DF. Harnessing genomics and genome biology to understand malaria biology. *Nat Rev Genet*. Nature Publishing Group; 2012;13: 315–28. doi:10.1038/nrg3187
37. Allentoft ME, Collins M, Harker D, Haile J, Oskam CL, Hale ML, et al. The half-life of DNA in bone: measuring decay kinetics in 158 dated fossils. *Proc Biol Sci*. 2012;279: 4724–33. doi:10.1098/rspb.2012.1745
38. Branzei D, Foiani M. Regulation of DNA repair throughout the cell cycle. *Nat Rev Mol Cell Biol*. 2008;9: 297–308. doi:10.1038/nrm2351
39. McVey M, Lee SE. MMEJ repair of double-strand breaks (director's cut): deleted sequences and alternative endings. *Trends Genet*. 2008;24: 529–38. doi:10.1016/j.tig.2008.08.007

40. Kirkman LA, Lawrence EA, Deitsch KW. Malaria parasites utilize both homologous recombination and alternative end joining pathways to maintain genome integrity. *Nucleic Acids Res.* 2014;42: 370–9. doi:10.1093/nar/gkt881
41. Moynahan ME, Jasin M. Mitotic homologous recombination maintains genomic stability and suppresses tumorigenesis. *Nat Rev Mol Cell Biol.* 2010;11: 196–207. doi:10.1038/nrm2851
42. Ramiro RS, Reece SE, Obbard DJ. Molecular evolution and phylogenetics of rodent malaria parasites. *BMC Evol Biol.* 2012;12: 219. doi:10.1186/1471-2148-12-219
43. Limenitakis J, Soldati-Favre D. Functional genetics in Apicomplexa: potentials and limits. *FEBS Lett. Federation of European Biochemical Societies;* 2011;585: 1579–88. doi:10.1016/j.febslet.2011.05.002
44. Janse CJ, Ramesar J, Waters AP. High-efficiency transfection and drug selection of genetically transformed blood stages of the rodent malaria parasite *Plasmodium berghei*. *Nat Protoc.* 2006;1: 346–56. doi:10.1038/nprot.2006.53
45. Amino R, Thibierge S, Blazquez S, Baldacci P, Renaud O, Shorte S, et al. Imaging malaria sporozoites in the dermis of the mammalian host. *Nat Protoc.* 2007;2: 1705–12. doi:10.1038/nprot.2007.120
46. Fonager J, Franke-Fayard BMD, Adams JH, Ramesar J, Klop O, Khan SM, et al. Development of the piggyBac transposable system for *Plasmodium berghei* and its application for random mutagenesis in malaria parasites. *BMC Genomics.* 2011;12: 155. doi:10.1186/1471-2164-12-155
47. Balu B, Chauhan C, Maher SP, Shoue DA, Kissinger JC, Fraser MJ, et al. piggyBac is an effective tool for functional analysis of the *Plasmodium falciparum* genome. *BMC Microbiol.* 2009;9: 83. doi:10.1186/1471-2180-9-83
48. Goonewardene R, Daily J, Kaslow D, Sullivan TJ, Duffy P, Carter R, et al. Transfection of the malaria parasite and expression of firefly luciferase. *Proc Natl Acad Sci U S A.* 1993;90: 5234–6. Available: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC46690/>&tool=pmcentrez&rendertype=abstract
49. Wu Y, Kirkman LA, Wellemes TE. Transformation of *Plasmodium falciparum* malaria parasites by homologous integration of plasmids that confer resistance to pyrimethamine. *Proc Natl Acad Sci U S A.* 1996;93: 1130–4. Available: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC40043/>&tool=pmcentrez&rendertype=abstract
50. Van der Wel AM, Tomás AM, Kocken CH, Malhotra P, Janse CJ, Waters AP, et al. Transfection of the primate malaria parasite *Plasmodium knowlesi* using entirely heterologous constructs. *J Exp Med.* 1997;185: 1499–503. Available: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2196274/>&tool=pmcentrez&rendertype=abstract

51. Van Dijk MR, Waters AP, Janse CJ. Stable transfection of malaria parasite blood stages. *Science*. 1995;268: 1358–62. Available: <http://www.ncbi.nlm.nih.gov/pubmed/7761856>
52. Ferone R, Burchall JJ, Hitchings GH. Plasmodium berghei dihydrofolate reductase. Isolation, properties, and inhibition by antifolates. *Mol Pharmacol*. 1969;5: 49–59. Available: <http://www.ncbi.nlm.nih.gov/pubmed/4392112>
53. Orr RY, Philip N, Waters AP. Improved negative selection protocol for Plasmodium berghei in the rodent malarial model. *Malar J*. 2012;11: 103. doi:10.1186/1475-2875-11-103
54. Braks JAM, Franke-Fayard B, Kroeze H, Janse CJ, Waters AP. Development and application of a positive-negative selectable marker system for use in reverse genetics in Plasmodium. *Nucleic Acids Res*. 2006;34: e39. doi:10.1093/nar/gnj033
55. Drinnenberg IA, Weinberg DE, Xie KT, Mower JP, Wolfe KH, Fink GR, et al. RNAi in budding yeast. *Science*. 2009;326: 544–50. doi:10.1126/science.1176945
56. Clemens JC, Worby CA, Simonson-Leff N, Muda M, Maehama T, Hemmings BA, et al. Use of double-stranded RNA interference in Drosophila cell lines to dissect signal transduction pathways. *Proc Natl Acad Sci U S A*. 2000;97: 6499–503. doi:10.1073/pnas.110149597
57. Ngô H, Tschudi C, Gull K, Ullu E. Double-stranded RNA induces mRNA degradation in Trypanosoma brucei. *Proc Natl Acad Sci U S A*. 1998;95: 14687–92. Available: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC18313/>
58. Baum J, Papenfuss AT, Mair GR, Janse CJ, Vlachou D, Waters AP, et al. Molecular genetics and comparative genomics reveal RNAi is not functional in malaria parasites. *Nucleic Acids Res*. 2009;37: 3788–98. doi:10.1093/nar/gkp239
59. Meissner M, Krejany E, Gilson PR, de Koning-Ward TF, Soldati D, Crabb BS. Tetracycline analogue-regulated transgene expression in Plasmodium falciparum blood stages using Toxoplasma gondii transactivators. *Proc Natl Acad Sci U S A*. 2005;102: 2980–5. doi:10.1073/pnas.0500112102
60. Pino P, Sebastian S, Kim EA, Bush E, Brochet M, Volkmann K, et al. A tetracycline-repressible transactivator system to study essential genes in malaria parasites. *Cell Host Microbe*. 2012;12: 824–34. doi:10.1016/j.chom.2012.10.016
61. Armstrong CM, Goldberg DE. An FKBP destabilization domain modulates protein levels in Plasmodium falciparum. *Nat Methods*. 2007;4: 1007–9. doi:10.1038/nmeth1132
62. Sebastian S, Brochet M, Collins MOO, Schwach F, Jones MLL, Goulding D, et al. A Plasmodium Calcium-Dependent Protein Kinase Controls Zygote Development and Transmission by Translationally Activating Repressed mRNAs. *Cell Host Microbe*. 2012;12: 9–19. doi:10.1016/j.chom.2012.05.014

63. Suarez C, Volkmann K, Gomes AR, Billker O, Blackman MJ. The malarial serine protease SUB1 plays an essential role in parasite liver stage development. *PLoS Pathog.* 2013;9: e1003811. doi:10.1371/journal.ppat.1003811
64. Lacroix C, Giovannini D, Combe A, Bargieri DY, Späth S, Panchal D, et al. FLP/FRT-mediated conditional mutagenesis in pre-erythrocytic stages of *Plasmodium berghei*. *Nat Protoc.* 2011;6: 1412–28. doi:10.1038/nprot.2011.363
65. Landy A. Dynamic, structural, and regulatory aspects of lambda site-specific recombination. *Annu Rev Biochem.* 1989;58: 913–49. doi:10.1146/annurev.bi.58.070189.004405
66. Hartley JL, Temple GF, Brasch MA. DNA cloning using in vitro site-specific recombination. *Genome Res.* 2000;10: 1788–95. Available: <http://www.ncbi.nlm.nih.gov/article/fcgi?artid=310948&tool=pmcentrez&rendertype=abstract>
67. Katzen F. Gateway(®) recombinational cloning: a biological operating system. *Expert Opin Drug Discov.* 2007;2: 571–89. doi:10.1517/17460441.2.4.571
68. Copeland NG, Jenkins NA, Court DL. Recombineering: a powerful new tool for mouse functional genomics. *Nat Rev Genet.* 2001;2: 769–79. doi:10.1038/35093556
69. Murphy KC. Phage recombinases and their applications. [Internet]. 1st ed. Advances in virus research. Elsevier Inc.; 2012. pp. 367–414. doi:10.1016/B978-0-12-394438-2.00008-6
70. Muyrers JP, Zhang Y, Testa G, Stewart AF. Rapid modification of bacterial artificial chromosomes by ET-recombination. *Nucleic Acids Res.* 1999;27: 1555–7. Available: <http://www.ncbi.nlm.nih.gov/article/fcgi?artid=148353&tool=pmcentrez&rendertype=abstract>
71. Zhang Y, Buchholz F, Muyrers JP, Stewart AF. A new logic for DNA engineering using recombination in *Escherichia coli*. *Nat Genet.* 1998;20: 123–8. doi:10.1038/2417
72. Ravin V, Ravin N, Casjens S, Ford ME, Hatfull GF, Hendrix RW. Genomic sequence and analysis of the atypical temperate bacteriophage N15. *J Mol Biol.* 2000;299: 53–73. doi:10.1006/jmbi.2000.3731
73. Pfander C, Anar B, Schwach F, Otto TD, Brochet M, Volkmann K, et al. A scalable pipeline for highly effective genetic modification of a malaria parasite. *Nat Methods.* 2011;8: 1078–82. doi:10.1038/nmeth.1742
74. Miller CA, Ingmer H, Cohen SN. Boundaries of the pSC101 minimal replicon are conditional. *J Bacteriol.* 1995;177: 4865–71. Available: <http://www.ncbi.nlm.nih.gov/article/fcgi?artid=177259&tool=pmcentrez&rendertype=abstract>
75. Marinelli LJ, Hatfull GF, Piuri M. Recombineering: A powerful tool for modification of bacteriophage genomes. 2012; 5–14.

76. Wang J, Sarov M, Rientjes J, Fu J, Hollak H, Kranz H, et al. An improved recombineering approach by adding RecA to lambda Red recombination. *Mol Biotechnol.* 2006;32: 43–53. Available: <http://www.ncbi.nlm.nih.gov/pubmed/16382181>
77. Hasty P, Rivera-Pérez J, Bradley A. The length of homology required for gene targeting in embryonic stem cells. *Mol Cell Biol.* 1991;11: 5586–91. Available: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC361929/>&tool=pmcentrez&rendertype=abstract
78. Pierce SE, Davis RW, Nislow C, Giaever G. Genome-wide analysis of barcoded *Saccharomyces cerevisiae* gene-deletion mutants in pooled cultures. *Nat Protoc.* 2007;2: 2958–74. doi:10.1038/nprot.2007.427
79. Skarnes WC, Rosen B, West AP, Koutsourakis M, Bushell W, Iyer V, et al. A conditional knockout resource for the genome-wide study of mouse gene function. *Nature.* 2011;474: 337–42. doi:10.1038/nature10163
80. Hayes F. Transposon-based strategies for microbial functional genomics and proteomics. *Annu Rev Genet.* 2003;37: 3–29. doi:10.1146/annurev.genet.37.110801.142807
81. Smith V, Chou KN, Lashkari D, Botstein D, Brown PO. Functional analysis of the genes of yeast chromosome V by genetic footprinting. *Science.* 1996;274: 2069–74. Available: <http://www.ncbi.nlm.nih.gov/pubmed/8953036>
82. Hensel M, Shea JE, Gleeson C, Jones MD, Dalton E, Holden DW. Simultaneous identification of bacterial virulence genes by negative selection. *Science.* 1995;269: 400–3. Available: <http://www.ncbi.nlm.nih.gov/pubmed/7618105>
83. Autret N, Charbit A. Lessons from signature-tagged mutagenesis on the infectious mechanisms of pathogenic bacteria. *FEMS Microbiol Rev.* 2005;29: 703–717. Available: <http://www.sciencedirect.com/science/article/pii/S0168644504000865>
84. Darwin AJ, Miller VL. Identification of *Yersinia enterocolitica* genes affecting survival in an animal host using signature-tagged transposon mutagenesis. *Mol Microbiol.* 1999;32: 51–62. Available: <http://www.ncbi.nlm.nih.gov/pubmed/10216859>
85. Camacho LR, Ensergueix D, Perez E, Gicquel B, Guilhot C. Identification of a virulence gene cluster of *Mycobacterium tuberculosis* by signature-tagged transposon mutagenesis. *Mol Microbiol.* 1999;34: 257–67. Available: <http://www.ncbi.nlm.nih.gov/pubmed/10564470>
86. Chiang SL, Mekalanos JJ. Use of signature-tagged transposon mutagenesis to identify *Vibrio cholerae* genes critical for colonization. *Mol Microbiol.* 1998;27: 797–805. Available: <http://www.ncbi.nlm.nih.gov/pubmed/9515705>
87. Mei JM, Nourbakhsh F, Ford CW, Holden DW. Identification of *Staphylococcus aureus* virulence genes in a murine model of bacteraemia using signature-tagged

- mutagenesis. *Mol Microbiol*. 1997;26: 399–407. Available: <http://www.ncbi.nlm.nih.gov/pubmed/9383163>
88. Cormack BP, Ghori N, Falkow S. An adhesin of the yeast pathogen *Candida glabrata* mediating adherence to human epithelial cells. *Science*. 1999;285: 578–82. Available: <http://www.ncbi.nlm.nih.gov/pubmed/10417386>
89. Knoll LJ, Furie GL, Boothroyd JC. Adaptation of signature-tagged mutagenesis for *Toxoplasma gondii*: a negative screening strategy to isolate genes that are essential in restrictive growth conditions. *Mol Biochem Parasitol*. 2001;116: 11–16. doi:10.1016/S0166-6851(01)00295-X
90. Saenz HL, Dehio C. Signature-tagged mutagenesis: technical advances in a negative selection method for virulence gene identification. *Curr Opin Microbiol*. 2005;8: 612–9. doi:10.1016/j.mib.2005.08.013
91. Mazurkiewicz P, Tang CM, Boone C, Holden DW. Signature-tagged mutagenesis : barcoding mutants for genome-wide screens. *Nat Rev Genet*. 2006;7: 929–939. doi:10.1038/nrg1984
92. Hunt TA, Kooi C, Sokol PA, Valvano MA. Identification of *Burkholderia cenocepacia* genes required for bacterial survival in vivo. *Infect Immun*. 2004;72: 4010–22. doi:10.1128/IAI.72.7.4010-4022.2004
93. Shoemaker DD, Lashkari DA, Morris D, Mittmann M, Davis RW. Quantitative phenotypic analysis of yeast deletion mutants using a highly parallel molecular bar-coding strategy. *Nat Genet*. 1996;14: 450–6. doi:10.1038/ng1296-450
94. Winzeler EA. Functional Characterization of the *S. cerevisiae* Genome by Gene Deletion and Parallel Analysis. *Science* (80-). 1999;285: 901–906. doi:10.1126/science.285.5429.901
95. Smith AM, Heisler LE, Mellor J, Kaper F, Thompson MJ, Chee M, et al. Quantitative phenotyping via deep barcode sequencing. *Genome Res*. 2009;19: 1836–42. doi:10.1101/gr.093955.109
96. Han TX, Xu X-Y, Zhang M-J, Peng X, Du L-L. Global fitness profiling of fission yeast deletion strains by barcode sequencing. *Genome Biol*. 2010;11: R60. doi:10.1186/gb-2010-11-6-r60
97. Bateson W. FACTS LIMITING THE THEORY OF HEREDITY. *Science*. 1907;26: 649–60. doi:10.1126/science.26.672.649
98. Guarente L. Synthetic enhancement in gene interaction: a genetic tool come of age. *Trends Genet*. 1993;9: 362–366. doi:10.1016/0168-9525(93)90042-G
99. Roth FP, Lipshitz HD, Andrews BJ. Q&A: epistasis. *J Biol*. 2009;8: 35. doi:10.1186/jbiol144

100. Boone C, Bussey H, Andrews BJ. Exploring genetic interactions and networks with yeast. *Nat Rev Genet.* 2007;8: 437–49. doi:10.1038/nrg2085
101. Mani R, St Onge RP, Hartman JL, Giaever G, Roth FP. Defining genetic interaction. *Proc Natl Acad Sci U S A.* 2008;105: 3461–6. doi:10.1073/pnas.0712255105
102. Tong AHY, Lesage G, Bader GD, Ding H, Xu H, Xin X, et al. Global mapping of the yeast genetic interaction network. *Science.* 2004;303: 808–13. doi:10.1126/science.1091317
103. Giaever G, Chu AM, Ni L, Connelly C, Riles L, Véronneau S, et al. Functional profiling of the *Saccharomyces cerevisiae* genome. *Nature.* 2002;418: 387–91. doi:10.1038/nature00935
104. Costanzo M, Baryshnikova A, Bellay J, Kim Y, Spear ED, Sevier CS, et al. The genetic landscape of a cell. *Science.* 2010;327: 425–31. doi:10.1126/science.1180823
105. Tewari R, Straschil U, Bateman A, Böhme U, Cherevach I, Gong P, et al. The systematic functional analysis of Plasmodium protein kinases identifies essential regulators of mosquito transmission. *Cell Host Microbe.* 2010;8: 377–87. doi:10.1016/j.chom.2010.09.006
106. Bimbó A, Jia Y, Poh SL, Karuturi RKM, den Elzen N, Peng X, et al. Systematic deletion analysis of fission yeast protein kinases. *Eukaryot Cell.* 2005;4: 799–813. doi:10.1128/EC.4.4.799-813.2005
107. Tremp AZ, Dessens JT. Malaria IMC1 membrane skeleton proteins operate autonomously and participate in motility independently of cell shape. *J Biol Chem.* 2011;286: 5383–91. doi:10.1074/jbc.M110.187195
108. Lavazec C, Moreira CK, Mair GR, Waters AP, Janse CJ, Templeton TJ. Analysis of mutant Plasmodium berghei parasites lacking expression of multiple PbCCp genes. *Mol Biochem Parasitol.* 2009;163: 1–7. doi:10.1016/j.molbiopara.2008.09.002
109. Sharifpoor S, van Dyk D, Costanzo M, Baryshnikova A, Friesen H, Douglas AC, et al. Functional wiring of the yeast kinase revealed by global analysis of genetic network motifs. *Genome Res.* 2012;22: 791–801. doi:10.1101/gr.129213.111
110. Ptacek J, Devgan G, Michaud G, Zhu H, Zhu X, Fasolo J, et al. Global analysis of protein phosphorylation in yeast. *Nature.* 2005;438: 679–84. doi:10.1038/nature04187
111. Sharifpoor S, Nguyen Ba AN, Youn J-Y, Young J-Y, van Dyk D, Friesen H, et al. A quantitative literature-curated gold standard for kinase-substrate pairs. *Genome Biol.* 2011;12: R39. doi:10.1186/gb-2011-12-4-r39
112. Doerig C, Billker O, Haystead T, Sharma P, Tobin AB, Waters NC. Protein kinases of malaria parasites: an update. *Trends Parasitol.* 2008;24: 570–7. doi:10.1016/j.pt.2008.08.007

113. Lim DC, Cooke BM, Doerig C, Saeij JPJ. Toxoplasma and Plasmodium protein kinases: roles in invasion and host cell remodelling. *Int J Parasitol. Australian Society for Parasitology Inc.*; 2012;42: 21–32. doi:10.1016/j.ijpara.2011.11.007
114. Sopko R, Andrews BJ. Linking the kinase and phosphorylome--a comprehensive review of approaches to find kinase targets. *Mol Biosyst.* 2008;4: 920–33. doi:10.1039/b801724g
115. Hanks SK. Genomic analysis of the eukaryotic protein kinase superfamily: a perspective. *Genome Biol.* 2003;4: 111. Available: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1470002/>
116. Hanks SK, Hunter T. The eukaryotic protein kinase superfamily: kinase (catalytic) domain structure and classification. *FASEB J.* 1995;9: 576–96. Available: <http://www.ncbi.nlm.nih.gov/pubmed/7768349>
117. Miranda-Saavedra D, Gabaldón T, Barton GJ, Langsley G, Doerig C. The kinomes of apicomplexan parasites. *Microbes Infect.* 2012;14: 796–810. doi:10.1016/j.micinf.2012.04.007
118. Ward P, Equinet L, Packer J, Doerig C. Protein kinases of the human malaria parasite Plasmodium falciparum: the kinase of a divergent eukaryote. *BMC Genomics.* 2004;5: 79. doi:10.1186/1471-2164-5-79
119. Talevich E, Mirza A, Kannan N. Structural and evolutionary divergence of eukaryotic protein kinases in Apicomplexa. *BMC Evol Biol.* 2011;11: 321. doi:10.1186/1471-2148-11-321
120. Anamika, Srinivasan N, Krupa A. A genomic perspective of protein kinases in Plasmodium falciparum. *Proteins.* 2005;58: 180–9. doi:10.1002/prot.20278
121. Manning G. Genomic overview of protein kinases. *WormBook.* 2005; 1–19. doi:10.1895/wormbook.1.60.1
122. Lasonder E, Treeck M, Alam M, Tobin AB. Insights into the Plasmodium falciparum schizont phospho-proteome. *Microbes Infect.* 2012;14: 811–9. doi:10.1016/j.micinf.2012.04.008
123. Schneider AG, Mercereau-Puijalon O. A new Apicomplexa-specific protein kinase family: multiple members in Plasmodium falciparum, all with an export signature. *BMC Genomics.* 2005;6: 30. doi:10.1186/1471-2164-6-30
124. LaRonde-LeBlanc N, Wlodawer A. A family portrait of the RIO kinases. *J Biol Chem.* 2005;280: 37297–300. doi:10.1074/jbc.R500013200
125. Nag S, Prasad KMN, Bhowmick A, Deshmukh R, Trivedi V. PfRIO-2 kinase is a potential therapeutic target of antimalarial protein kinase inhibitors. *Curr Drug Discov Technol.* 2013;10: 85–91. Available: <http://www.ncbi.nlm.nih.gov/pubmed/23082912>

126. Lovejoy CA, Cortez D. Common mechanisms of PIKK regulation. *DNA Repair* (Amst). 2009;8: 1004–8. doi:10.1016/j.dnarep.2009.04.006
127. Pearson G, Robinson F, Beers Gibson T, Xu BE, Karandikar M, Berman K, et al. Mitogen-activated protein (MAP) kinase pathways: regulation and physiological functions. *Endocr Rev.* 2001;22: 153–83. doi:10.1210/edrv.22.2.0428
128. Doerig C, Abdi A, Bland N, Eschenlauer S, Dorin-Semblat D, Fennell C, et al. Malaria: targeting parasite and host cell kinomes. *Biochim Biophys Acta.* Elsevier B.V.; 2010;1804: 604–12. doi:10.1016/j.bbapap.2009.10.009
129. Dorin-Semblat D, Quashie N, Halbert J, Sicard A, Doerig C, Peat E, et al. Functional characterization of both MAP kinases of the human malaria parasite *Plasmodium falciparum* by reverse genetics. *Mol Microbiol.* 2007;65: 1170–80. doi:10.1111/j.1365-2958.2007.05859.x
130. Tewari R, Dorin D, Moon R, Doerig C, Billker O. An atypical mitogen-activated protein kinase controls cytokinesis and flagellar motility during male gamete formation in a malaria parasite. *Mol Microbiol.* 2005;58: 1253–63. doi:10.1111/j.1365-2958.2005.04793.x
131. Harmon AC, Gribskov M, Harper JF. CDPKs - a kinase for every Ca²⁺ signal? *Trends Plant Sci.* 2000;5: 154–9. Available: <http://www.ncbi.nlm.nih.gov/pubmed/10740296>
132. Zhang XS, Choi JH. Molecular evolution of calmodulin-like domain protein kinases (CDPKs) in plants and protists. *J Mol Evol.* 2001;53: 214–24. doi:10.1007/s002390010211
133. Harper JF, Harmon A. Plants, symbiosis and parasites: a calcium signalling connection. *Nat Rev Mol Cell Biol.* Nature Publishing Group; 2005;6: 555–66. doi:10.1038/nrm1679
134. Vaid A, Thomas DC, Sharma P. Role of Ca²⁺/calmodulin-PfPKB signaling pathway in erythrocyte invasion by *Plasmodium falciparum*. *J Biol Chem.* 2008;283: 5589–97. doi:10.1074/jbc.M708465200
135. Gantt S, Persson C, Rose K, Birkett AJ, Abagyan R, Nussenzweig V. Antibodies against thrombospondin-related anonymous protein do not inhibit *Plasmodium* sporozoite infectivity in vivo. *Infect Immun.* 2000;68: 3667–73. Available: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=97657&tool=pmcentrez&rendertype=abstract>
136. Ishino T, Orito Y, Chinzei Y, Yuda M. A calcium-dependent protein kinase regulates *Plasmodium* ookinete access to the midgut epithelial cell. *Mol Microbiol.* 2006;59: 1175–84. doi:10.1111/j.1365-2958.2005.05014.x
137. Ono T, Cabrita-Santos L, Leitao R, Bettoli E, Purcell LA, Diaz-Pulido O, et al. Adenylyl cyclase alpha and cAMP signaling mediate *Plasmodium* sporozoite apical regulated exocytosis and hepatocyte infection. *PLoS Pathog.* 2008;4: e1000008. doi:10.1371/journal.ppat.1000008

138. Billker O, Dechamps S, Tewari R, Wenig G, Franke-Fayard B, Brinkmann V. Calcium and a calcium-dependent protein kinase regulate gamete formation and mosquito transmission in a malaria parasite. *Cell*. 2004;117: 503–14. Available: <http://www.ncbi.nlm.nih.gov/pubmed/15137943>
139. Green JL, Rees-Channer RR, Howell SA, Martin SR, Knuepfer E, Taylor HM, et al. The motor complex of Plasmodium falciparum: phosphorylation by a calcium-dependent protein kinase. *J Biol Chem*. 2008;283: 30980–9. doi:10.1074/jbc.M803129200
140. Bansal A, Singh S, More KR, Hans D, Nangalia K, Yogavel M, et al. Characterization of Plasmodium falciparum calcium-dependent protein kinase 1 (PfCDPK1) and its role in microneme secretion during erythrocyte invasion. *J Biol Chem*. 2013;288: 1590–602. doi:10.1074/jbc.M112.411934
141. Lauciello L, Kappes B, Scapozza L, Perozzo R. Expression, purification and biochemical characterization of recombinant Ca-dependent protein kinase 2 of the malaria parasite Plasmodium falciparum. *Protein Expr Purif*. 2013;90: 170–177. Available: <http://www.sciencedirect.com/science/article/pii/S1046592813001125>
142. Li JL, Baker DA, Cox LS. Sexual stage-specific expression of a third calcium-dependent protein kinase from Plasmodium falciparum. *Biochim Biophys Acta*. 2000;1491: 341–9. Available: <http://www.ncbi.nlm.nih.gov/pubmed/10760601>
143. Kato K, Sudo A, Kobayashi K, Sugi T, Tohya Y, Akashi H. Characterization of Plasmodium falciparum calcium-dependent protein kinase 4. *Parasitol Int*. 2009;58: 394–400. doi:10.1016/j.parint.2009.08.001
144. Dvorin JD, Martyn DC, Patel SD, Grimley JS, Collins CR, Hopp CS, et al. A plant-like kinase in Plasmodium falciparum regulates parasite egress from erythrocytes. *Science*. 2010;328: 910–2. doi:10.1126/science.1188191
145. Solyakov L, Halbert J, Alam MM, Semblat J-P, Dorin-Semblat D, Reininger L, et al. Global kinomic and phospho-proteomic analyses of the human malaria parasite Plasmodium falciparum. *Nat Commun*. Nature Publishing Group; 2011;2: 565. doi:10.1038/ncomms1558
146. Jebiwott S, Govindaswamy K, Mbugua A, Bhanot P. Plasmodium berghei calcium dependent protein kinase 1 is not required for host cell invasion. *PLoS One*. 2013;8: e79171. doi:10.1371/journal.pone.0079171
147. Coppi A, Tewari R, Bishop JR, Bennett BL, Lawrence R, Esko JD, et al. Heparan Sulfate Proteoglycans Provide a Signal to Plasmodium Sporozoites to Stop Migrating and Productively Invade Host Cells. *Cell Host Microbe*. 2007;2: 316–327. Available: <http://www.sciencedirect.com/science/article/pii/S193131280700248X>
148. Möskes C, Burghaus PA, Wernli B, Sauder U, Dürrenberger M, Kappes B. Export of Plasmodium falciparum calcium-dependent protein kinase 1 to the parasitophorous vacuole is dependent on three N-terminal membrane anchor motifs. *Mol Microbiol*. 2004;54: 676–91. doi:10.1111/j.1365-2958.2004.04313.x

149. Macek B, Gnad F, Soufi B, Kumar C, Olsen J V, Mijakovic I, et al. Phosphoproteome analysis of *E. coli* reveals evolutionary conservation of bacterial Ser/Thr/Tyr phosphorylation. *Mol Cell Proteomics*. 2008;7: 299–307. doi:10.1074/mcp.M700311-MCP200
150. Gruhler A, Olsen J V, Mohammed S, Mortensen P, Faergeman NJ, Mann M, et al. Quantitative phosphoproteomics applied to the yeast pheromone signaling pathway. *Mol Cell Proteomics*. 2005;4: 310–27. doi:10.1074/mcp.M400219-MCP200
151. Krüger M, Moser M, Ussar S, Thievessen I, Luber CA, Forner F, et al. SILAC mouse for quantitative proteomics uncovers kindlin-3 as an essential factor for red blood cell function. *Cell*. 2008;134: 353–64. doi:10.1016/j.cell.2008.05.033
152. Lasonder E, Green JL, Camarda G, Talabani H, Holder AA, Langsley G, et al. The *Plasmodium falciparum* Schizont Phosphoproteome Reveals Extensive Phosphatidylinositol and cAMP-Protein Kinase A Signaling. *J Proteome Res*. 2012;11: 5323–5337. doi:10.1021/pr300557m
153. Treeck M, Sanders JL, Elias JE, Boothroyd JC. The Phosphoproteomes of *Plasmodium falciparum* and *Toxoplasma gondii* Reveal Unusual Adaptations Within and Beyond the Parasites' Boundaries. *Cell Host Microbe*. 2011;10: 410–419. doi:10.1016/j.chom.2011.09.004
154. Brochet M, Collins MO, Smith TK, Thompson E, Sebastian S, Volkmann K, et al. Phosphoinositide metabolism links cGMP-dependent protein kinase G to essential Ca^{2+} signals at key decision points in the life cycle of malaria parasites. *PLoS Biol*. 2014;12: e1001806. doi:10.1371/journal.pbio.1001806
155. Trager W, Gill GS. Enhanced gametocyte formation in young erythrocytes by *Plasmodium falciparum* in vitro. *J Protozool*. 1992;39: 429–32. Available: <http://www.ncbi.nlm.nih.gov/pubmed/1640389>
156. Winger LA, Tirawanchai N, Nicholas J, Carter HE, Smith JE, Sinden RE. Ookinete antigens of *Plasmodium berghei*. Appearance on the zygote surface of an Mr 21 kD determinant identified by transmission-blocking monoclonal antibodies. *Parasite Immunol*. 1988;10: 193–207. Available: <http://www.ncbi.nlm.nih.gov/pubmed/2453831>
157. Saxena AK, Wu Y, Garboczi DN. Plasmodium P25 and P28 Surface Proteins: Potential Transmission-Blocking Vaccines. *Eukaryot Cell*. 2007;6: 1260–1265. doi:10.1128/EC.00060-07
158. Hamming RW. Error Detecting and Error Correcting Codes. *Bell Syst Tech J*. 1950;29: 147–160. doi:10.1002/j.1538-7305.1950.tb00463.x
159. Janse CJ, Franke-Fayard B, Mair GR, Ramesar J, Thiel C, Engelmann S, et al. High efficiency transfection of *Plasmodium berghei* facilitates novel selection procedures. *Mol Biochem Parasitol*. 2006;145: 60–70. doi:10.1016/j.molbiopara.2005.09.007

160. Janse CJ, Haghparast A, Sperança MA, Ramesar J, Kroeze H, del Portillo HA, et al. Malaria parasites lacking eef1a have a normal S/M phase yet grow more slowly due to a longer G1 phase. *Mol Microbiol*. 2003;50: 1539–51. Available: <http://www.ncbi.nlm.nih.gov/pubmed/14651637>
161. Semrov D, Miklavčič D. Numerical modeling for in vivo electroporation. *Methods Mol Med*. 2000;37: 63–81. doi:10.1385/1-59259-080-2:63
162. Kotnik T, Bobanović F, Miklavčič D. Sensitivity of transmembrane voltage induced by applied electric fields—A theoretical analysis. *Bioelectrochemistry Bioenerg*. 1997;43: 285–291. doi:10.1016/S0302-4598(97)00023-8
163. Polz MF, Cavanaugh CM. Bias in template-to-product ratios in multitemplate PCR. *Appl Environ Microbiol*. 1998;64: 3724–30. Available: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC106531/>
164. Tomas AM, Margos G, Dimopoulos G, van Lin LH, de Koning-Ward TF, Sinha R, et al. P25 and P28 proteins of the malaria ookinete surface have multiple and partially redundant functions. *EMBO J*. 2001;20: 3975–83. doi:10.1093/emboj/20.15.3975
165. Dessens JT, Sidén-Kiamos I, Mendoza J, Mahairaki V, Khater E, Vlachou D, et al. SOAP, a novel malaria ookinete protein involved in mosquito midgut invasion and oocyst development. *Mol Microbiol*. 2003;49: 319–29. Available: <http://www.ncbi.nlm.nih.gov/pubmed/12828632>
166. Van Dijk MR, van Schaijk BCL, Khan SM, van Dooren MW, Ramesar J, Kaczanowski S, et al. Three members of the 6-cys protein family of Plasmodium play a role in gamete fertility. *PLoS Pathog*. 2010;6: e1000853. doi:10.1371/journal.ppat.1000853
167. Spaccapelo R, Janse CJ, Caterbi S, Franke-Fayard B, Bonilla JA, Syphard LM, et al. Plasmeprin 4-deficient Plasmodium berghei are virulence attenuated and induce protective immunity against experimental malaria. *Am J Pathol*. 2010;176: 205–17. doi:10.2353/ajpath.2010.090504
168. Günther S, McMillan PJ, Wallace LJM, Müller S. Plasmodium falciparum possesses organelle-specific alpha-keto acid dehydrogenase complexes and lipoylation pathways. *Biochem Soc Trans*. 2005;33: 977–80. doi:10.1042/BST20050977
169. Droucheau E, Primot A, Thomas V, Mattei D, Knockaert M, Richardson C, et al. Plasmodium falciparum glycogen synthase kinase-3: molecular model, expression, intracellular localisation and selective inhibitors. *Biochim Biophys Acta*. 2004;1697: 181–96. doi:10.1016/j.bbapap.2003.11.023
170. Kato N, Sakata T, Breton G, Le Roch KG, Nagle A, Andersen C, et al. Gene expression signatures and small-molecule compounds link a protein kinase to Plasmodium falciparum motility. *Nat Chem Biol*. 2008;4: 347–56. doi:10.1038/nchembio.87

171. Angermayr M, Roidl A, Bandlow W. Yeast Rio1p is the founding member of a novel subfamily of protein serine kinases involved in the control of cell cycle progression. *Mol Microbiol*. 2002;44: 309–24. doi:10.1046/j.1365-2958.2002.02881.x
172. Geerlings TH, Faber AW, Bister MD, Vos JC, Raué HA. Rio2p, an evolutionarily conserved, low abundant protein kinase essential for processing of 20 S Pre-rRNA in *Saccharomyces cerevisiae*. *J Biol Chem*. 2003;278: 22537–45. doi:10.1074/jbc.M300759200
173. Widmann B, Wandrey F, Badertscher L, Wyler E, Pfannstiel J, Zemp I, et al. The kinase activity of human Rio1 is required for final steps of cytoplasmic maturation of 40S subunits. *Mol Biol Cell*. 2012;23: 22–35. doi:10.1091/mbc.E11-07-0639
174. Spahn CM, Beckmann R, Eswar N, Penczek PA, Sali A, Blobel G, et al. Structure of the 80S ribosome from *Saccharomyces cerevisiae*--tRNA-ribosome and subunit-subunit interactions. *Cell*. 2001;107: 373–86. Available: <http://www.ncbi.nlm.nih.gov/pubmed/11701127>
175. Schäfer T, Strauss D, Petfalski E, Tollervey D, Hurt E. The path from nucleolar 90S to cytoplasmic 40S pre-ribosomes. *EMBO J*. 2003;22: 1370–80. doi:10.1093/emboj/cdg121
176. Guler JL, Freeman DL, Ahyong V, Patrapuvich R, White J, Gujjar R, et al. Asexual populations of the human malaria parasite, *Plasmodium falciparum*, use a two-step genomic strategy to acquire accurate, beneficial DNA amplifications. *PLoS Pathog*. 2013;9: e1003375. doi:10.1371/journal.ppat.1003375
177. Embi N, Rylatt DB, Cohen P. Glycogen synthase kinase-3 from rabbit skeletal muscle. Separation from cyclic-AMP-dependent protein kinase and phosphorylase kinase. *Eur J Biochem*. 1980;107: 519–27. Available: <http://www.ncbi.nlm.nih.gov/pubmed/6249596>
178. Harwood AJ. Regulation of GSK-3: a cellular multiprocessor. *Cell*. 2001;105: 821–4. Available: <http://www.ncbi.nlm.nih.gov/pubmed/11439177>
179. Nurul Aiezzah Z, Noor E, Hasidah MS. Suppression of *Plasmodium berghei* parasitemia by LiCl in an animal infection model. *Trop Biomed*. 2010;27: 624–31. Available: <http://www.ncbi.nlm.nih.gov/pubmed/21399604>
180. Trager W, Rudzinska MA, Bradbury PC. The fine structure of *Plasmodium falciparum* and its host erythrocytes in natural malarial infections in man. *Bull World Health Organ*. 1966;35: 883–5. Available: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2476278&tool=pmcentrez&rendertype=abstract>
181. Sam-Yellowe TY. The role of the Maurer's clefts in protein transport in *Plasmodium falciparum*. *Trends Parasitol*. 2009;25: 277–84. doi:10.1016/j.pt.2009.03.009

182. Ingmundson A, Nahar C, Brinkmann V, Lehmann MJ, Matuschewski K. The exported Plasmodium berghei protein IBIS1 delineates membranous structures in infected red blood cells. *Mol Microbiol*. 2012;83: 1229–43. doi:10.1111/j.1365-2958.2012.08004.x
183. Haase S, Hanssen E, Matthews K, Kalanon M, de Koning-Ward TF. The exported protein PbCP1 localises to cleft-like structures in the rodent malaria parasite Plasmodium berghei. *PLoS One*. 2013;8: e61482. doi:10.1371/journal.pone.0061482
184. Cromer D, Evans KJ, Schofield L, Davenport MP. Preferential invasion of reticulocytes during late-stage Plasmodium berghei infection accounts for reduced circulating reticulocyte levels. *Int J Parasitol*. 2006;36: 1389–97. doi:10.1016/j.ijpara.2006.07.009
185. Chang K-H, Tam M, Stevenson MM. Modulation of the course and outcome of blood-stage malaria by erythropoietin-induced reticulocytosis. *J Infect Dis*. 2004;189: 735–43. doi:10.1086/381458
186. Mombaerts P, Iacomini J, Johnson RS, Herrup K, Tonegawa S, Papaioannou VE. RAG-1-deficient mice have no mature B and T lymphocytes. *Cell*. Elsevier; 1992;68: 869–877. doi:10.1016/0092-8674(92)90030-G
187. Tullai JW, Graham JR, Cooper GM. A GSK-3-mediated transcriptional network maintains repression of immediate early genes in quiescent cells. *Cell Cycle*. 2011;10: 3072–7. Available: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3218618&tool=pmcentrez&rendertype=abstract>
188. Ojo KK, Pfander C, Mueller NR, Burstroem C, Larson ET, Bryan CM, et al. Transmission of malaria to mosquitoes blocked by bumped kinase inhibitors. *J Clin Invest*. 2012;122: 2301–5. doi:10.1172/JCI61822
189. Billker O, Lourido S, Sibley LD. Calcium-dependent signaling and kinases in apicomplexan parasites. *Cell Host Microbe*. 2009;5: 612–22. doi:10.1016/j.chom.2009.05.017
190. Francis SH, Busch JL, Corbin JD, Sibley D. cGMP-dependent protein kinases and cGMP phosphodiesterases in nitric oxide and cGMP action. *Pharmacol Rev*. 2010;62: 525–63. doi:10.1124/pr.110.002907
191. Shokat K, Velleca M. Novel chemical genetic approaches to the discovery of signal transduction inhibitors. *Drug Discov Today*. 2002;7: 872–9. Available: <http://www.ncbi.nlm.nih.gov/pubmed/12546954>
192. Taylor HM, McRobert L, Grainger M, Sicard A, Dluzewski AR, Hopp CS, et al. The malaria parasite cyclic GMP-dependent protein kinase plays a central role in blood-stage schizogony. *Eukaryot Cell*. 2010;9: 37–45. doi:10.1128/EC.00186-09
193. Diaz CA, Allocco J, Powles MA, Yeung L, Donald RGK, Anderson JW, et al. Characterization of Plasmodium falciparum cGMP-dependent protein kinase (PfPKG):

- antiparasitic activity of a PKG inhibitor. *Mol Biochem Parasitol.* 2006;146: 78–88. doi:10.1016/j.molbiopara.2005.10.020
194. McRobert L, Taylor CJ, Deng W, Fivelman QL, Cummings RM, Polley SD, et al. Gametogenesis in malaria parasites is mediated by the cGMP-dependent protein kinase. Ward GE, editor. *PLoS Biol.* Public Library of Science; 2008;6: e139. doi:10.1371/journal.pbio.0060139
195. Shimizu H, Nagamori I, Yabuta N, Nojima H. GAK, a regulator of clathrin-mediated membrane traffic, also controls centrosome integrity and chromosome congression. *J Cell Sci.* 2009;122: 3145–52. doi:10.1242/jcs.052795
196. Dearsly AL, Sinden RE, Self IA. Sexual development in malarial parasites: gametocyte production, fertility and infectivity to the mosquito vector. *Parasitology.* 1990;100 Pt 3: 359–68. Available: <http://www.ncbi.nlm.nih.gov/pubmed/2194152>
197. Shimomura T, Ando S, Matsumoto K, Sugimoto K. Functional and physical interaction between Rad24 and Rfc5 in the yeast checkpoint pathways. *Mol Cell Biol.* 1998;18: 5485–91. Available: <http://www.ncbi.nlm.nih.gov/article/fcgi?artid=109133&tool=pmcentrez&rendertype=abstract>
198. Fujioka Y, Kimata Y, Nomaguchi K, Watanabe K, Kohno K. Identification of a novel non-structural maintenance of chromosomes (SMC) component of the SMC5-SMC6 complex involved in DNA repair. *J Biol Chem.* 2002;277: 21585–91. doi:10.1074/jbc.M201523200
199. Ranjan R, Ahmed A, Gourinath S, Sharma P. Dissection of mechanisms involved in the regulation of Plasmodium falciparum calcium-dependent protein kinase 4. *J Biol Chem.* 2009;284: 15267–76. doi:10.1074/jbc.M900656200
200. Glushakova S, Lizunov V, Blank PS, Melikov K, Humphrey G, Zimmerberg J. Cytoplasmic free Ca²⁺ is essential for multiple steps in malaria parasite egress from infected erythrocytes. *Malar J.* 2013;12: 41. doi:10.1186/1475-2875-12-41
201. Collins CR, Hackett F, Strath M, Penzo M, Withers-Martinez C, Baker DA, et al. Malaria parasite cGMP-dependent protein kinase regulates blood stage merozoite secretory organelle discharge and egress. *PLoS Pathog.* 2013;9: e1003344. doi:10.1371/journal.ppat.1003344
202. Collins CR, Das S, Wong EH, Andenmatten N, Stallmach R, Hackett F, et al. Robust inducible Cre recombinase activity in the human malaria parasite Plasmodium falciparum enables efficient gene deletion within a single asexual erythrocytic growth cycle. *Mol Microbiol.* 2013;88: 687–701. doi:10.1111/mmi.12206
203. Parsons AB, Brost RL, Ding H, Li Z, Zhang C, Sheikh B, et al. Integration of chemical-genetic and genetic interaction data links bioactive compounds to cellular target pathways. *Nat Biotechnol.* Nature Publishing Group; 2004;22: 62–9. doi:10.1038/nbt919

204. Polley SD, Weedall GD, Thomas AW, Golightly LM, Conway DJ. Orthologous gene sequences of merozoite surface protein 1 (MSP1) from *Plasmodium reichenowi* and *P. gallinaceum* confirm an ancient divergence of *P. falciparum* alleles. *Mol Biochem Parasitol.* 2005;142: 25–31. doi:10.1016/j.molbiopara.2005.02.012
205. Straimer J, Lee MCS, Lee AH, Zeitler B, Williams AE, Pearl JR, et al. Site-specific genome editing in *Plasmodium falciparum* using engineered zinc-finger nucleases. *Nat Methods.* 2012;9: 993–8. doi:10.1038/nmeth.2143
206. Wagner JC, Platt RJ, Goldfless SJ, Zhang F, Niles JC. Efficient CRISPR-Cas9-mediated genome editing in *Plasmodium falciparum*. *Nat Methods.* 2014;11: 915–8. doi:10.1038/nmeth.3063
207. Moon RW, Hall J, Rangkuti F, Ho YS, Almond N, Mitchell GH, et al. Adaptation of the genetically tractable malaria pathogen *Plasmodium knowlesi* to continuous culture in human erythrocytes. *Proc Natl Acad Sci U S A.* 2013;110: 531–6. doi:10.1073/pnas.1216457110