

# References

1. Darwin C. On the origin of species by means of natural selection. London,: J. Murray; 1859. ix, 1 , 502 p. p.
2. Mayr E. The growth of biological thought : diversity, evolution, and inheritance. Cambridge, Mass.: Belknap Press; 1982. ix, 974 p. p.
3. Grafen A, Ridley M. Richard Dawkins : how a scientist changed the way we think : reflections by scientists, writers, and philosophers. Oxford ; New York: Oxford University Press; 2006. xiii, 283 p. p.
4. Fisher RA. The genetical theory of natural selection. Oxford,: The Clarendon press; 1930. xiv, 272 p. p.
5. Bowler PJ. The Mendelian revolution : the emergence of hereditarian concepts in modern science and society. Baltimore: Johns Hopkins University Press; 1989. viii, 207 p. p.
6. Provine WB. The origins of theoretical population genetics. Chicago,: University of Chicago Press; 1971. xi, 201 p. p.
7. Huxley J. Evolution, the modern synthesis. London,: G. Allen & Unwin ltd; 1942. 645, 1 p. p.
8. Akey JM. Constructing genomic maps of positive selection in humans: where do we go from here? *Genome research*. 2009;19(5):711-22.
9. Nielsen R. Molecular signatures of natural selection. *Annual review of genetics*. 2005;39:197-218.
10. Vitti JJ, Grossman SR, Sabeti PC. Detecting natural selection in genomic data. *Annual review of genetics*. 2013;47:97-120.
11. Charlesworth B, Morgan MT, Charlesworth D. The effect of deleterious mutations on neutral molecular variation. *Genetics*. 1993;134(4):1289-303.
12. Charlesworth B. The effect of background selection against deleterious mutations on weakly selected, linked variants. *Genetical research*. 1994;63(3):213-27.
13. Charlesworth D. Balancing selection and its effects on sequences in nearby genome regions. *PLoS genetics*. 2006;2(4):e64.
14. Kimura M. The neutral theory of molecular evolution. Cambridge Cambridgeshire ; New York: Cambridge University Press; 1983. xv, 367 p. p.
15. Kimura M. Evolutionary rate at the molecular level. *Nature*. 1968;217(5129):624-6.
16. Sabeti PC, Schaffner SF, Fry B, Lohmueller J, Vavilily P, Shamovsky O, et al. Positive natural selection in the human lineage. *Science*. 2006;312(5780):1614-20.
17. Scheinfeldt LB, Tishkoff SA. Recent human adaptation: genomic approaches, interpretation and insights. *Nature reviews Genetics*. 2013;14(10):692-702.
18. Pritchard JK, Pickrell JK, Coop G. The genetics of human adaptation: hard sweeps, soft sweeps, and polygenic adaptation. *Current biology : CB*. 2010;20(4):R208-15.
19. Smith JM, Haigh J. The hitch-hiking effect of a favourable gene. *Genetical research*. 1974;23(1):23-35.

20. Hernandez RD, Kelley JL, Elyashiv E, Melton SC, Auton A, McVean G, et al. Classic selective sweeps were rare in recent human evolution. *Science*. 2011;331(6019):920-4.
21. Novembre J, Di Rienzo A. Spatial patterns of variation due to natural selection in humans. *Nature reviews Genetics*. 2009;10(11):745-55.
22. Nielsen R, Hellmann I, Hubisz M, Bustamante C, Clark AG. Recent and ongoing selection in the human genome. *Nature reviews Genetics*. 2007;8(11):857-68.
23. Jeong C, Di Rienzo A. Adaptations to local environments in modern human populations. *Current opinion in genetics & development*. 2014;29:1-8.
24. Schlotterer C. Towards a molecular characterization of adaptation in local populations. *Current opinion in genetics & development*. 2002;12(6):683-7.
25. Przeworski M, Coop G, Wall JD. The signature of positive selection on standing genetic variation. *Evolution; international journal of organic evolution*. 2005;59(11):2312-23.
26. Hermisson J, Pennings PS. Soft sweeps: molecular population genetics of adaptation from standing genetic variation. *Genetics*. 2005;169(4):2335-52.
27. Turchin MC, Chiang CW, Palmer CD, Sankararaman S, Reich D, Genetic Investigation of ATC, et al. Evidence of widespread selection on standing variation in Europe at height-associated SNPs. *Nature genetics*. 2012;44(9):1015-9.
28. Berg JJ, Coop G. A population genetic signal of polygenic adaptation. *PLoS genetics*. 2014;10(8):e1004412.
29. Robinson MR, Hemani G, Medina-Gomez C, Mezzavilla M, Esko T, Shakhbazov K, et al. Population genetic differentiation of height and body mass index across Europe. *Nature genetics*. 2015;47(11):1357-62.
30. Racimo F, Sankararaman S, Nielsen R, Huerta-Sanchez E. Evidence for archaic adaptive introgression in humans. *Nature reviews Genetics*. 2015;16(6):359-71.
31. Jobling MA, Hurler M, Tyler-Smith C. *Human evolutionary genetics*. 2nd ed. New York: Garland Science; 2013. xviii, 670 p. p.
32. Bamshad M, Wooding S, Salisbury BA, Stephens JC. Deconstructing the relationship between genetics and race. *Nature reviews Genetics*. 2004;5(8):598-609.
33. Jablonski NG, Chaplin G. The evolution of skin pigmentation and hair texture in people of African ancestry. *Dermatologic clinics*. 2014;32(2):113-21.
34. Perry GH, Dominy NJ. Evolution of the human pygmy phenotype. *Trends Ecol Evol*. 2009;24(4):218-25.
35. Beall CM. Tibetan and Andean contrasts in adaptation to high-altitude hypoxia. *Adv Exp Med Biol*. 2000;475:63-74.
36. Moore LG. Human genetic adaptation to high altitude. *High Alt Med Biol*. 2001;2(2):257-79.
37. Li WH, Sadler LA. Low nucleotide diversity in man. *Genetics*. 1991;129(2):513-23.
38. Harpending H, Rogers A. Genetic perspectives on human origins and differentiation. *Annu Rev Genomics Hum Genet*. 2000;1:361-85.
39. Fischer A, Wiebe V, Paabo S, Przeworski M. Evidence for a complex demographic history of chimpanzees. *Molecular biology and evolution*. 2004;21(5):799-808.

40. Kittles RA, Weiss KM. Race, ancestry, and genes: implications for defining disease risk. *Annu Rev Genomics Hum Genet.* 2003;4:33-67.
41. Youmans WJ. *Appleton's popular science monthly.* New York: D. Appleton and Co.; 1895.
42. Rodriguez JA, Marigorta UM, Navarro A. Integrating genomics into evolutionary medicine. *Current opinion in genetics & development.* 2014;29:97-102.
43. Wilson TW, Grim CE. Biohistory of slavery and blood pressure differences in blacks today. A hypothesis. *Hypertension.* 1991;17(1 Suppl):1122-8.
44. Neel JV. Diabetes mellitus: a "thrifty" genotype rendered detrimental by "progress"? *American journal of human genetics.* 1962;14:353-62.
45. Di Rienzo A, Hudson RR. An evolutionary framework for common diseases: the ancestral-susceptibility model. *Trends in genetics : TIG.* 2005;21(11):596-601.
46. Minster RL, Hawley NL, Su CT, Sun G, Kershaw EE, Cheng H, et al. A thrifty variant in CREBRF strongly influences body mass index in Samoans. *Nature genetics.* 2016;48(9):1049-54.
47. Ayub Q, Moutsianas L, Chen Y, Panoutsopoulou K, Colonna V, Pagani L, et al. Revisiting the thrifty gene hypothesis via 65 loci associated with susceptibility to type 2 diabetes. *American journal of human genetics.* 2014;94(2):176-85.
48. Williams GC, Nesse RM. The dawn of Darwinian medicine. *Q Rev Biol.* 1991;66(1):1-22.
49. Ewald PW. Evolutionary biology and the treatment of signs and symptoms of infectious disease. *J Theor Biol.* 1980;86(1):169-76.
50. Xue Y, Daly A, Yngvadottir B, Liu M, Coop G, Kim Y, et al. Spread of an inactive form of caspase-12 in humans is due to recent positive selection. *American journal of human genetics.* 2006;78(4):659-70.
51. Novembre J, Galvani AP, Slatkin M. The geographic spread of the CCR5 Delta32 HIV-resistance allele. *PLoS biology.* 2005;3(11):e339.
52. Lindesmith L, Moe C, Marionneau S, Ruvoen N, Jiang X, Lindblad L, et al. Human susceptibility and resistance to Norwalk virus infection. *Nature medicine.* 2003;9(5):548-53.
53. Raj T, Kuchroo M, Replogle JM, Raychaudhuri S, Stranger BE, De Jager PL. Common risk alleles for inflammatory diseases are targets of recent positive selection. *American journal of human genetics.* 2013;92(4):517-29.
54. Biswas S, Akey JM. Genomic insights into positive selection. *Trends in genetics : TIG.* 2006;22(8):437-46.
55. Cardona A, Pagani L, Antao T, Lawson DJ, Eichstaedt CA, Yngvadottir B, et al. Genome-wide analysis of cold adaptation in indigenous Siberian populations. *PloS one.* 2014;9(5):e98076.
56. Clemente FJ, Cardona A, Inchley CE, Peter BM, Jacobs G, Pagani L, et al. A Selective Sweep on a Deleterious Mutation in CPT1A in Arctic Populations. *American journal of human genetics.* 2014;95(5):584-9.
57. Ko WY, Rajan P, Gomez F, Scheinfeldt L, An P, Winkler CA, et al. Identifying Darwinian selection acting on different human APOL1 variants among diverse African populations. *American journal of human genetics.* 2013;93(1):54-66.

58. Genovese G, Friedman DJ, Ross MD, Lecordier L, Uzureau P, Freedman BI, et al. Association of trypanolytic ApoL1 variants with kidney disease in African Americans. *Science*. 2010;329(5993):841-5.
59. Spyropoulos B, Moens PB, Davidson J, Lowden JA. Heterozygote advantage in Tay-Sachs carriers? *American journal of human genetics*. 1981;33(3):375-80.
60. Schroeder SA, Gaughan DM, Swift M. Protection against bronchial asthma by CFTR delta F508 mutation: a heterozygote advantage in cystic fibrosis. *Nature medicine*. 1995;1(7):703-5.
61. Woolf LI, McBean MS, Woolf FM, Cahalane SF. Phenylketonuria as a balanced polymorphism: the nature of the heterozygote advantage. *Ann Hum Genet*. 1975;38(4):461-9.
62. Allison AC. Protection afforded by sickle-cell trait against subtertian malarial infection. *British medical journal*. 1954;1(4857):290-4.
63. Bamshad M, Wooding SP. Signatures of natural selection in the human genome. *Nature reviews Genetics*. 2003;4(2):99-111.
64. Gillespie JH. Genetic drift in an infinite population. The pseudohitchhiking model. *Genetics*. 2000;155(2):909-19.
65. Gillespie JH. Is the population size of a species relevant to its evolution? *Evolution; international journal of organic evolution*. 2001;55(11):2161-9.
66. Zlotogora J. Multiple mutations responsible for frequent genetic diseases in isolated populations. *European journal of human genetics : EJHG*. 2007;15(3):272-8.
67. McVean GA, Myers SR, Hunt S, Deloukas P, Bentley DR, Donnelly P. The fine-scale structure of recombination rate variation in the human genome. *Science*. 2004;304(5670):581-4.
68. Cavalli-Sforza LL. Population structure and human evolution. *Proc R Soc Lond B Biol Sci*. 1966;164(995):362-79.
69. Burbano HA, Green RE, Maricic T, Lalueza-Fox C, de la Rasilla M, Rosas A, et al. Analysis of human accelerated DNA regions using archaic hominin genomes. *PloS one*. 2012;7(3):e32877.
70. Lindblad-Toh K, Garber M, Zuk O, Lin MF, Parker BJ, Washietl S, et al. A high-resolution map of human evolutionary constraint using 29 mammals. *Nature*. 2011;478(7370):476-82.
71. Pollard KS, Salama SR, King B, Kern AD, Dreszer T, Katzman S, et al. Forces shaping the fastest evolving regions in the human genome. *PLoS genetics*. 2006;2(10):e168.
72. Prabhakar S, Noonan JP, Paabo S, Rubin EM. Accelerated evolution of conserved noncoding sequences in humans. *Science*. 2006;314(5800):786.
73. Nielsen R, Yang Z. Likelihood models for detecting positively selected amino acid sites and applications to the HIV-1 envelope gene. *Genetics*. 1998;148(3):929-36.
74. Suzuki Y, Gojobori T. A method for detecting positive selection at single amino acid sites. *Molecular biology and evolution*. 1999;16(10):1315-28.
75. Yang Z, Nielsen R. Codon-substitution models for detecting molecular adaptation at individual sites along specific lineages. *Molecular biology and evolution*. 2002;19(6):908-17.

76. Yang Z, Nielsen R. Estimating synonymous and nonsynonymous substitution rates under realistic evolutionary models. *Molecular biology and evolution*. 2000;17(1):32-43.
77. Yang Z, Nielsen R. Synonymous and nonsynonymous rate variation in nuclear genes of mammals. *J Mol Evol*. 1998;46(4):409-18.
78. Wong WS, Nielsen R. Detecting selection in noncoding regions of nucleotide sequences. *Genetics*. 2004;167(2):949-58.
79. McDonald JH, Kreitman M. Adaptive protein evolution at the Adh locus in *Drosophila*. *Nature*. 1991;351(6328):652-4.
80. Hudson RR, Kreitman M, Aguade M. A test of neutral molecular evolution based on nucleotide data. *Genetics*. 1987;116(1):153-9.
81. Lewontin RC, Krakauer J. Distribution of gene frequency as a test of the theory of the selective neutrality of polymorphisms. *Genetics*. 1973;74(1):175-95.
82. Wright S. The genetical structure of populations. *Ann Eugen*. 1951;15(4):323-54.
83. Akey JM, Zhang G, Zhang K, Jin L, Shriver MD. Interrogating a high-density SNP map for signatures of natural selection. *Genome research*. 2002;12(12):1805-14.
84. Beaumont MA, Balding DJ. Identifying adaptive genetic divergence among populations from genome scans. *Mol Ecol*. 2004;13(4):969-80.
85. Porter AH. A test for deviation from island-model population structure. *Mol Ecol*. 2003;12(4):903-15.
86. Kayser M, Brauer S, Stoneking M. A genome scan to detect candidate regions influenced by local natural selection in human populations. *Molecular biology and evolution*. 2003;20(6):893-900.
87. Vitalis R, Dawson K, Boursot P. Interpretation of variation across marker loci as evidence of selection. *Genetics*. 2001;158(4):1811-23.
88. Meirmans PG, Hedrick PW. Assessing population structure: F(ST) and related measures. *Mol Ecol Resour*. 2011;11(1):5-18.
89. Bonhomme M, Chevalet C, Servin B, Boitard S, Abdallah J, Blott S, et al. Detecting selection in population trees: the Lewontin and Krakauer test extended. *Genetics*. 2010;186(1):241-62.
90. Excoffier L, Hofer T, Foll M. Detecting loci under selection in a hierarchically structured population. *Heredity (Edinb)*. 2009;103(4):285-98.
91. Shriver MD, Kennedy GC, Parra EJ, Lawson HA, Sonpar V, Huang J, et al. The genomic distribution of population substructure in four populations using 8,525 autosomal SNPs. *Hum Genomics*. 2004;1(4):274-86.
92. Yi X, Liang Y, Huerta-Sanchez E, Jin X, Cuo ZX, Pool JE, et al. Sequencing of 50 human exomes reveals adaptation to high altitude. *Science*. 2010;329(5987):75-8.
93. Chen H, Patterson N, Reich D. Population differentiation as a test for selective sweeps. *Genome research*. 2010;20(3):393-402.
94. Fariello MI, Boitard S, Naya H, SanCristobal M, Servin B. Detecting signatures of selection through haplotype differentiation among hierarchically structured populations. *Genetics*. 2013;193(3):929-41.
95. Colonna V, Ayub Q, Chen Y, Pagani L, Luisi P, Pybus M, et al. Human genomic regions with exceptionally high levels of population differentiation

- identified from 911 whole-genome sequences. *Genome biology*. 2014;15(6):R88.
96. Wilde S, Timpson A, Kirsanow K, Kaiser E, Kayser M, Unterlander M, et al. Direct evidence for positive selection of skin, hair, and eye pigmentation in Europeans during the last 5,000 y. *Proceedings of the National Academy of Sciences of the United States of America*. 2014;111(13):4832-7.
  97. Mathieson I, Lazaridis I, Rohland N, Mallick S, Patterson N, Roodenberg SA, et al. Genome-wide patterns of selection in 230 ancient Eurasians. *Nature*. 2015;528(7583):499-503.
  98. Tajima F. Statistical method for testing the neutral mutation hypothesis by DNA polymorphism. *Genetics*. 1989;123(3):585-95.
  99. Fu YX, Li WH. Statistical tests of neutrality of mutations. *Genetics*. 1993;133(3):693-709.
  100. Fu YX. New statistical tests of neutrality for DNA samples from a population. *Genetics*. 1996;143(1):557-70.
  101. Fu YX. Statistical tests of neutrality of mutations against population growth, hitchhiking and background selection. *Genetics*. 1997;147(2):915-25.
  102. Fay JC, Wu CI. Hitchhiking under positive Darwinian selection. *Genetics*. 2000;155(3):1405-13.
  103. Kim Y, Stephan W. Detecting a local signature of genetic hitchhiking along a recombining chromosome. *Genetics*. 2002;160(2):765-77.
  104. Sabeti PC, Reich DE, Higgins JM, Levine HZ, Richter DJ, Schaffner SF, et al. Detecting recent positive selection in the human genome from haplotype structure. *Nature*. 2002;419(6909):832-7.
  105. Depaulis F, Veuille M. Neutrality tests based on the distribution of haplotypes under an infinite-site model. *Molecular biology and evolution*. 1998;15(12):1788-90.
  106. Kelly JK. A test of neutrality based on interlocus associations. *Genetics*. 1997;146(3):1197-206.
  107. Kim Y, Nielsen R. Linkage disequilibrium as a signature of selective sweeps. *Genetics*. 2004;167(3):1513-24.
  108. Zhang C, Bailey DK, Awad T, Liu G, Xing G, Cao M, et al. A whole genome long-range haplotype (WGLRH) test for detecting imprints of positive selection in human populations. *Bioinformatics*. 2006;22(17):2122-8.
  109. Hanchard NA, Rockett KA, Spencer C, Coop G, Pinder M, Jallow M, et al. Screening for recently selected alleles by analysis of human haplotype similarity. *American journal of human genetics*. 2006;78(1):153-9.
  110. Voight BF, Kudaravalli S, Wen X, Pritchard JK. A map of recent positive selection in the human genome. *PLoS biology*. 2006;4(3):e72.
  111. Sabeti PC, Varilly P, Fry B, Lohmueller J, Hostetter E, Cotsapas C, et al. Genome-wide detection and characterization of positive selection in human populations. *Nature*. 2007;449(7164):913-8.
  112. Tang K, Thornton KR, Stoneking M. A new approach for using genome scans to detect recent positive selection in the human genome. *PLoS biology*. 2007;5(7):e171.
  113. Albrechtsen A, Moltke I, Nielsen R. Natural selection and the distribution of identity-by-descent in the human genome. *Genetics*. 2010;186(1):295-308.

114. Cai Z, Camp NJ, Cannon-Albright L, Thomas A. Identification of regions of positive selection using Shared Genomic Segment analysis. *European journal of human genetics : EJHG*. 2011;19(6):667-71.
115. Han L, Abney M. Using identity by descent estimation with dense genotype data to detect positive selection. *European journal of human genetics : EJHG*. 2013;21(2):205-11.
116. Wiener P, Pong-Wong R. A regression-based approach to selection mapping. *J Hered*. 2011;102(3):294-305.
117. Zeng K, Fu YX, Shi S, Wu CI. Statistical tests for detecting positive selection by utilizing high-frequency variants. *Genetics*. 2006;174(3):1431-9.
118. Ayub Q, Yngvadottir B, Chen Y, Xue Y, Hu M, Vernes SC, et al. FOXP2 targets show evidence of positive selection in European populations. *American journal of human genetics*. 2013;92(5):696-706.
119. Ewens WJ. The sampling theory of selectively neutral alleles. *Theoretical population biology*. 1972;3(1):87-112.
120. Watterson GA. The homozygosity test of neutrality. *Genetics*. 1978;88(2):405-17.
121. Zeng K, Shi S, Wu CI. Compound tests for the detection of hitchhiking under positive selection. *Molecular biology and evolution*. 2007;24(8):1898-908.
122. Nielsen R, Hubisz MJ, Hellmann I, Torgerson D, Andres AM, Albrechtsen A, et al. Darwinian and demographic forces affecting human protein coding genes. *Genome research*. 2009;19(5):838-49.
123. Grossman SR, Shlyakhter I, Karlsson EK, Byrne EH, Morales S, Frieden G, et al. A composite of multiple signals distinguishes causal variants in regions of positive selection. *Science*. 2010;327(5967):883-6.
124. Pybus M, Luisi P, Dall'Olio GM, Uzkudun M, Laayouni H, Bertranpetit J, et al. Hierarchical boosting: a machine-learning framework to detect and classify hard selective sweeps in human populations. *Bioinformatics*. 2015;31(24):3946-52.
125. Green RE, Krause J, Briggs AW, Maricic T, Stenzel U, Kircher M, et al. A draft sequence of the Neandertal genome. *Science*. 2010;328(5979):710-22.
126. Durand EY, Patterson N, Reich D, Slatkin M. Testing for ancient admixture between closely related populations. *Molecular biology and evolution*. 2011;28(8):2239-52.
127. Patterson N, Moorjani P, Luo Y, Mallick S, Rohland N, Zhan Y, et al. Ancient admixture in human history. *Genetics*. 2012;192(3):1065-93.
128. Plagnol V, Wall JD. Possible ancestral structure in human populations. *PLoS genetics*. 2006;2(7):e105.
129. Vernot B, Akey JM. Resurrecting surviving Neandertal lineages from modern human genomes. *Science*. 2014;343(6174):1017-21.
130. Seguin-Orlando A, Korneliussen TS, Sikora M, Malaspina AS, Manica A, Moltke I, et al. Paleogenomics. Genomic structure in Europeans dating back at least 36,200 years. *Science*. 2014;346(6213):1113-8.
131. Sankararaman S, Patterson N, Li H, Paabo S, Reich D. The date of interbreeding between Neandertals and modern humans. *PLoS genetics*. 2012;8(10):e1002947.
132. Mendez FL, Watkins JC, Hammer MF. A haplotype at STAT2 Introgressed from neanderthals and serves as a candidate of positive selection in Papua New Guinea. *American journal of human genetics*. 2012;91(2):265-74.

133. Prufer K, Racimo F, Patterson N, Jay F, Sankararaman S, Sawyer S, et al. The complete genome sequence of a Neanderthal from the Altai Mountains. *Nature*. 2014;505(7481):43-9.
134. Sankararaman S, Mallick S, Dannemann M, Prufer K, Kelso J, Paabo S, et al. The genomic landscape of Neanderthal ancestry in present-day humans. *Nature*. 2014;507(7492):354-7.
135. Pavlidis P, Jensen JD, Stephan W, Stamatakis A. A critical assessment of storytelling: gene ontology categories and the importance of validating genomic scans. *Molecular biology and evolution*. 2012;29(10):3237-48.
136. Kelley JL, Madeoy J, Calhoun JC, Swanson W, Akey JM. Genomic signatures of positive selection in humans and the limits of outlier approaches. *Genome research*. 2006;16(8):980-9.
137. Oleksyk TK, Smith MW, O'Brien SJ. Genome-wide scans for footprints of natural selection. *Philosophical transactions of the Royal Society of London Series B, Biological sciences*. 2010;365(1537):185-205.
138. Kamberov YG, Wang S, Tan J, Gerbault P, Wark A, Tan L, et al. Modeling recent human evolution in mice by expression of a selected EDAR variant. *Cell*. 2013;152(4):691-702.
139. Lamason RL, Mohideen MA, Mest JR, Wong AC, Norton HL, Aros MC, et al. SLC24A5, a putative cation exchanger, affects pigmentation in zebrafish and humans. *Science*. 2005;310(5755):1782-6.
140. Enattah NS, Sahi T, Savilahti E, Terwilliger JD, Peltonen L, Jarvela I. Identification of a variant associated with adult-type hypolactasia. *Nature genetics*. 2002;30(2):233-7.
141. Olds LC, Sibley E. Lactase persistence DNA variant enhances lactase promoter activity in vitro: functional role as a cis regulatory element. *Human molecular genetics*. 2003;12(18):2333-40.
142. Genomes Project C, Auton A, Brooks LD, Durbin RM, Garrison EP, Kang HM, et al. A global reference for human genetic variation. *Nature*. 2015;526(7571):68-74.
143. Liu X, Ong RT, Pillai EN, Elzein AM, Small KS, Clark TG, et al. Detecting and characterizing genomic signatures of positive selection in global populations. *American journal of human genetics*. 2013;92(6):866-81.
144. Barreiro LB, Laval G, Quach H, Patin E, Quintana-Murci L. Natural selection has driven population differentiation in modern humans. *Nature genetics*. 2008;40(3):340-5.
145. Carlson CS, Thomas DJ, Eberle MA, Swanson JE, Livingston RJ, Rieder MJ, et al. Genomic regions exhibiting positive selection identified from dense genotype data. *Genome research*. 2005;15(11):1553-65.
146. International HapMap C, Frazer KA, Ballinger DG, Cox DR, Hinds DA, Stuve LL, et al. A second generation human haplotype map of over 3.1 million SNPs. *Nature*. 2007;449(7164):851-61.
147. Fagny M, Patin E, Enard D, Barreiro LB, Quintana-Murci L, Laval G. Exploring the occurrence of classic selective sweeps in humans using whole-genome sequencing data sets. *Molecular biology and evolution*. 2014;31(7):1850-68.
148. Hofer T, Foll M, Excoffier L. Evolutionary forces shaping genomic islands of population differentiation in humans. *BMC genomics*. 2012;13:107.
149. Tennessen JA, Akey JM. Parallel adaptive divergence among geographically diverse human populations. *PLoS genetics*. 2011;7(6):e1002127.



150. Johansson A, Gyllensten U. Identification of local selective sweeps in human populations since the exodus from Africa. *Hereditas*. 2008;145(3):126-37.
151. Kimura R, Fujimoto A, Tokunaga K, Ohashi J. A practical genome scan for population-specific strong selective sweeps that have reached fixation. *PloS one*. 2007;2(3):e286.
152. Lopez Herraez D, Bauchet M, Tang K, Theunert C, Pugach I, Li J, et al. Genetic variation and recent positive selection in worldwide human populations: evidence from nearly 1 million SNPs. *PloS one*. 2009;4(11):e7888.
153. Pickrell JK, Coop G, Novembre J, Kudaravalli S, Li JZ, Absher D, et al. Signals of recent positive selection in a worldwide sample of human populations. *Genome research*. 2009;19(5):826-37.
154. Rafajlovic M, Klassmann A, Eriksson A, Wiehe T, Mehlig B. Demography-adjusted tests of neutrality based on genome-wide SNP data. *Theoretical population biology*. 2014;95:1-12.
155. Grossman SR, Andersen KG, Shlyakhter I, Tabrizi S, Winnicki S, Yen A, et al. Identifying recent adaptations in large-scale genomic data. *Cell*. 2013;152(4):703-13.
156. Zhong M, Lange K, Papp JC, Fan R. A powerful score test to detect positive selection in genome-wide scans. *European journal of human genetics : EJHG*. 2010;18(10):1148-59.
157. Wang ET, Kodama G, Baldi P, Moyzis RK. Global landscape of recent inferred Darwinian selection for *Homo sapiens*. *Proceedings of the National Academy of Sciences of the United States of America*. 2006;103(1):135-40.
158. Williamson SH, Hubisz MJ, Clark AG, Payseur BA, Bustamante CD, Nielsen R. Localizing recent adaptive evolution in the human genome. *PLoS genetics*. 2007;3(6):e90.
159. Genomes Project C, Abecasis GR, Auton A, Brooks LD, DePristo MA, Durbin RM, et al. An integrated map of genetic variation from 1,092 human genomes. *Nature*. 2012;491(7422):56-65.
160. Cunningham F, Amode MR, Barrell D, Beal K, Billis K, Brent S, et al. Ensembl 2015. *Nucleic acids research*. 2015;43(Database issue):D662-9.
161. Mou C, Thomason HA, Willan PM, Clowes C, Harris WE, Drew CF, et al. Enhanced ectodysplasin-A receptor (EDAR) signaling alters multiple fiber characteristics to produce the East Asian hair form. *Human mutation*. 2008;29(12):1405-11.
162. Sturm RA, Duffy DL, Zhao ZZ, Leite FP, Stark MS, Hayward NK, et al. A single SNP in an evolutionary conserved region within intron 86 of the *HERC2* gene determines human blue-brown eye color. *American journal of human genetics*. 2008;82(2):424-31.
163. Eiberg H, Troelsen J, Nielsen M, Mikkelsen A, Mengel-From J, Kjaer KW, et al. Blue eye color in humans may be caused by a perfectly associated founder mutation in a regulatory element located within the *HERC2* gene inhibiting *OCA2* expression. *Human genetics*. 2008;123(2):177-87.
164. Visser M, Kayser M, Palstra RJ. *HERC2* rs12913832 modulates human pigmentation by attenuating chromatin-loop formation between a long-range enhancer and the *OCA2* promoter. *Genome research*. 2012;22(3):446-55.
165. Engelken J, Carnero-Montoro E, Pybus M, Andrews GK, Lalueza-Fox C, Comas D, et al. Extreme population differences in the human zinc transporter ZIP4

- (SLC39A4) are explained by positive selection in Sub-Saharan Africa. *PLoS genetics*. 2014;10(2):e1004128.
166. Li JZ, Absher DM, Tang H, Southwick AM, Casto AM, Ramachandran S, et al. Worldwide human relationships inferred from genome-wide patterns of variation. *Science*. 2008;319(5866):1100-4.
  167. Peacock E, Whiteley P. Perlegen sciences, inc. *Pharmacogenomics*. 2005;6(4):439-42.
  168. Kircher M, Witten DM, Jain P, O'Roak BJ, Cooper GM, Shendure J. A general framework for estimating the relative pathogenicity of human genetic variants. *Nature genetics*. 2014;46(3):310-5.
  169. Breiman L. *Classification and regression trees*. Belmont, Calif.: Wadsworth International Group; 1984. x, 358 p. p.
  170. Carroll SB. Evo-devo and an expanding evolutionary synthesis: a genetic theory of morphological evolution. *Cell*. 2008;134(1):25-36.
  171. King MC, Wilson AC. Evolution at two levels in humans and chimpanzees. *Science*. 1975;188(4184):107-16.
  172. Wray GA. The evolutionary significance of cis-regulatory mutations. *Nature reviews Genetics*. 2007;8(3):206-16.
  173. Tournamille C, Colin Y, Cartron JP, Le Van Kim C. Disruption of a GATA motif in the Duffy gene promoter abolishes erythroid gene expression in Duffy-negative individuals. *Nature genetics*. 1995;10(2):224-8.
  174. Iwamoto S, Li J, Omi T, Ikemoto S, Kajii E. Identification of a novel exon and spliced form of Duffy mRNA that is the predominant transcript in both erythroid and postcapillary venule endothelium. *Blood*. 1996;87(1):378-85.
  175. Iwamoto S, Li J, Sugimoto N, Okuda H, Kajii E. Characterization of the Duffy gene promoter: evidence for tissue-specific abolishment of expression in Fy(a-b-) of black individuals. *Biochemical and biophysical research communications*. 1996;222(3):852-9.
  176. Miller LH, Mason SJ, Clyde DF, McGinniss MH. The resistance factor to *Plasmodium vivax* in blacks. The Duffy-blood-group genotype, FyFy. *The New England journal of medicine*. 1976;295(6):302-4.
  177. Yoshiura K, Kinoshita A, Ishida T, Ninokata A, Ishikawa T, Kaname T, et al. A SNP in the ABCC11 gene is the determinant of human earwax type. *Nature genetics*. 2006;38(3):324-30.
  178. Martin A, Saathoff M, Kuhn F, Max H, Terstegen L, Natsch A. A functional ABCC11 allele is essential in the biochemical formation of human axillary odor. *The Journal of investigative dermatology*. 2010;130(2):529-40.
  179. Tsetschlhadze ZR, Canfield VA, Ang KC, Wentzel SM, Reid KP, Berg AS, et al. Functional assessment of human coding mutations affecting skin pigmentation using zebrafish. *PloS one*. 2012;7(10):e47398.
  180. Graf J, Hodgson R, van Daal A. Single nucleotide polymorphisms in the MATP gene are associated with normal human pigmentation variation. *Human mutation*. 2005;25(3):278-84.
  181. Cook AL, Chen W, Thurber AE, Smit DJ, Smith AG, Bladen TG, et al. Analysis of cultured human melanocytes based on polymorphisms within the SLC45A2/MATP, SLC24A5/NCKX5, and OCA2/P loci. *The Journal of investigative dermatology*. 2009;129(2):392-405.

182. Paten B, Herrero J, Fitzgerald S, Beal K, Flicek P, Holmes I, et al. Genome-wide nucleotide-level mammalian ancestor reconstruction. *Genome research*. 2008;18(11):1829-43.
183. Peng B, Kimmel M. simuPOP: a forward-time population genetics simulation environment. *Bioinformatics*. 2005;21(18):3686-7.
184. Gutenkunst RN, Hernandez RD, Williamson SH, Bustamante CD. Inferring the joint demographic history of multiple populations from multidimensional SNP frequency data. *PLoS genetics*. 2009;5(10):e1000695.
185. Genomes Project C, Abecasis GR, Altshuler D, Auton A, Brooks LD, Durbin RM, et al. A map of human genome variation from population-scale sequencing. *Nature*. 2010;467(7319):1061-73.
186. Gulko B, Hubisz MJ, Gronau I, Siepel A. A method for calculating probabilities of fitness consequences for point mutations across the human genome. *Nature genetics*. 2015;47(3):276-83.
187. Ritchie GR, Dunham I, Zeggini E, Flicek P. Functional annotation of noncoding sequence variants. *Nature methods*. 2014;11(3):294-6.
188. Edwards M, Bigham A, Tan J, Li S, Gozdzik A, Ross K, et al. Association of the OCA2 polymorphism His615Arg with melanin content in east Asian populations: further evidence of convergent evolution of skin pigmentation. *PLoS genetics*. 2010;6(3):e1000867.
189. Eaton K, Edwards M, Krithika S, Cook G, Norton H, Parra EJ. Association study confirms the role of two OCA2 polymorphisms in normal skin pigmentation variation in East Asian populations. *American journal of human biology : the official journal of the Human Biology Council*. 2015;27(4):520-5.
190. Donnelly MP, Paschou P, Grigorenko E, Gurwitz D, Barta C, Lu RB, et al. A global view of the OCA2-HERC2 region and pigmentation. *Human genetics*. 2012;131(5):683-96.
191. Stokowski RP, Pant PV, Dadd T, Fereday A, Hinds DA, Jarman C, et al. A genomewide association study of skin pigmentation in a South Asian population. *American journal of human genetics*. 2007;81(6):1119-32.
192. Hutton SM, Spritz RA. A comprehensive genetic study of autosomal recessive ocular albinism in Caucasian patients. *Investigative ophthalmology & visual science*. 2008;49(3):868-72.
193. Sulem P, Gudbjartsson DF, Stacey SN, Helgason A, Rafnar T, Magnusson KP, et al. Genetic determinants of hair, eye and skin pigmentation in Europeans. *Nature genetics*. 2007;39(12):1443-52.
194. Visser M, Palstra RJ, Kayser M. Human skin color is influenced by an intergenic DNA polymorphism regulating transcription of the nearby BNC2 pigmentation gene. *Human molecular genetics*. 2014;23(21):5750-62.
195. Kudo T, Iwasaki H, Nishihara S, Shinya N, Ando T, Narimatsu I, et al. Molecular genetic analysis of the human Lewis histo-blood group system. II. Secretor gene inactivation by a novel single missense mutation A385T in Japanese nonsecretor individuals. *The Journal of biological chemistry*. 1996;271(16):9830-7.
196. Adhikari K, Fontanil T, Cal S, Mendoza-Revilla J, Fuentes-Guajardo M, Chacon-Duque JC, et al. A genome-wide association scan in admixed Latin Americans identifies loci influencing facial and scalp hair features. *Nature communications*. 2016;7:10815.

197. Mackenzie FE, Romero R, Williams D, Gillingwater T, Hilton H, Dick J, et al. Upregulation of PKD1L2 provokes a complex neuromuscular disease in the mouse. *Human molecular genetics*. 2009;18(19):3553-66.
198. Oh HJ, Li Y, Lau YF. Sry associates with the heterochromatin protein 1 complex by interacting with a KRAB domain protein. *Biology of reproduction*. 2005;72(2):407-15.
199. Young P, Ehler E, Gautel M. Obscurin, a giant sarcomeric Rho guanine nucleotide exchange factor protein involved in sarcomere assembly. *The Journal of cell biology*. 2001;154(1):123-36.
200. Consortium GT. Human genomics. The Genotype-Tissue Expression (GTEx) pilot analysis: multitissue gene regulation in humans. *Science*. 2015;348(6235):648-60.
201. Randazzo D, Giacomello E, Lorenzini S, Rossi D, Pierantozzi E, Blaauw B, et al. Obscurin is required for ankyrinB-dependent dystrophin localization and sarcolemma integrity. *The Journal of cell biology*. 2013;200(4):523-36.
202. Tardif S, Wilson MD, Wagner R, Hunt P, Gertsenstein M, Nagy A, et al. Zonadhesin is essential for species specificity of sperm adhesion to the egg zona pellucida. *The Journal of biological chemistry*. 2010;285(32):24863-70.
203. Wassarman PM, Jovine L, Litscher ES. A profile of fertilization in mammals. *Nature cell biology*. 2001;3(2):E59-64.
204. Gasper J, Swanson WJ. Molecular population genetics of the gene encoding the human fertilization protein zonadhesin reveals rapid adaptive evolution. *American journal of human genetics*. 2006;79(5):820-30.
205. Tardif S, Brady HA, Breazeale KR, Bi M, Thompson LD, Bruemmer JE, et al. Zonadhesin D3-polypeptides vary among species but are similar in Equus species capable of interbreeding. *Biology of reproduction*. 2010;82(2):413-21.
206. Yngvadottir B, Xue Y, Searle S, Hunt S, Delgado M, Morrison J, et al. A genome-wide survey of the prevalence and evolutionary forces acting on human nonsense SNPs. *American journal of human genetics*. 2009;84(2):224-34.
207. Thibaut S, Cavusoglu N, de Becker E, Zerbib F, Bednarczyk A, Schaeffer C, et al. Transglutaminase-3 enzyme: a putative actor in human hair shaft scaffolding? *The Journal of investigative dermatology*. 2009;129(2):449-59.
208. John S, Thiebach L, Frie C, Mokkapati S, Bechtel M, Nischt R, et al. Epidermal transglutaminase (TGase 3) is required for proper hair development, but not the formation of the epidermal barrier. *PloS one*. 2012;7(4):e34252.
209. Bognar P, Nemeth I, Mayer B, Haluszka D, Wikonkal N, Ostorhazi E, et al. Reduced inflammatory threshold indicates skin barrier defect in transglutaminase 3 knockout mice. *The Journal of investigative dermatology*. 2014;134(1):105-11.
210. Brennan BM, Huynh MT, Rabah MA, Shaw HE, Bisailon JJ, Radden LA, 2nd, et al. The mouse wellhaarig (we) mutations result from defects in epidermal-type transglutaminase 3 (Tgm3). *Molecular genetics and metabolism*. 2015;116(3):187-91.
211. Steinert PM, Parry DA, Marekov LN. Trichohyalin mechanically strengthens the hair follicle: multiple cross-bridging roles in the inner root sheath. *The Journal of biological chemistry*. 2003;278(42):41409-19.
212. FB UB, Cau L, Tafazzoli A, Mechin MC, Wolf S, Romano MT, et al. Mutations in Three Genes Encoding Proteins Involved in Hair Shaft Formation Cause

- Uncombable Hair Syndrome. *American journal of human genetics*. 2016;99(6):1292-304.
213. Fujimoto A, Nishida N, Kimura R, Miyagawa T, Yuliwulandari R, Batubara L, et al. FGFR2 is associated with hair thickness in Asian populations. *Journal of human genetics*. 2009;54(8):461-5.
  214. Laatsch CN, Durbin-Johnson BP, Rocke DM, Mukwana S, Newland AB, Flagler MJ, et al. Human hair shaft proteomic profiling: individual differences, site specificity and cuticle analysis. *PeerJ*. 2014;2:e506.
  215. Robbins CR. *Chemical and physical behavior of human hair*. 4th ed. New York: Springer; 2002. xvii, 483 p. p.
  216. Iolascon A, King MJ, Robertson S, Avvisati RA, Vitiello F, Asci R, et al. A genomic deletion causes truncation of alpha-spectrin and ellipto-poikilocytosis. *Blood cells, molecules & diseases*. 2011;46(3):195-200.
  217. Salomao M, An X, Guo X, Gratzler WB, Mohandas N, Baines AJ. Mammalian alpha I-spectrin is a neofunctionalized polypeptide adapted to small highly deformable erythrocytes. *Proceedings of the National Academy of Sciences of the United States of America*. 2006;103(3):643-8.
  218. Burke JP, Van Zyl D, Zail SS, Coetzer TL. Reduced spectrin-ankyrin binding in a South African hereditary elliptocytosis kindred homozygous for spectrin St Claude. *Blood*. 1998;92(7):2591-2.
  219. Soranzo N, Sanna S, Wheeler E, Gieger C, Radke D, Dupuis J, et al. Common variants at 10 genomic loci influence hemoglobin A(1)(C) levels via glycemic and nonglycemic pathways. *Diabetes*. 2010;59(12):3229-39.
  220. Ding K, Shameer K, Jouni H, Masys DR, Jarvik GP, Kho AN, et al. Genetic Loci implicated in erythroid differentiation and cell cycle regulation are associated with red blood cell traits. *Mayo Clinic proceedings*. 2012;87(5):461-74.
  221. Ganesh SK, Zakai NA, van Rooij FJ, Soranzo N, Smith AV, Nalls MA, et al. Multiple loci influence erythrocyte phenotypes in the CHARGE Consortium. *Nature genetics*. 2009;41(11):1191-8.
  222. Birkenmeier CS, McFarland-Starr EC, Barker JE. Chromosomal location of three spectrin genes: relationship to the inherited hemolytic anemias of mouse and man. *Proceedings of the National Academy of Sciences of the United States of America*. 1988;85(21):8121-5.
  223. Grossmann A, Maggio-Price L, Shiota FM, Liggitt DV. Pathologic features associated with decreased longevity of mutant sphha/sphha mice with chronic hemolytic anemia: similarities to sequelae of sickle cell anemia in humans. *Laboratory animal science*. 1993;43(3):217-21.
  224. Lecomte MC, Dhermy D, Gautero H, Bournier O, Galand C, Boivin P. [Hereditary elliptocytosis in West Africa: frequency and repartition of spectrin variants]. *Comptes rendus de l'Academie des sciences Serie III, Sciences de la vie*. 1988;306(2):43-6.
  225. Delaunay J, Dhermy D. Mutations involving the spectrin heterodimer contact site: clinical expression and alterations in specific function. *Seminars in hematology*. 1993;30(1):21-33.
  226. Delaunay J. The molecular basis of hereditary red cell membrane disorders. *Blood reviews*. 2007;21(1):1-20.
  227. Schulman S, Roth EF, Jr., Cheng B, Rybicki AC, Sussman, II, Wong M, et al. Growth of *Plasmodium falciparum* in human erythrocytes containing

- abnormal membrane proteins. *Proceedings of the National Academy of Sciences of the United States of America*. 1990;87(18):7339-43.
228. Shear HL, Roth EF, Jr., Ng C, Nagel RL. Resistance to malaria in ankyrin and spectrin deficient mice. *British journal of haematology*. 1991;78(4):555-60.
  229. Lappalainen T, Sammeth M, Friedlander MR, t Hoen PA, Monlong J, Rivas MA, et al. Transcriptome and genome sequencing uncovers functional variation in humans. *Nature*. 2013;501(7468):506-11.
  230. Spiekerkoetter U, Sun B, Khuchua Z, Bennett MJ, Strauss AW. Molecular and phenotypic heterogeneity in mitochondrial trifunctional protein deficiency due to beta-subunit mutations. *Human mutation*. 2003;21(6):598-607.
  231. Purevsuren J, Fukao T, Hasegawa Y, Kobayashi H, Li H, Mushimoto Y, et al. Clinical and molecular aspects of Japanese patients with mitochondrial trifunctional protein deficiency. *Molecular genetics and metabolism*. 2009;98(4):372-7.
  232. Naiki M, Ochi N, Kato YS, Purevsuren J, Yamada K, Kimura R, et al. Mutations in HADHB, which encodes the beta-subunit of mitochondrial trifunctional protein, cause infantile onset hypoparathyroidism and peripheral polyneuropathy. *American journal of medical genetics Part A*. 2014;164A(5):1180-7.
  233. Valbuena A, Lopez-Sanchez I, Lazo PA. Human VRK1 is an early response gene and its loss causes a block in cell cycle progression. *PloS one*. 2008;3(2):e1642.
  234. Valbuena A, Sanz-Garcia M, Lopez-Sanchez I, Vega FM, Lazo PA. Roles of VRK1 as a new player in the control of biological processes required for cell division. *Cell Signal*. 2011;23(8):1267-72.
  235. Lancaster OM, Breuer M, Cullen CF, Ito T, Ohkura H. The meiotic recombination checkpoint suppresses NHK-1 kinase to prevent reorganisation of the oocyte nucleus in *Drosophila*. *PLoS genetics*. 2010;6(10):e1001179.
  236. Waters K, Yang AZ, Reinke V. Genome-wide analysis of germ cell proliferation in *C.elegans* identifies VRK-1 as a key regulator of CEP-1/p53. *Dev Biol*. 2010;344(2):1011-25.
  237. Dobrzynska A, Askjaer P. Vaccinia-related kinase 1 is required for early uterine development in *Caenorhabditis elegans*. *Dev Biol*. 2016;411(2):246-56.
  238. Ivanovska I, Khandan T, Ito T, Orr-Weaver TL. A histone code in meiosis: the histone kinase, NHK-1, is required for proper chromosomal architecture in *Drosophila* oocytes. *Genes Dev*. 2005;19(21):2571-82.
  239. Kim J, Choi YH, Chang S, Kim KT, Je JH. Defective folliculogenesis in female mice lacking Vaccinia-related kinase 1. *Sci Rep*. 2012;2:468.
  240. Schober CS, Aydiner F, Booth CJ, Seli E, Reinke V. The kinase VRK1 is required for normal meiotic progression in mammalian oogenesis. *Mech Dev*. 2011;128(3-4):178-90.
  241. Choi YH, Park CH, Kim W, Ling H, Kang A, Chang MW, et al. Vaccinia-related kinase 1 is required for the maintenance of undifferentiated spermatogonia in mouse male germ cells. *PloS one*. 2010;5(12):e15254.
  242. Wiebe MS, Nichols RJ, Molitor TP, Lindgren JK, Traktman P. Mice deficient in the serine/threonine protein kinase VRK1 are infertile due to a progressive loss of spermatogonia. *Biology of reproduction*. 2010;82(1):182-93.

243. Ionita-Laza I, Capanu M, De Rubeis S, McCallum K, Buxbaum JD. Identification of rare causal variants in sequence-based studies: methods and applications to VPS13B, a gene involved in Cohen syndrome and autism. *PLoS genetics*. 2014;10(12):e1004729.
244. MacArthur DG, Manolio TA, Dimmock DP, Rehm HL, Shendure J, Abecasis GR, et al. Guidelines for investigating causality of sequence variants in human disease. *Nature*. 2014;508(7497):469-76.
245. Deschamps M, Laval G, Fagny M, Itan Y, Abel L, Casanova JL, et al. Genomic Signatures of Selective Pressures and Introgression from Archaic Hominins at Human Innate Immunity Genes. *American journal of human genetics*. 2016;98(1):5-21.
246. Meyer M, Kircher M, Gansauge MT, Li H, Racimo F, Mallick S, et al. A high-coverage genome sequence from an archaic Denisovan individual. *Science*. 2012;338(6104):222-6.
247. Pagani L, Schiffels S, Gurdasani D, Danecek P, Scally A, Chen Y, et al. Tracing the route of modern humans out of Africa by using 225 human genome sequences from Ethiopians and Egyptians. *American journal of human genetics*. 2015;96(6):986-91.
248. Liu Y, DeBoer K, de Kretser DM, O'Donnell L, O'Connor AE, Merriner DJ, et al. LRGUK-1 is required for basal body and manchette function during spermatogenesis and male fertility. *PLoS genetics*. 2015;11(3):e1005090.
249. Wu BY, Lee SP, Hsiao HC, Chiu H, Chen CY, Yeo YH, et al. Matriptase expression and zymogen activation in human pilosebaceous unit. *J Histochem Cytochem*. 2014;62(1):50-9.
250. Alef T, Torres S, Hausser I, Metze D, Tursen U, Lestringant GG, et al. Ichthyosis, follicular atrophoderma, and hypotrichosis caused by mutations in ST14 is associated with impaired profilaggrin processing. *The Journal of investigative dermatology*. 2009;129(4):862-9.
251. List K, Currie B, Scharschmidt TC, Szabo R, Shireman J, Molinolo A, et al. Autosomal ichthyosis with hypotrichosis syndrome displays low matriptase proteolytic activity and is phenocopied in ST14 hypomorphic mice. *The Journal of biological chemistry*. 2007;282(50):36714-23.
252. Basel-Vanagaite L, Attia R, Ishida-Yamamoto A, Rainshtein L, Ben Amitai D, Lurie R, et al. Autosomal recessive ichthyosis with hypotrichosis caused by a mutation in ST14, encoding type II transmembrane serine protease matriptase. *American journal of human genetics*. 2007;80(3):467-77.
253. List K, Szabo R, Molinolo A, Nielsen BS, Bugge TH. Delineation of matriptase protein expression by enzymatic gene trapping suggests diverging roles in barrier function, hair formation, and squamous cell carcinogenesis. *Am J Pathol*. 2006;168(5):1513-25.
254. List K, Haudenschild CC, Szabo R, Chen W, Wahl SM, Swaim W, et al. Matriptase/MT-SP1 is required for postnatal survival, epidermal barrier function, hair follicle development, and thymic homeostasis. *Oncogene*. 2002;21(23):3765-79.
255. Harris H. The relation of hair-growth on the body to baldness. *Br J Dermatol Syph*. 1947;59(8-9):300-9.
256. Hindley SW, Damon A. Some genetic traits in Solomon Island populations. IV. Mid-phalangeal hair. *Am J Phys Anthropol*. 1973;39(2):191-4.

257. Chen YW, Wang JK, Chou FP, Wu BY, Hsiao HC, Chiu H, et al. Matriptase regulates proliferation and early, but not terminal, differentiation of human keratinocytes. *The Journal of investigative dermatology*. 2014;134(2):405-14.
258. Buzza MS, Netzel-Arnett S, Shea-Donohue T, Zhao A, Lin CY, List K, et al. Membrane-anchored serine protease matriptase regulates epithelial barrier formation and permeability in the intestine. *Proceedings of the National Academy of Sciences of the United States of America*. 2010;107(9):4200-5.
259. List K, Kosa P, Szabo R, Bey AL, Wang CB, Molinolo A, et al. Epithelial integrity is maintained by a matriptase-dependent proteolytic pathway. *Am J Pathol*. 2009;175(4):1453-63.
260. Szabo R, Kosa P, List K, Bugge TH. Loss of matriptase suppression underlies spint1 mutation-associated ichthyosis and postnatal lethality. *Am J Pathol*. 2009;174(6):2015-22.
261. Scharschmidt TC, List K, Grice EA, Szabo R, Program NCS, Renaud G, et al. Matriptase-deficient mice exhibit ichthyotic skin with a selective shift in skin microbiota. *The Journal of investigative dermatology*. 2009;129(10):2435-42.
262. Netzel-Arnett S, Currie BM, Szabo R, Lin CY, Chen LM, Chai KX, et al. Evidence for a matriptase-prostasin proteolytic cascade regulating terminal epidermal differentiation. *The Journal of biological chemistry*. 2006;281(44):32941-5.
263. Yin H, Kosa P, Liu X, Swaim WD, Lai Z, Cabrera-Perez J, et al. Matriptase deletion initiates a Sjogren's syndrome-like disease in mice. *PloS one*. 2014;9(2):e82852.
264. Beaulieu A, Gravel E, Cloutier A, Marois I, Colombo E, Desilets A, et al. Matriptase proteolytically activates influenza virus and promotes multicycle replication in the human airway epithelium. *J Virol*. 2013;87(8):4237-51.
265. Baron J, Tarnow C, Mayoli-Nussle D, Schilling E, Meyer D, Hammami M, et al. Matriptase, HAT, and TMPRSS2 activate the hemagglutinin of H9N2 influenza A viruses. *J Virol*. 2013;87(3):1811-20.
266. Hamilton BS, Gludish DW, Whittaker GR. Cleavage activation of the human-adapted influenza virus subtypes by matriptase reveals both subtype and strain specificities. *J Virol*. 2012;86(19):10579-86.
267. Lebreton A, Lakisic G, Job V, Fritsch L, Tham TN, Camejo A, et al. A bacterial protein targets the BAHD1 chromatin complex to stimulate type III interferon response. *Science*. 2011;331(6022):1319-21.
268. Zhu C, Xiao F, Hong J, Wang K, Liu X, Cai D, et al. EFTUD2 Is a Novel Innate Immune Regulator Restricting Hepatitis C Virus Infection through the RIG-I/MDA5 Pathway. *J Virol*. 2015;89(13):6608-18.
269. Kim HJ, Kim CH, Kim MJ, Ryu JH, Seong SY, Kim S, et al. The Induction of Pattern-Recognition Receptor Expression against Influenza A Virus through Duox2-Derived Reactive Oxygen Species in Nasal Mucosa. *Am J Respir Cell Mol Biol*. 2015;53(4):525-35.
270. Ebrahim M, Mirzaei V, Bidaki R, Shabani Z, Daneshvar H, Karimi-Googheri M, et al. Are RIG-1 and MDA5 Expressions Associated with Chronic HBV Infection? *Viral Immunol*. 2015;28(9):504-8.



271. Cao X, Ding Q, Lu J, Tao W, Huang B, Zhao Y, et al. MDA5 plays a critical role in interferon response during hepatitis C virus infection. *J Hepatol.* 2015;62(4):771-8.
272. Hoffmann FS, Schmidt A, Dittmann Chevillotte M, Wisskirchen C, Hellmuth J, Willms S, et al. Polymorphisms in melanoma differentiation-associated gene 5 link protein function to clearance of hepatitis C virus. *Hepatology.* 2015;61(2):460-70.
273. Grandvaux N, Guan X, Yoboua F, Zucchini N, Fink K, Doyon P, et al. Sustained activation of interferon regulatory factor 3 during infection by paramyxoviruses requires MDA5. *J Innate Immun.* 2014;6(5):650-62.
274. Runge S, Sparrer KM, Lassig C, Hembach K, Baum A, Garcia-Sastre A, et al. In vivo ligands of MDA5 and RIG-I in measles virus-infected cells. *PLoS Pathog.* 2014;10(4):e1004081.
275. Pang L, Gong X, Liu N, Xie G, Gao W, Kong G, et al. A polymorphism in melanoma differentiation-associated gene 5 may be a risk factor for enterovirus 71 infection. *Clin Microbiol Infect.* 2014;20(10):O711-7.
276. Feng Q, Langereis MA, Lork M, Nguyen M, Hato SV, Lanke K, et al. Enterovirus 2Apro targets MDA5 and MAVS in infected cells. *J Virol.* 2014;88(6):3369-78.
277. Nasirudeen AM, Wong HH, Thien P, Xu S, Lam KP, Liu DX. RIG-I, MDA5 and TLR3 synergistically play an important role in restriction of dengue virus infection. *PLoS Negl Trop Dis.* 2011;5(1):e926.
278. Broquet AH, Hirata Y, McAllister CS, Kagnoff MF. RIG-I/MDA5/MAVS are required to signal a protective IFN response in rotavirus-infected intestinal epithelium. *J Immunol.* 2011;186(3):1618-26.
279. Melchjorsen J, Rintahaka J, Soby S, Horan KA, Poltajainen A, Ostergaard L, et al. Early innate recognition of herpes simplex virus in human primary macrophages is mediated via the MDA5/MAVS-dependent and MDA5/MAVS/RNA polymerase III-independent pathways. *J Virol.* 2010;84(21):11350-8.
280. Ikegame S, Takeda M, Ohno S, Nakatsu Y, Nakanishi Y, Yanagi Y. Both RIG-I and MDA5 RNA helicases contribute to the induction of alpha/beta interferon in measles virus-infected human cells. *J Virol.* 2010;84(1):372-9.
281. Lifland AW, Jung J, Alonas E, Zurla C, Crowe JE, Jr., Santangelo PJ. Human respiratory syncytial virus nucleoprotein and inclusion bodies antagonize the innate immune response mediated by MDA5 and MAVS. *J Virol.* 2012;86(15):8245-58.
282. Siren J, Imaizumi T, Sarkar D, Pietila T, Noah DL, Lin R, et al. Retinoic acid inducible gene-I and mda-5 are involved in influenza A virus-induced expression of antiviral cytokines. *Microbes Infect.* 2006;8(8):2013-20.
283. Berghall H, Siren J, Sarkar D, Julkunen I, Fisher PB, Vainionpaa R, et al. The interferon-inducible RNA helicase, mda-5, is involved in measles virus-induced expression of antiviral cytokines. *Microbes Infect.* 2006;8(8):2138-44.
284. Zalinger ZB, Elliott R, Rose KM, Weiss SR. MDA5 Is Critical to Host Defense during Infection with Murine Coronavirus. *J Virol.* 2015;89(24):12330-40.
285. Lu HL, Liao F. Melanoma differentiation-associated gene 5 senses hepatitis B virus and activates innate immune signaling to suppress virus replication. *J Immunol.* 2013;191(6):3264-76.

286. McCartney EM, Beard MR. Impact of alcohol on hepatitis C virus replication and interferon signaling. *World J Gastroenterol.* 2010;16(11):1337-43.
287. Gitlin L, Benoit L, Song C, Cella M, Gilfillan S, Holtzman MJ, et al. Melanoma differentiation-associated gene 5 (MDA5) is involved in the innate immune response to Paramyxoviridae infection in vivo. *PLoS Pathog.* 2010;6(1):e1000734.
288. Kato H, Takeuchi O, Sato S, Yoneyama M, Yamamoto M, Matsui K, et al. Differential roles of MDA5 and RIG-I helicases in the recognition of RNA viruses. *Nature.* 2006;441(7089):101-5.
289. Goldman FD, Ballas ZK, Schutte BC, Kemp J, Hollenback C, Noraz N, et al. Defective expression of p56lck in an infant with severe combined immunodeficiency. *J Clin Invest.* 1998;102(2):421-9.
290. Molina TJ, Kishihara K, Siderovski DP, van Ewijk W, Narendran A, Timms E, et al. Profound block in thymocyte development in mice lacking p56lck. *Nature.* 1992;357(6374):161-4.
291. Levin SD, Anderson SJ, Forbush KA, Perlmutter RM. A dominant-negative transgene defines a role for p56lck in thymopoiesis. *The EMBO journal.* 1993;12(4):1671-80.
292. Welte T, Leitenberg D, Dittel BN, al-Ramadi BK, Xie B, Chin YE, et al. STAT5 interaction with the T cell receptor complex and stimulation of T cell proliferation. *Science.* 1999;283(5399):222-5.
293. Kim PW, Sun ZY, Blacklow SC, Wagner G, Eck MJ. A zinc clasp structure tethers Lck to T cell coreceptors CD4 and CD8. *Science.* 2003;301(5640):1725-8.
294. Sawabe T, Horiuchi T, Nakamura M, Tsukamoto H, Nakahara K, Harashima SI, et al. Defect of lck in a patient with common variable immunodeficiency. *Int J Mol Med.* 2001;7(6):609-14.
295. Hauck F, Randriamampita C, Martin E, Gerart S, Lambert N, Lim A, et al. Primary T-cell immunodeficiency with immunodysregulation caused by autosomal recessive LCK deficiency. *J Allergy Clin Immunol.* 2012;130(5):1144-52 e11.
296. Legname G, Seddon B, Lovatt M, Tomlinson P, Sarner N, Tolaini M, et al. Inducible expression of a p56Lck transgene reveals a central role for Lck in the differentiation of CD4 SP thymocytes. *Immunity.* 2000;12(5):537-46.
297. Chiang YJ, Hodes RJ. Regulation of T cell development by c-Cbl: essential role of Lck. *Int Immunol.* 2015;27(5):245-51.
298. Karlas A, Machuy N, Shin Y, Pleissner KP, Artarini A, Heuer D, et al. Genome-wide RNAi screen identifies human host factors crucial for influenza virus replication. *Nature.* 2010;463(7282):818-22.
299. Sun CT, Lo WY, Wang IH, Lo YH, Shiou SR, Lai CK, et al. Transcription repression of human hepatitis B virus genes by negative regulatory element-binding protein/SON. *The Journal of biological chemistry.* 2001;276(26):24059-67.
300. Komori T, Doi A, Furuta H, Wakao H, Nakao N, Nakazato M, et al. Regulation of ghrelin signaling by a leptin-induced gene, negative regulatory element-binding protein, in the hypothalamic neurons. *The Journal of biological chemistry.* 2010;285(48):37884-94.
301. Tschop M, Smiley DL, Heiman ML. Ghrelin induces adiposity in rodents. *Nature.* 2000;407(6806):908-13.

302. Nakazato M, Murakami N, Date Y, Kojima M, Matsuo H, Kangawa K, et al. A role for ghrelin in the central regulation of feeding. *Nature*. 2001;409(6817):194-8.
303. Theander-Carrillo C, Wiedmer P, Cettour-Rose P, Nogueiras R, Perez-Tilve D, Pfluger P, et al. Ghrelin action in the brain controls adipocyte metabolism. *J Clin Invest*. 2006;116(7):1983-93.
304. Wortley KE, Anderson KD, Garcia K, Murray JD, Malinova L, Liu R, et al. Genetic deletion of ghrelin does not decrease food intake but influences metabolic fuel preference. *Proceedings of the National Academy of Sciences of the United States of America*. 2004;101(21):8227-32.
305. Chebani Y, Marion C, Zizzari P, Chettab K, Pastor M, Korostelev M, et al. Enhanced responsiveness of Ghrelin Q343X rats to ghrelin results in enhanced adiposity without increased appetite. *Sci Signal*. 2016;9(424):ra39.
306. Wortley KE, del Rincon JP, Murray JD, Garcia K, Iida K, Thorner MO, et al. Absence of ghrelin protects against early-onset obesity. *J Clin Invest*. 2005;115(12):3573-8.
307. Zigman JM, Nakano Y, Coppari R, Balthasar N, Marcus JN, Lee CE, et al. Mice lacking ghrelin receptors resist the development of diet-induced obesity. *J Clin Invest*. 2005;115(12):3564-72.
308. Li RL, Sherbet DP, Elsbernd BL, Goldstein JL, Brown MS, Zhao TJ. Profound hypoglycemia in starved, ghrelin-deficient mice is caused by decreased gluconeogenesis and reversed by lactate or fatty acids. *The Journal of biological chemistry*. 2012;287(22):17942-50.
309. Szentirmai E, Kapas L, Sun Y, Smith RG, Krueger JM. The preproghrelin gene is required for the normal integration of thermoregulation and sleep in mice. *Proceedings of the National Academy of Sciences of the United States of America*. 2009;106(33):14069-74.
310. Farquhar J, Heiman M, Wong AC, Wach R, Chessex P, Chanoine JP. Elevated umbilical cord ghrelin concentrations in small for gestational age neonates. *J Clin Endocrinol Metab*. 2003;88(9):4324-7.
311. Zhang JV, Ren PG, Avsian-Kretchmer O, Luo CW, Rauch R, Klein C, et al. Obestatin, a peptide encoded by the ghrelin gene, opposes ghrelin's effects on food intake. *Science*. 2005;310(5750):996-9.
312. Nouh O, Abd Elfattah MM, Hassouna AA. Association between ghrelin levels and BMD: a cross sectional trial. *Gynecol Endocrinol*. 2012;28(7):570-2.
313. Shojima N, Hara K, Fujita H, Horikoshi M, Takahashi N, Takamoto I, et al. Depletion of homeodomain-interacting protein kinase 3 impairs insulin secretion and glucose tolerance in mice. *Diabetologia*. 2012;55(12):3318-30.
314. Hahm S, Mizuno TM, Wu TJ, Wisor JP, Priest CA, Kozak CA, et al. Targeted deletion of the Vgf gene indicates that the encoded secretory peptide precursor plays a novel role in the regulation of energy balance. *Neuron*. 1999;23(3):537-48.
315. Watson E, Fargali S, Okamoto H, Sadahiro M, Gordon RE, Chakraborty T, et al. Analysis of knockout mice suggests a role for VGF in the control of fat storage and energy expenditure. *BMC Physiol*. 2009;9:19.
316. D'Amato F, Noli B, Angioni L, Cossu E, Incani M, Messina I, et al. VGF Peptide Profiles in Type 2 Diabetic Patients' Plasma and in Obese Mice. *PloS one*. 2015;10(11):e0142333.

317. Rahimi M, Vinciguerra M, Daghighi M, Ozcan B, Akbarkhanzadeh V, Sheedfar F, et al. Age-related obesity and type 2 diabetes dysregulate neuronal associated genes and proteins in humans. *Oncotarget*. 2015;6(30):29818-32.
318. Kim JW, Rhee M, Park JH, Yamaguchi H, Sasaki K, Minamino N, et al. Chronic effects of neuroendocrine regulatory peptide (NERP-1 and -2) on insulin secretion and gene expression in pancreatic beta-cells. *Biochemical and biophysical research communications*. 2015;457(2):148-53.
319. Bartolomucci A, La Corte G, Possenti R, Locatelli V, Rigamonti AE, Torsello A, et al. TLQP-21, a VGF-derived peptide, increases energy expenditure and prevents the early phase of diet-induced obesity. *Proceedings of the National Academy of Sciences of the United States of America*. 2006;103(39):14584-9.
320. Watson E, Hahm S, Mizuno TM, Windsor J, Montgomery C, Scherer PE, et al. VGF ablation blocks the development of hyperinsulinemia and hyperglycemia in several mouse models of obesity. *Endocrinology*. 2005;146(12):5151-63.
321. Henn BM, Botigue LR, Gravel S, Wang W, Brisbin A, Byrnes JK, et al. Genomic ancestry of North Africans supports back-to-Africa migrations. *PLoS genetics*. 2012;8(1):e1002397.
322. Pagani L, Kivisild T, Tarekegn A, Ekong R, Plaster C, Gallego Romero I, et al. Ethiopian genetic diversity reveals linguistic stratification and complex influences on the Ethiopian gene pool. *American journal of human genetics*. 2012;91(1):83-96.
323. Fry AE, Ghansa A, Small KS, Palma A, Auburn S, Diakite M, et al. Positive selection of a CD36 nonsense variant in sub-Saharan Africa, but no association with severe malaria phenotypes. *Human molecular genetics*. 2009;18(14):2683-92.
324. Ayodo G, Price AL, Keinan A, Ajwang A, Otieno MF, Orago AS, et al. Combining evidence of natural selection with association analysis increases power to detect malaria-resistance variants. *American journal of human genetics*. 2007;81(2):234-42.
325. Love-Gregory L, Sherva R, Sun L, Wasson J, Schappe T, Doria A, et al. Variants in the CD36 gene associate with the metabolic syndrome and high-density lipoprotein cholesterol. *Human molecular genetics*. 2008;17(11):1695-704.
326. Matsuo Y, Yokoyama R, Yokoyama S. The genes for human alcohol dehydrogenases beta 1 and beta 2 differ by only one nucleotide. *Eur J Biochem*. 1989;183(2):317-20.
327. Jornvall H, Hempel J, Vallee BL, Bosron WF, Li TK. Human liver alcohol dehydrogenase: amino acid substitution in the beta 2 beta 2 Oriental isozyme explains functional properties, establishes an active site structure, and parallels mutational exchanges in the yeast enzyme. *Proceedings of the National Academy of Sciences of the United States of America*. 1984;81(10):3024-8.
328. Hurley TD, Edenberg HJ, Bosron WF. Expression and kinetic characterization of variants of human beta 1 beta 1 alcohol dehydrogenase containing substitutions at amino acid 47. *The Journal of biological chemistry*. 1990;265(27):16366-72.

329. Han Y, Gu S, Oota H, Osier MV, Pakstis AJ, Speed WC, et al. Evidence of positive selection on a class I ADH locus. *American journal of human genetics*. 2007;80(3):441-56.
330. Mendez R, Hake LE, Andresson T, Littlepage LE, Ruderman JV, Richter JD. Phosphorylation of CPE binding factor by Eg2 regulates translation of c-mos mRNA. *Nature*. 2000;404(6775):302-7.
331. Prasad CK, Mahadevan M, MacNicol MC, MacNicol AM. Mos 3' UTR regulatory differences underlie species-specific temporal patterns of Mos mRNA cytoplasmic polyadenylation and translational recruitment during oocyte maturation. *Mol Reprod Dev*. 2008;75(8):1258-68.
332. Hashimoto N, Watanabe N, Furuta Y, Tamemoto H, Sagata N, Yokoyama M, et al. Parthenogenetic activation of oocytes in c-mos-deficient mice. *Nature*. 1994;370(6484):68-71.
333. Singh B, Arlinghaus RB. Mos and the cell cycle. *Prog Cell Cycle Res*. 1997;3:251-9.
334. Haber M, Gauguier D, Youhanna S, Patterson N, Moorjani P, Botigue LR, et al. Genome-wide diversity in the levant reveals recent structuring by culture. *PLoS genetics*. 2013;9(2):e1003316.
335. Huang AL, Chen X, Hoon MA, Chandrashekar J, Guo W, Trankner D, et al. The cells and logic for mammalian sour taste detection. *Nature*. 2006;442(7105):934-8.
336. Ishimaru Y, Inada H, Kubota M, Zhuang H, Tominaga M, Matsunami H. Transient receptor potential family members PKD1L3 and PKD2L1 form a candidate sour taste receptor. *Proceedings of the National Academy of Sciences of the United States of America*. 2006;103(33):12569-74.
337. Jalalvand E, Robertson B, Tostivint H, Wallen P, Grillner S. The Spinal Cord Has an Intrinsic System for the Control of pH. *Current biology : CB*. 2016;26(10):1346-51.
338. Horio N, Yoshida R, Yasumatsu K, Yanagawa Y, Ishimaru Y, Matsunami H, et al. Sour taste responses in mice lacking PKD channels. *PloS one*. 2011;6(5):e20007.
339. Ishimaru Y. Molecular mechanisms underlying the reception and transmission of sour taste information. *Biosci Biotechnol Biochem*. 2015;79(2):171-6.
340. Yu B, Zheng Y, Alexander D, Morrison AC, Coresh J, Boerwinkle E. Genetic determinants influencing human serum metabolome among African Americans. *PLoS genetics*. 2014;10(3):e1004212.
341. Wu JH, Lemaitre RN, Manichaikul A, Guan W, Tanaka T, Foy M, et al. Genome-wide association study identifies novel loci associated with concentrations of four plasma phospholipid fatty acids in the de novo lipogenesis pathway: results from the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) consortium. *Circ Cardiovasc Genet*. 2013;6(2):171-83.
342. Demirkan A, van Duijn CM, Ugocsai P, Isaacs A, Pramstaller PP, Liebisch G, et al. Genome-wide association study identifies novel loci associated with circulating phospho- and sphingolipid concentrations. *PLoS genetics*. 2012;8(2):e1002490.
343. Tremblay F, Revett T, Huard C, Zhang Y, Tobin JF, Martinez RV, et al. Bidirectional modulation of adipogenesis by the secreted protein

- Ccdc80/DR01/URB. *The Journal of biological chemistry*. 2009;284(12):8136-47.
344. Aoki K, Sun YJ, Aoki S, Wada K, Wada E. Cloning, expression, and mapping of a gene that is upregulated in adipose tissue of mice deficient in bombesin receptor subtype-3. *Biochemical and biophysical research communications*. 2002;290(4):1282-8.
345. Okada T, Nishizawa H, Kurata A, Tamba S, Sonoda M, Yasui A, et al. URB is abundantly expressed in adipose tissue and dysregulated in obesity. *Biochemical and biophysical research communications*. 2008;367(2):370-6.
346. Tremblay F, Huard C, Dow J, Gareski T, Will S, Richard AM, et al. Loss of coiled-coil domain containing 80 negatively modulates glucose homeostasis in diet-induced obese mice. *Endocrinology*. 2012;153(9):4290-303.
347. Li L, Zhang Y, Du H, He P, Li G, Liu X, et al. [Correlation between the expression level of coiled-coil domain-containing protein 80 and obesity]. *Zhonghua Yu Fang Yi Xue Za Zhi*. 2015;49(3):248-53.
348. Kowalski MP, Dubouix-Bourandy A, Bajmoczy M, Golan DE, Zaidi T, Coutinho-Sledge YS, et al. Host resistance to lung infection mediated by major vault protein in epithelial cells. *Science*. 2007;317(5834):130-2.
349. Suprenant KA, Bloom N, Fang J, Lushington G. The major vault protein is related to the toxic anion resistance protein (TelA) family. *J Exp Biol*. 2007;210(Pt 6):946-55.
350. Dortet L, Mostowy S, Samba-Louaka A, Gouin E, Nahori MA, Wiemer EA, et al. Recruitment of the major vault protein by InlK: a *Listeria monocytogenes* strategy to avoid autophagy. *PLoS Pathog*. 2011;7(8):e1002168.
351. Lara PC, Pruschy M, Zimmermann M, Henriquez-Hernandez LA. MVP and vaults: a role in the radiation response. *Radiat Oncol*. 2011;6:148.
352. Lara PC, Lloret M, Clavo B, Apolinario RM, Henriquez-Hernandez LA, Bordon E, et al. Severe hypoxia induces chemo-resistance in clinical cervical tumors through MVP over-expression. *Radiat Oncol*. 2009;4:29.
353. Reich D, Thangaraj K, Patterson N, Price AL, Singh L. Reconstructing Indian population history. *Nature*. 2009;461(7263):489-94.
354. Bamshad M, Kivisild T, Watkins WS, Dixon ME, Ricker CE, Rao BB, et al. Genetic evidence on the origins of Indian caste populations. *Genome research*. 2001;11(6):994-1004.
355. Alchon SA. *A pest in the land : new world epidemics in a global perspective*. 1st ed. Albuquerque: University of New Mexico Press; 2003. ix, 214 p. p.
356. Cook ND. *Demographic collapse, Indian Peru, 1520-1620*. Cambridge Cambridgeshire ; New York: Cambridge University Press; 1981. x, 310 p. p.
357. Aberth J. *The first horseman : disease in human history*. Upper Saddle River, N.J.: Pearson Prentice Hall; 2007. xii, 177 p. p.
358. Francis JM. *Iberia and the Americas : culture, politics, and history : a multidisciplinary encyclopedia*. Santa Barbara, Calif.: ABC-CLIO; 2006.
359. Cook ND. *Born to die : disease and New World conquest, 1492-1650*. Cambridge ; New York: Cambridge University Press; 1998. xiii, 248 p. p.
360. Fumagalli M, Cagliani R, Riva S, Pozzoli U, Biasin M, Piacentini L, et al. Population genetics of IFIH1: ancient population structure, local selection, and implications for susceptibility to type 1 diabetes. *Molecular biology and evolution*. 2010;27(11):2555-66.

361. Nejentsev S, Walker N, Riches D, Egholm M, Todd JA. Rare variants of IFIH1, a gene implicated in antiviral responses, protect against type 1 diabetes. *Science*. 2009;324(5925):387-9.
362. Liu S, Wang H, Jin Y, Podolsky R, Reddy MV, Pedersen J, et al. IFIH1 polymorphisms are significantly associated with type 1 diabetes and IFIH1 gene expression in peripheral blood mononuclear cells. *Human molecular genetics*. 2009;18(2):358-65.
363. Schell LM, Gallo MV. Overweight and obesity among North American Indian infants, children, and youth. *American journal of human biology : the official journal of the Human Biology Council*. 2012;24(3):302-13.
364. Story M, Evans M, Fabsitz RR, Clay TE, Holy Rock B, Broussard B. The epidemic of obesity in American Indian communities and the need for childhood obesity-prevention programs. *Am J Clin Nutr*. 1999;69(4 Suppl):747S-54S.
365. Ravussin E. Energy metabolism in obesity. *Studies in the Pima Indians*. *Diabetes Care*. 1993;16(1):232-8.
366. Wang SP, Yang H, Wu JW, Gauthier N, Fukao T, Mitchell GA. Metabolism as a tool for understanding human brain evolution: lipid energy metabolism as an example. *J Hum Evol*. 2014;77:41-9.
367. Gessner BD, Gillingham MB, Birch S, Wood T, Koeller DM. Evidence for an association between infant mortality and a carnitine palmitoyltransferase 1A genetic variant. *Pediatrics*. 2010;126(5):945-51.
368. Boyce VL, Swinburn BA. The traditional Pima Indian diet. Composition and adaptation for use in a dietary intervention study. *Diabetes Care*. 1993;16(1):369-71.
369. Smith CJ, Nelson RG, Hardy SA, Manahan EM, Bennett PH, Knowler WC. Survey of the diet of Pima Indians using quantitative food frequency assessment and 24-hour recall. *Diabetic Renal Disease Study*. *J Am Diet Assoc*. 1996;96(8):778-84.
370. Tekola-Ayele F, Adeyemo A, Chen G, Hailu E, Aseffa A, Davey G, et al. Novel genomic signals of recent selection in an Ethiopian population. *European journal of human genetics : EJHG*. 2015;23(8):1085-92.
371. Carrillo-Larco RM, Bernabe-Ortiz A, Pillay TD, Gilman RH, Sanchez JF, Poterico JA, et al. Obesity risk in rural, urban and rural-to-urban migrants: prospective results of the PERU MIGRANT study. *Int J Obes (Lond)*. 2016;40(1):181-5.
372. Antiporta DA, Smeeth L, Gilman RH, Miranda JJ. Length of urban residence and obesity among within-country rural-to-urban Andean migrants. *Public Health Nutr*. 2016;19(7):1270-8.
373. Lindgarde F, Ercilla MB, Correa LR, Ahren B. Body adiposity, insulin, and leptin in subgroups of Peruvian Amerindians. *High Alt Med Biol*. 2004;5(1):27-31.
374. Revilla L, Lopez T, Sanchez S, Yasuda M, Sanjines G. [Prevalence of hypertension and diabetes in residents from Lima and Callao, Peru]. *Rev Peru Med Exp Salud Publica*. 2014;31(3):437-44.
375. Nunez-Robles E, Huapaya-Pizarro C, Torres-Lao R, Esquivel-Leon S, Suarez-Moreno V, Yasuda-Espinoza M, et al. [Prevalence of cardiovascular and metabolic risk factors in school students, university students, and women from community-based organizations in the districts of Lima, Callao, la

- Libertad and Arequipa, Peru 2011]. *Rev Peru Med Exp Salud Publica*. 2014;31(4):652-9.
376. Lozano-Rojas G, Cabello-Morales E, Hernadez-Diaz H, Loza-Munarriz C. [Prevalence of overweight and obesity in adolescents from an urban district of Lima, Peru 2012]. *Rev Peru Med Exp Salud Publica*. 2014;31(3):494-500.
377. Bustamante A, Maia J. [Weight status and cardiorespiratory fitness in school students in the central region of Peru]. *Rev Peru Med Exp Salud Publica*. 2013;30(3):399-407.
378. Nam EW, Sharma B, Kim HY, Paja DJ, Yoon YM, Lee SH, et al. Obesity and Hypertension among School-going Adolescents in Peru. *J Lifestyle Med*. 2015;5(2):60-7.
379. Mohanna S, Baracco R, Seclen S. Lipid profile, waist circumference, and body mass index in a high altitude population. *High Alt Med Biol*. 2006;7(3):245-55.
380. Medina-Lezama J, Zea-Diaz H, Morey-Vargas OL, Bolanos-Salazar JF, Munoz-Atahualpa E, Postigo-MacDowall M, et al. Prevalence of the metabolic syndrome in Peruvian Andean hispanics: the PREVENCION study. *Diabetes Res Clin Pract*. 2007;78(2):270-81.
381. Baracco R, Mohanna S, Seclen S. A comparison of the prevalence of metabolic syndrome and its components in high and low altitude populations in peru. *Metab Syndr Relat Disord*. 2007;5(1):55-62.
382. Seclen SN, Rosas ME, Arias AJ, Huayta E, Medina CA. Prevalence of diabetes and impaired fasting glucose in Peru: report from PERUDIAB, a national urban population-based longitudinal study. *BMJ Open Diabetes Res Care*. 2015;3(1):e000110.
383. Abrha S, Shiferaw S, Ahmed KY. Overweight and obesity and its socio-demographic correlates among urban Ethiopian women: evidence from the 2011 EDHS. *BMC Public Health*. 2016;16:636.
384. Helelo TP, Gelaw YA, Adane AA. Prevalence and associated factors of hypertension among adults in Durame Town, Southern Ethiopia. *PloS one*. 2014;9(11):e112790.
385. Moges B, Amare B, Fantahun B, Kassu A. High prevalence of overweight, obesity, and hypertension with increased risk to cardiovascular disorders among adults in northwest Ethiopia: a cross sectional study. *BMC Cardiovasc Disord*. 2014;14:155.
386. Tebekaw Y, Teller C, Colon-Ramos U. The burden of underweight and overweight among women in Addis Ababa, Ethiopia. *BMC Public Health*. 2014;14:1126.
387. Tadesse T, Alemu H. Hypertension and associated factors among university students in Gondar, Ethiopia: a cross-sectional study. *BMC Public Health*. 2014;14:937.
388. Awoke A, Awoke T, Alemu S, Megabiaw B. Prevalence and associated factors of hypertension among adults in Gondar, Northwest Ethiopia: a community based cross-sectional study. *BMC Cardiovasc Disord*. 2012;12:113.
389. Regev-Tobias H, Reifen R, Endevelt R, Havkin O, Cohen E, Stern G, et al. Dietary acculturation and increasing rates of obesity in Ethiopian women living in Israel. *Nutrition*. 2012;28(1):30-4.



390. Tesfaye F, Byass P, Wall S. Population based prevalence of high blood pressure among adults in Addis Ababa: uncovering a silent epidemic. *BMC Cardiovasc Disord.* 2009;9:39.
391. Holden JE, Stone CK, Clark CM, Brown WD, Nickles RJ, Stanley C, et al. Enhanced cardiac metabolism of plasma glucose in high-altitude natives: adaptation against chronic hypoxia. *J Appl Physiol* (1985). 1995;79(1):222-8.
392. Hochachka PW, Clark CM, Brown WD, Stanley C, Stone CK, Nickles RJ, et al. The brain at high altitude: hypometabolism as a defense against chronic hypoxia? *J Cereb Blood Flow Metab.* 1994;14(4):671-9.
393. Wang P, Ha AY, Kidd KK, Koehle MS, Rupert JL. A variant of the endothelial nitric oxide synthase gene (NOS3) associated with AMS susceptibility is less common in the Quechua, a high altitude Native population. *High Alt Med Biol.* 2010;11(1):27-30.
394. Sivakumaran S, Agakov F, Theodoratou E, Prendergast JG, Zgaga L, Manolio T, et al. Abundant pleiotropy in human complex diseases and traits. *American journal of human genetics.* 2011;89(5):607-18.
395. Malnic B, Godfrey PA, Buck LB. The human olfactory receptor gene family. *Proceedings of the National Academy of Sciences of the United States of America.* 2004;101(8):2584-9.
396. Buettner JA, Glusman G, Ben-Arie N, Ramos P, Lancet D, Evans GA. Organization and evolution of olfactory receptor genes on human chromosome 11. *Genomics.* 1998;53(1):56-68.
397. Gilad Y, Segre D, Skorecki K, Nachman MW, Lancet D, Sharon D. Dichotomy of single-nucleotide polymorphism haplotypes in olfactory receptor genes and pseudogenes. *Nature genetics.* 2000;26(2):221-4.
398. Gaillard I, Rouquier S, Giorgi D. Olfactory receptors. *Cell Mol Life Sci.* 2004;61(4):456-69.
399. Zozulya S, Echeverri F, Nguyen T. The human olfactory receptor repertoire. *Genome biology.* 2001;2(6):RESEARCH0018.
400. Younger RM, Amadou C, Bethel G, Ehlers A, Lindahl KF, Forbes S, et al. Characterization of clustered MHC-linked olfactory receptor genes in human and mouse. *Genome research.* 2001;11(4):519-30.
401. Mainland JD, Keller A, Li YR, Zhou T, Trimmer C, Snyder LL, et al. The missense of smell: functional variability in the human odorant receptor repertoire. *Nat Neurosci.* 2014;17(1):114-20.
402. Keller A, Zhuang H, Chi Q, Vosshall LB, Matsunami H. Genetic variation in a human odorant receptor alters odour perception. *Nature.* 2007;449(7161):468-72.
403. Jaeger SR, McRae JF, Bava CM, Beresford MK, Hunter D, Jia Y, et al. A Mendelian trait for olfactory sensitivity affects odor experience and food selection. *Current biology : CB.* 2013;23(16):1601-5.
404. McRae JF, Mainland JD, Jaeger SR, Adipietro KA, Matsunami H, Newcomb RD. Genetic variation in the odorant receptor OR2J3 is associated with the ability to detect the "grassy" smelling odor, cis-3-hexen-1-ol. *Chem Senses.* 2012;37(7):585-93.
405. Katada S, Hirokawa T, Oka Y, Suwa M, Touhara K. Structural basis for a broad but selective ligand spectrum of a mouse olfactory receptor: mapping the

- odorant-binding site. *The Journal of neuroscience : the official journal of the Society for Neuroscience*. 2005;25(7):1806-15.
406. Hasin-Brumshtein Y, Lancet D, Olender T. Human olfaction: from genomic variation to phenotypic diversity. *Trends in genetics : TIG*. 2009;25(4):178-84.
  407. Adipietro KA, Mainland JD, Matsunami H. Functional evolution of mammalian odorant receptors. *PLoS genetics*. 2012;8(7):e1002821.
  408. Hayden S, Bekaert M, Crider TA, Mariani S, Murphy WJ, Teeling EC. Ecological adaptation determines functional mammalian olfactory subgenomes. *Genome research*. 2010;20(1):1-9.
  409. Keller A, Vosshall LB. Better smelling through genetics: mammalian odor perception. *Curr Opin Neurobiol*. 2008;18(4):364-9.
  410. Capittini C, Martinetti M, Cuccia M. MHC variation, mate choice and natural selection: the scent of evolution. *Riv Biol*. 2008;101(3):463-80.
  411. Apfelbach R, Blanchard CD, Blanchard RJ, Hayes RA, McGregor IS. The effects of predator odors in mammalian prey species: a review of field and laboratory studies. *Neurosci Biobehav Rev*. 2005;29(8):1123-44.
  412. Gilad Y, Man O, Paabo S, Lancet D. Human specific loss of olfactory receptor genes. *Proceedings of the National Academy of Sciences of the United States of America*. 2003;100(6):3324-7.
  413. Niimura Y, Nei M. Extensive gains and losses of olfactory receptor genes in mammalian evolution. *PloS one*. 2007;2(8):e708.
  414. Gimelbrant AA, Skaletsky H, Chess A. Selective pressures on the olfactory receptor repertoire since the human-chimpanzee divergence. *Proceedings of the National Academy of Sciences of the United States of America*. 2004;101(24):9019-22.
  415. Glusman G, Yanai I, Rubin I, Lancet D. The complete human olfactory subgenome. *Genome research*. 2001;11(5):685-702.
  416. Rouquier S, Blancher A, Giorgi D. The olfactory receptor gene repertoire in primates and mouse: evidence for reduction of the functional fraction in primates. *Proceedings of the National Academy of Sciences of the United States of America*. 2000;97(6):2870-4.
  417. Sharon D, Glusman G, Pilpel Y, Khen M, Gruetzner F, Haaf T, et al. Primate evolution of an olfactory receptor cluster: diversification by gene conversion and recent emergence of pseudogenes. *Genomics*. 1999;61(1):24-36.
  418. Go Y, Niimura Y. Similar numbers but different repertoires of olfactory receptor genes in humans and chimpanzees. *Molecular biology and evolution*. 2008;25(9):1897-907.
  419. Gilad Y, Lancet D. Population differences in the human functional olfactory repertoire. *Molecular biology and evolution*. 2003;20(3):307-14.
  420. Pierron D, Cortes NG, Letellier T, Grossman LI. Current relaxation of selection on the human genome: tolerance of deleterious mutations on olfactory receptors. *Mol Phylogenet Evol*. 2013;66(2):558-64.
  421. Gilad Y, Bustamante CD, Lancet D, Paabo S. Natural selection on the olfactory receptor gene family in humans and chimpanzees. *American journal of human genetics*. 2003;73(3):489-501.
  422. Moreno-Estrada A, Casals F, Ramirez-Soriano A, Oliva B, Calafell F, Bertranpetit J, et al. Signatures of selection in the human olfactory receptor OR511 gene. *Molecular biology and evolution*. 2008;25(1):144-54.

423. Saito H, Chi Q, Zhuang H, Matsunami H, Mainland JD. Odor coding by a Mammalian receptor repertoire. *Sci Signal*. 2009;2(60):ra9.
424. Trimmer C, Snyder LL, Mainland JD. High-throughput analysis of mammalian olfactory receptors: measurement of receptor activation via luciferase activity. *J Vis Exp*. 2014(88).
425. Zhuang H, Matsunami H. Evaluating cell-surface expression and measuring activation of mammalian odorant receptors in heterologous cells. *Nat Protoc*. 2008;3(9):1402-13.
426. Saito H, Kubota M, Roberts RW, Chi Q, Matsunami H. RTP family members induce functional expression of mammalian odorant receptors. *Cell*. 2004;119(5):679-91.
427. Zhuang H, Matsunami H. Synergism of accessory factors in functional expression of mammalian odorant receptors. *The Journal of biological chemistry*. 2007;282(20):15284-93.
428. Petryszak R, Keays M, Tang YA, Fonseca NA, Barrera E, Burdett T, et al. Expression Atlas update--an integrated database of gene and protein expression in humans, animals and plants. *Nucleic acids research*. 2016;44(D1):D746-52.
429. Flegel C, Manteniots S, Osthold S, Hatt H, Gisselmann G. Expression profile of ectopic olfactory receptors determined by deep sequencing. *PloS one*. 2013;8(2):e55368.
430. Bandelt HJ, Forster P, Rohl A. Median-joining networks for inferring intraspecific phylogenies. *Molecular biology and evolution*. 1999;16(1):37-48.
431. Feldmesser E, Olender T, Khen M, Yanai I, Ophir R, Lancet D. Widespread ectopic expression of olfactory receptor genes. *BMC genomics*. 2006;7:121.
432. De la Cruz O, Blekhman R, Zhang X, Nicolae D, Firestein S, Gilad Y. A signature of evolutionary constraint on a subset of ectopically expressed olfactory receptor genes. *Molecular biology and evolution*. 2009;26(3):491-4.
433. Braun T, Volland P, Kunz L, Prinz C, Gratzl M. Enterochromaffin cells of the human gut: sensors for spices and odorants. *Gastroenterology*. 2007;132(5):1890-901.
434. Vanderhaeghen P, Schurmans S, Vassart G, Parmentier M. Molecular cloning and chromosomal mapping of olfactory receptor genes expressed in the male germ line: evidence for their wide distribution in the human genome. *Biochemical and biophysical research communications*. 1997;237(2):283-7.
435. Vanderhaeghen P, Schurmans S, Vassart G, Parmentier M. Specific repertoire of olfactory receptor genes in the male germ cells of several mammalian species. *Genomics*. 1997;39(3):239-46.
436. Spehr M, Gisselmann G, Poplawski A, Riffell JA, Wetzel CH, Zimmer RK, et al. Identification of a testicular odorant receptor mediating human sperm chemotaxis. *Science*. 2003;299(5615):2054-8.
437. Veitinger T, Riffell JR, Veitinger S, Nascimento JM, Triller A, Chandsawangbhuwana C, et al. Chemosensory Ca<sup>2+</sup> dynamics correlate with diverse behavioral phenotypes in human sperm. *The Journal of biological chemistry*. 2011;286(19):17311-25.
438. Spehr M, Schwane K, Heilmann S, Gisselmann G, Hummel T, Hatt H. Dual capacity of a human olfactory receptor. *Current biology : CB*. 2004;14(19):R832-3.

439. Gakamsky A, Armon L, Eisenbach M. Behavioral response of human spermatozoa to a concentration jump of chemoattractants or intracellular cyclic nucleotides. *Hum Reprod.* 2009;24(5):1152-63.
440. Ziegler A, Dohr G, Uchanska-Ziegler B. Possible roles for products of polymorphic MHC and linked olfactory receptor genes during selection processes in reproduction. *Am J Reprod Immunol.* 2002;48(1):34-42.
441. Dreyer WJ. The area code hypothesis revisited: olfactory receptors and other related transmembrane receptors may function as the last digits in a cell surface code for assembling embryos. *Proceedings of the National Academy of Sciences of the United States of America.* 1998;95(16):9072-7.
442. Parmentier M, Libert F, Schurmans S, Schiffmann S, Lefort A, Eggerickx D, et al. Expression of members of the putative olfactory receptor gene family in mammalian germ cells. *Nature.* 1992;355(6359):453-5.
443. Solovieff N, Milton JN, Hartley SW, Sherva R, Sebastiani P, Dworkis DA, et al. Fetal hemoglobin in sickle cell anemia: genome-wide association studies suggest a regulatory region in the 5' olfactory receptor gene cluster. *Blood.* 2010;115(9):1815-22.
444. Dean A. Chromatin remodelling and the interaction between enhancers and promoters in the beta-globin locus. *Brief Funct Genomic Proteomic.* 2004;2(4):344-54.
445. Bulger M, Bender MA, van Doorninck JH, Wertman B, Farrell CM, Felsenfeld G, et al. Comparative structural and functional analysis of the olfactory receptor genes flanking the human and mouse beta-globin gene clusters. *Proceedings of the National Academy of Sciences of the United States of America.* 2000;97(26):14560-5.
446. Feingold EA, Penny LA, Nienhuis AW, Forget BG. An olfactory receptor gene is located in the extended human beta-globin gene cluster and is expressed in erythroid cells. *Genomics.* 1999;61(1):15-23.
447. Kim A, Kiefer CM, Dean A. Distinctive signatures of histone methylation in transcribed coding and noncoding human beta-globin sequences. *Molecular and cellular biology.* 2007;27(4):1271-9.
448. Epner E, Reik A, Cimborra D, Telling A, Bender MA, Fiering S, et al. The beta-globin LCR is not necessary for an open chromatin structure or developmentally regulated transcription of the native mouse beta-globin locus. *Mol Cell.* 1998;2(4):447-55.
449. Uda M, Galanello R, Sanna S, Lettre G, Sankaran VG, Chen W, et al. Genome-wide association study shows BCL11A associated with persistent fetal hemoglobin and amelioration of the phenotype of beta-thalassemia. *Proceedings of the National Academy of Sciences of the United States of America.* 2008;105(5):1620-5.
450. Sherva R, Sripichai O, Abel K, Ma Q, Whitacre J, Angkachatchai V, et al. Genetic modifiers of Hb E/beta0 thalassemia identified by a two-stage genome-wide association study. *BMC Med Genet.* 2010;11:51.
451. Bulger M, Schubeler D, Bender MA, Hamilton J, Farrell CM, Hardison RC, et al. A complex chromatin landscape revealed by patterns of nuclease sensitivity and histone modification within the mouse beta-globin locus. *Molecular and cellular biology.* 2003;23(15):5234-44.

452. Ferrer-Admetlla A, Sikora M, Laayouni H, Esteve A, Roubinet F, Blancher A, et al. A natural history of FUT2 polymorphism in humans. *Molecular biology and evolution*. 2009;26(9):1993-2003.
453. Karlsson EK, Kwiatkowski DP, Sabeti PC. Natural selection and infectious disease in human populations. *Nature reviews Genetics*. 2014;15(6):379-93.
454. Imbert-Marcille BM, Barbe L, Dupe M, Le Moullac-Vaidye B, Besse B, Peltier C, et al. A FUT2 gene common polymorphism determines resistance to rotavirus A of the P[8] genotype. *J Infect Dis*. 2014;209(8):1227-30.
455. Tate JE, Burton AH, Boschi-Pinto C, Steele AD, Duque J, Parashar UD, et al. 2008 estimate of worldwide rotavirus-associated mortality in children younger than 5 years before the introduction of universal rotavirus vaccination programmes: a systematic review and meta-analysis. *Lancet Infect Dis*. 2012;12(2):136-41.
456. Debbink K, Lindesmith LC, Donaldson EF, Baric RS. Norovirus immunity and the great escape. *PLoS Pathog*. 2012;8(10):e1002921.
457. Huang P, Xia M, Tan M, Zhong W, Wei C, Wang L, et al. Spike protein VP8\* of human rotavirus recognizes histo-blood group antigens in a type-specific manner. *J Virol*. 2012;86(9):4833-43.
458. Hu L, Crawford SE, Czako R, Cortes-Penfield NW, Smith DF, Le Pendu J, et al. Cell attachment protein VP8\* of a human rotavirus specifically interacts with A-type histo-blood group antigen. *Nature*. 2012;485(7397):256-9.
459. Liu Y, Huang P, Tan M, Liu Y, Biesiada J, Meller J, et al. Rotavirus VP8\*: phylogeny, host range, and interaction with histo-blood group antigens. *J Virol*. 2012;86(18):9899-910.
460. Ramani S, Cortes-Penfield NW, Hu L, Crawford SE, Czako R, Smith DF, et al. The VP8\* domain of neonatal rotavirus strain G10P[11] binds to type II precursor glycans. *J Virol*. 2013;87(13):7255-64.
461. Kambhampati A, Payne DC, Costantini V, Lopman BA. Host Genetic Susceptibility to Enteric Viruses: A Systematic Review and Metaanalysis. *Clin Infect Dis*. 2016;62(1):11-8.
462. Marionneau S, Cailleau-Thomas A, Rocher J, Le Moullac-Vaidye B, Ruvoen N, Clement M, et al. ABH and Lewis histo-blood group antigens, a model for the meaning of oligosaccharide diversity in the face of a changing world. *Biochimie*. 2001;83(7):565-73.
463. Shirato H. Norovirus and histo-blood group antigens. *Jpn J Infect Dis*. 2011;64(2):95-103.
464. Koda Y, Tachida H, Pang H, Liu Y, Soejima M, Ghaderi AA, et al. Contrasting patterns of polymorphisms at the ABO-secretor gene (FUT2) and plasma alpha(1,3)fucosyltransferase gene (FUT6) in human populations. *Genetics*. 2001;158(2):747-56.
465. Kelly RJ, Rouquier S, Giorgi D, Lennon GG, Lowe JB. Sequence and expression of a candidate for the human Secretor blood group alpha(1,2)fucosyltransferase gene (FUT2). Homozygosity for an enzyme-inactivating nonsense mutation commonly correlates with the non-secretor phenotype. *The Journal of biological chemistry*. 1995;270(9):4640-9.
466. Yu LC, Yang YH, Broadberry RE, Chen YH, Chan YS, Lin M. Correlation of a missense mutation in the human Secretor alpha 1,2-fucosyltransferase gene with the Lewis(a+b+) phenotype: a potential molecular basis for the weak Secretor allele (Sew). *Biochem J*. 1995;312 ( Pt 2):329-32.

467. Henry S, Mollicone R, Fernandez P, Samuelsson B, Oriol R, Larson G. Molecular basis for erythrocyte Le(a+ b+) and salivary ABH partial-secretor phenotypes: expression of a FUT2 secretor allele with an A-->T mutation at nucleotide 385 correlates with reduced alpha(1,2) fucosyltransferase activity. *Glycoconj J*. 1996;13(6):985-93.
468. Thorven M, Grahn A, Hedlund KO, Johansson H, Wahlfrid C, Larson G, et al. A homozygous nonsense mutation (428G-->A) in the human secretor (FUT2) gene provides resistance to symptomatic norovirus (GGII) infections. *J Virol*. 2005;79(24):15351-5.
469. Larsson MM, Rydell GE, Grahn A, Rodriguez-Diaz J, Akerlind B, Hutson AM, et al. Antibody prevalence and titer to norovirus (genogroup II) correlate with secretor (FUT2) but not with ABO phenotype or Lewis (FUT3) genotype. *J Infect Dis*. 2006;194(10):1422-7.
470. Marionneau S, Airaud F, Bovin NV, Le Pendu J, Ruvoen-Clouet N. Influence of the combined ABO, FUT2, and FUT3 polymorphism on susceptibility to Norwalk virus attachment. *J Infect Dis*. 2005;192(6):1071-7.
471. Liu P, Wang X, Lee JC, Teunis P, Hu S, Paradise HT, et al. Genetic susceptibility to norovirus GII.3 and GII.4 infections in Chinese pediatric diarrheal disease. *Pediatr Infect Dis J*. 2014;33(11):e305-9.
472. Carlsson B, Kindberg E, Buesa J, Rydell GE, Lidon MF, Montava R, et al. The G428A nonsense mutation in FUT2 provides strong but not absolute protection against symptomatic GII.4 Norovirus infection. *PloS one*. 2009;4(5):e5593.
473. Magalhaes A, Rossez Y, Robbe-Masselot C, Maes E, Gomes J, Shevtsova A, et al. Muc5ac gastric mucin glycosylation is shaped by FUT2 activity and functionally impacts *Helicobacter pylori* binding. *Sci Rep*. 2016;6:25575.
474. Ilver D, Arnqvist A, Ogren J, Frick IM, Kersulyte D, Incecik ET, et al. *Helicobacter pylori* adhesin binding fucosylated histo-blood group antigens revealed by retagging. *Science*. 1998;279(5349):373-7.
475. Boren T, Falk P, Roth KA, Larson G, Normark S. Attachment of *Helicobacter pylori* to human gastric epithelium mediated by blood group antigens. *Science*. 1993;262(5141):1892-5.
476. Azevedo M, Eriksson S, Mendes N, Serpa J, Figueiredo C, Resende LP, et al. Infection by *Helicobacter pylori* expressing the BabA adhesin is influenced by the secretor phenotype. *J Pathol*. 2008;215(3):308-16.
477. Moore ME, Boren T, Solnick JV. Life at the margins: modulation of attachment proteins in *Helicobacter pylori*. *Gut Microbes*. 2011;2(1):42-6.
478. Polk DB, Peek RM, Jr. *Helicobacter pylori*: gastric cancer and beyond. *Nat Rev Cancer*. 2010;10(6):403-14.
479. Schreiber S, Konradt M, Groll C, Scheid P, Hanauer G, Werling HO, et al. The spatial orientation of *Helicobacter pylori* in the gastric mucus. *Proceedings of the National Academy of Sciences of the United States of America*. 2004;101(14):5024-9.
480. Ali S, Niang MA, N'Doye I, Critchlow CW, Hawes SE, Hill AV, et al. Secretor polymorphism and human immunodeficiency virus infection in Senegalese women. *J Infect Dis*. 2000;181(2):737-9.
481. Blackwell CC, James VS, Davidson S, Wyld R, Brettle RP, Robertson RJ, et al. Secretor status and heterosexual transmission of HIV. *BMJ*. 1991;303(6806):825-6.

482. Kindberg E, Hejdeman B, Bratt G, Wahren B, Lindblom B, Hinkula J, et al. A nonsense mutation (428G-->A) in the fucosyltransferase FUT2 gene affects the progression of HIV-1 infection. *AIDS*. 2006;20(5):685-9.
483. Raza MW, Blackwell CC, Molyneaux P, James VS, Ogilvie MM, Inglis JM, et al. Association between secretor status and respiratory viral illness. *BMJ*. 1991;303(6806):815-8.
484. Wacklin P, Tuimala J, Nikkila J, Sebastian T, Makivuokko H, Alakulppi N, et al. Faecal microbiota composition in adults is associated with the FUT2 gene determining the secretor status. *PloS one*. 2014;9(4):e94863.
485. Tong M, McHardy I, Ruegger P, Goudarzi M, Kashyap PC, Haritunians T, et al. Reprogramming of gut microbiome energy metabolism by the FUT2 Crohn's disease risk polymorphism. *ISME J*. 2014;8(11):2193-206.
486. Rausch P, Rehman A, Kunzel S, Hasler R, Ott SJ, Schreiber S, et al. Colonic mucosa-associated microbiota is influenced by an interaction of Crohn disease and FUT2 (Secretor) genotype. *Proceedings of the National Academy of Sciences of the United States of America*. 2011;108(47):19030-5.
487. Wacklin P, Makivuokko H, Alakulppi N, Nikkila J, Tenkanen H, Rabina J, et al. Secretor genotype (FUT2 gene) is strongly associated with the composition of Bifidobacteria in the human intestine. *PloS one*. 2011;6(5):e20113.
488. Pham TA, Clare S, Goulding D, Arasteh JM, Stares MD, Browne HP, et al. Epithelial IL-22RA1-mediated fucosylation promotes intestinal colonization resistance to an opportunistic pathogen. *Cell host & microbe*. 2014;16(4):504-16.
489. Pickard JM, Maurice CF, Kinnebrew MA, Abt MC, Schenten D, Golovkina TV, et al. Rapid fucosylation of intestinal epithelium sustains host-commensal symbiosis in sickness. *Nature*. 2014;514(7524):638-41.
490. Nanthakumar NN, Meng D, Newburg DS. Glucocorticoids and microbiota regulate ontogeny of intestinal fucosyltransferase 2 requisite for gut homeostasis. *Glycobiology*. 2013;23(10):1131-41.
491. McGuckin MA, Linden SK, Sutton P, Florin TH. Mucin dynamics and enteric pathogens. *Nat Rev Microbiol*. 2011;9(4):265-78.
492. Xiao Y, Wang XQ, Yu Y, Guo Y, Xu X, Gong L, et al. Comprehensive mutation screening for 10 genes in Chinese patients suffering very early onset inflammatory bowel disease. *World J Gastroenterol*. 2016;22(24):5578-88.
493. Hu DY, Shao XX, Xu CL, Xia SL, Yu LQ, Jiang LJ, et al. Associations of FUT2 and FUT3 gene polymorphisms with Crohn's disease in Chinese patients. *J Gastroenterol Hepatol*. 2014;29(10):1778-85.
494. Kaur M, Panikkath D, Yan X, Liu Z, Berel D, Li D, et al. Perianal Crohn's Disease is Associated with Distal Colonic Disease, Strictureing Disease Behavior, IBD-Associated Serologies and Genetic Variation in the JAK-STAT Pathway. *Inflamm Bowel Dis*. 2016;22(4):862-9.
495. Franke A, McGovern DP, Barrett JC, Wang K, Radford-Smith GL, Ahmad T, et al. Genome-wide meta-analysis increases to 71 the number of confirmed Crohn's disease susceptibility loci. *Nature genetics*. 2010;42(12):1118-25.
496. McGovern DP, Jones MR, Taylor KD, Marcianti K, Yan X, Dubinsky M, et al. Fucosyltransferase 2 (FUT2) non-secretor status is associated with Crohn's disease. *Human molecular genetics*. 2010;19(17):3468-76.

497. Aheman A, Luo HS, Gao F. Association of fucosyltransferase 2 gene variants with ulcerative colitis in Han and Uyghur patients in China. *World J Gastroenterol*. 2012;18(34):4758-64.
498. Rupp C, Friedrich K, Folseraas T, Wannhoff A, Bode KA, Weiss KH, et al. Fut2 genotype is a risk factor for dominant stenosis and biliary candida infections in primary sclerosing cholangitis. *Aliment Pharmacol Ther*. 2014;39(8):873-82.
499. Henriksen EK, Melum E, Karlsen TH. Update on primary sclerosing cholangitis genetics. *Curr Opin Gastroenterol*. 2014;30(3):310-9.
500. Folseraas T, Melum E, Rausch P, Juran BD, Ellinghaus E, Shiryaev A, et al. Extended analysis of a genome-wide association study in primary sclerosing cholangitis detects multiple novel risk loci. *J Hepatol*. 2012;57(2):366-75.
501. Parmar AS, Alakulppi N, Paavola-Sakki P, Kurppa K, Halme L, Farkkila M, et al. Association study of FUT2 (rs601338) with celiac disease and inflammatory bowel disease in the Finnish population. *Tissue Antigens*. 2012;80(6):488-93.
502. Soejima M, Pang H, Koda Y. Genetic variation of FUT2 in a Ghanaian population: identification of four novel mutations and inference of balancing selection. *Ann Hematol*. 2007;86(3):199-204.
503. Walsh EC, Sabeti P, Hutcheson HB, Fry B, Schaffner SF, de Bakker PI, et al. Searching for signals of evolutionary selection in 168 genes related to immune function. *Human genetics*. 2006;119(1-2):92-102.
504. Fumagalli M, Cagliani R, Pozzoli U, Riva S, Comi GP, Menozzi G, et al. Widespread balancing selection and pathogen-driven selection at blood group antigen genes. *Genome research*. 2009;19(2):199-212.
505. Lis-Kuberka J, Katnik-Prastowska I, Berghausen-Mazur M, Orczyk-Pawilowicz M. Lectin-based analysis of fucosylated glycoproteins of human skim milk during 47 days of lactation. *Glycoconj J*. 2015;32(9):665-74.
506. Guix S, Asanaka M, Katayama K, Crawford SE, Neill FH, Atmar RL, et al. Norwalk virus RNA is infectious in mammalian cells. *J Virol*. 2007;81(22):12238-48.
507. Silva LM, Carvalho AS, Guillon P, Seixas S, Azevedo M, Almeida R, et al. Infection-associated FUT2 (Fucosyltransferase 2) genetic variation and impact on functionality assessed by in vivo studies. *Glycoconj J*. 2010;27(1):61-8.
508. Kaufman WL, Kocman I, Agrawal V, Rahn HP, Besser D, Gossen M. Homogeneity and persistence of transgene expression by omitting antibiotic selection in cell line isolation. *Nucleic acids research*. 2008;36(17):e111.
509. Krishnan M, Park JM, Cao F, Wang D, Paulmurugan R, Tseng JR, et al. Effects of epigenetic modulation on reporter gene expression: implications for stem cell imaging. *FASEB journal : official publication of the Federation of American Societies for Experimental Biology*. 2006;20(1):106-8.
510. Davis RH. The age of model organisms. *Nature reviews Genetics*. 2004;5(1):69-76.
511. Koonin EV. Orthologs, paralogs, and evolutionary genomics. *Annual review of genetics*. 2005;39:309-38.
512. Studer RA, Robinson-Rechavi M. How confident can we be that orthologs are similar, but paralogs differ? *Trends in genetics : TIG*. 2009;25(5):210-6.



513. Nehrt NL, Clark WT, Radivojac P, Hahn MW. Testing the ortholog conjecture with comparative functional genomic data from mammals. *PLoS Comput Biol.* 2011;7(6):e1002073.
514. Gharib WH, Robinson-Rechavi M. When orthologs diverge between human and mouse. *Brief Bioinform.* 2011;12(5):436-41.
515. Rosenthal N, Brown S. The mouse ascending: perspectives for human-disease models. *Nature cell biology.* 2007;9(9):993-9.
516. Hardouin SN, Nagy A. Mouse models for human disease. *Clin Genet.* 2000;57(4):237-44.
517. Cox RD, Brown SD. Rodent models of genetic disease. *Current opinion in genetics & development.* 2003;13(3):278-83.
518. Enard W. Mouse models of human evolution. *Current opinion in genetics & development.* 2014;29:75-80.
519. Stedman HH, Kozyak BW, Nelson A, Thesier DM, Su LT, Low DW, et al. Myosin gene mutation correlates with anatomical changes in the human lineage. *Nature.* 2004;428(6981):415-8.
520. Hedlund M, Tangvoranuntakul P, Takematsu H, Long JM, Housley GD, Kozutsumi Y, et al. N-glycolylneuraminic acid deficiency in mice: implications for human biology and evolution. *Molecular and cellular biology.* 2007;27(12):4340-6.
521. Enard W, Gehre S, Hammerschmidt K, Holter SM, Blass T, Somel M, et al. A humanized version of Foxp2 affects cortico-basal ganglia circuits in mice. *Cell.* 2009;137(5):961-71.
522. Cotney J, Leng J, Yin J, Reilly SK, DeMare LE, Emera D, et al. The evolution of lineage-specific regulatory activities in the human embryonic limb. *Cell.* 2013;154(1):185-96.
523. McLean CY, Reno PL, Pollen AA, Bassan AI, Capellini TD, Guenther C, et al. Human-specific loss of regulatory DNA and the evolution of human-specific traits. *Nature.* 2011;471(7337):216-9.
524. Dominski Z, Yang XC, Purdy M, Wagner EJ, Marzluff WF. A CPSF-73 homologue is required for cell cycle progression but not cell growth and interacts with a protein having features of CPSF-100. *Molecular and cellular biology.* 2005;25(4):1489-500.
525. Otani Y, Nakatsu Y, Sakoda H, Fukushima T, Fujishiro M, Kushiyama A, et al. Integrator complex plays an essential role in adipose differentiation. *Biochemical and biophysical research communications.* 2013;434(2):197-202.
526. Hata T, Nakayama M. Targeted disruption of the murine large nuclear KIAA1440/Ints1 protein causes growth arrest in early blastocyst stage embryos and eventual apoptotic cell death. *Biochimica et biophysica acta.* 2007;1773(7):1039-51.
527. Tao S, Cai Y, Sampath K. The Integrator subunits function in hematopoiesis by modulating Smad/BMP signaling. *Development.* 2009;136(16):2757-65.
528. Grundberg E, Small KS, Hedman AK, Nica AC, Buil A, Keildson S, et al. Mapping cis- and trans-regulatory effects across multiple tissues in twins. *Nature genetics.* 2012;44(10):1084-9.
529. Jurica MS, Licklider LJ, Gygi SR, Grigorieff N, Moore MJ. Purification and characterization of native spliceosomes suitable for three-dimensional structural analysis. *Rna.* 2002;8(4):426-39.

530. Estrada K, Styrkarsdottir U, Evangelou E, Hsu YH, Duncan EL, Ntzani EE, et al. Genome-wide meta-analysis identifies 56 bone mineral density loci and reveals 14 loci associated with risk of fracture. *Nature genetics*. 2012;44(5):491-501.
531. Moayyeri A, Hsu YH, Karasik D, Estrada K, Xiao SM, Nielson C, et al. Genetic determinants of heel bone properties: genome-wide association meta-analysis and replication in the GEFOS/GENOMOS consortium. *Human molecular genetics*. 2014.
532. Olalde I, Allentoft ME, Sanchez-Quinto F, Santpere G, Chiang CW, DeGiorgio M, et al. Derived immune and ancestral pigmentation alleles in a 7,000-year-old Mesolithic European. *Nature*. 2014;507(7491):225-8.
533. Krishnan S, Chen S, Turcatel G, Arditi M, Prasadarao NV. Regulation of Toll-like receptor 2 interaction with Ecgp96 controls Escherichia coli K1 invasion of brain endothelial cells. *Cellular microbiology*. 2013;15(1):63-81.
534. Cal S, Moncada-Pazos A, Lopez-Otin C. Expanding the complexity of the human degradome: polyserases and their tandem serine protease domains. *Frontiers in bioscience : a journal and virtual library*. 2007;12:4661-9.
535. Cal S, Peinado JR, Llamazares M, Quesada V, Moncada-Pazos A, Garabaya C, et al. Identification and characterization of human polyserase-3, a novel protein with tandem serine-protease domains in the same polypeptide chain. *BMC biochemistry*. 2006;7:9.
536. Tonne JM, Sakuma T, Deeds MC, Munoz-Gomez M, Barry MA, Kudva YC, et al. Global gene expression profiling of pancreatic islets in mice during streptozotocin-induced beta-cell damage and pancreatic Glp-1 gene therapy. *Disease models & mechanisms*. 2013;6(5):1236-45.
537. Stuart PE, Nair RP, Ellinghaus E, Ding J, Tejasvi T, Gudjonsson JE, et al. Genome-wide association analysis identifies three psoriasis susceptibility loci. *Nature genetics*. 2010;42(11):1000-4.
538. Garcia-Gonzalo FR, Cruz C, Munoz P, Mazurek S, Eigenbrodt E, Ventura F, et al. Interaction between HERC1 and M2-type pyruvate kinase. *FEBS letters*. 2003;539(1-3):78-84.
539. Mashimo T, Hadjebi O, Amair-Pinedo F, Tsurumi T, Langa F, Serikawa T, et al. Progressive Purkinje cell degeneration in tambaleante mutant mice is a consequence of a missense mutation in HERC1 E3 ubiquitin ligase. *PLoS genetics*. 2009;5(12):e1000784.
540. Rosa JL, Casaroli-Marano RP, Buckler AJ, Vilaro S, Barbacid M. p619, a giant protein related to the chromosome condensation regulator RCC1, stimulates guanine nucleotide exchange on ARF1 and Rab proteins. *The EMBO journal*. 1996;15(16):4262-73.
541. Craig DW, O'Shaughnessy JA, Kiefer JA, Aldrich J, Sinari S, Moses TM, et al. Genome and transcriptome sequencing in prospective metastatic triple-negative breast cancer uncovers therapeutic vulnerabilities. *Molecular cancer therapeutics*. 2013;12(1):104-16.
542. Diouf B, Cheng Q, Krynetskaia NF, Yang W, Cheok M, Pei D, et al. Somatic deletions of genes regulating MSH2 protein stability cause DNA mismatch repair deficiency and drug resistance in human leukemia cells. *Nature medicine*. 2011;17(10):1298-303.

543. Yuasa I, Umetsu K, Nishimukai H, Fukumori Y, Harihara S, Saitou N, et al. HERC1 polymorphisms: population-specific variations in haplotype composition. *Cell biochemistry and function*. 2009;27(6):402-5.
544. Aggarwal S, Bhowmik AD, Ramprasad VL, Murugan S, Dalal A. A splice site mutation in HERC1 leads to syndromic intellectual disability with macrocephaly and facial dysmorphism: Further delineation of the phenotypic spectrum. *American journal of medical genetics Part A*. 2016;170(7):1868-73.
545. Ortega-Recalde O, Beltran OI, Galvez JM, Palma-Montero A, Restrepo CM, Mateus HE, et al. Biallelic HERC1 mutations in a syndromic form of overgrowth and intellectual disability. *Clin Genet*. 2015;88(4):e1-3.
546. Nguyen LS, Schneider T, Rio M, Moutton S, Siquier-Pernet K, Verny F, et al. A nonsense variant in HERC1 is associated with intellectual disability, megalencephaly, thick corpus callosum and cerebellar atrophy. *European journal of human genetics : EJHG*. 2016;24(3):455-8.
547. Hashimoto R, Nakazawa T, Tsurusaki Y, Yasuda Y, Nagayasu K, Matsumura K, et al. Whole-exome sequencing and neurite outgrowth analysis in autism spectrum disorder. *Journal of human genetics*. 2016;61(3):199-206.
548. Bachiller S, Rybkina T, Porrás-García E, Pérez-Villegas E, Tabares L, Armengol JA, et al. The HERC1 E3 Ubiquitin Ligase is essential for normal development and for neurotransmission at the mouse neuromuscular junction. *Cell Mol Life Sci*. 2015;72(15):2961-71.
549. Jablonski NG. *Skin : a natural history*. Berkeley: University of California Press; 2006. xiii, 266 p. p.
550. Iyengar B. The hair follicle: a specialised UV receptor in the human skin? *Biol Signals Recept*. 1998;7(3):188-94.
551. De la Mettrie R, Saint-Leger D, Loussouarn G, Garcel A, Porter C, Langaney A. Shape variability and classification of human hair: a worldwide approach. *Hum Biol*. 2007;79(3):265-81.
552. Koniukhov BV, Malinina NA, Martynov M. [The we gene is a modifier of the wal gene in mice]. *Genetika*. 2004;40(7):968-74.
553. Koniukhov BV, Kupriianov SD. [The mutant gene wellhaarig disturbs the differentiation of hair follicle cells in the mouse]. *Ontogenez*. 1990;21(1):56-62.
554. Loussouarn G. African hair growth parameters. *Br J Dermatol*. 2001;145(2):294-7.
555. Khumalo NP, Gumedze F. African hair length in a school population: a clue to disease pathogenesis? *J Cosmet Dermatol*. 2007;6(3):144-51.
556. Schwartz GG, Rosenblum LA. Allometry of primate hair density and the evolution of human hairlessness. *Am J Phys Anthropol*. 1981;55(1):9-12.
557. Moura DS, Fernandez IF, Marin-Royo G, Lopez-Sanchez I, Martin-Doncel E, Vega FM, et al. Oncogenic Sox2 regulates and cooperates with Vrk1 in cell cycle progression and differentiation. *Sci Rep*. 2016;6:28532.
558. Liu J, Wang Y, He S, Xu X, Huang Y, Tang J, et al. Expression of vaccinia-related kinase 1 (VRK1) accelerates cell proliferation but overcomes cell adhesion mediated drug resistance (CAM-DR) in multiple myeloma. *Hematology*. 2016:1-10.

559. Renbaum P, Kellerman E, Jaron R, Geiger D, Segel R, Lee M, et al. Spinal muscular atrophy with pontocerebellar hypoplasia is caused by a mutation in the VRK1 gene. *American journal of human genetics*. 2009;85(2):281-9.
560. Najmabadi H, Hu H, Garshasbi M, Zemojtel T, Abedini SS, Chen W, et al. Deep sequencing reveals 50 novel genes for recessive cognitive disorders. *Nature*. 2011;478(7367):57-63.
561. Stoll M, Teoh H, Lee J, Reddel S, Zhu Y, Buckley M, et al. Novel motor phenotypes in patients with VRK1 mutations without pontocerebellar hypoplasia. *Neurology*. 2016;87(1):65-70.
562. Nguyen TP, Biliciler S, Wiszniewski W, Sheikh K. Expanding Phenotype of VRK1 Mutations in Motor Neuron Disease. *J Clin Neuromuscul Dis*. 2015;17(2):69-71.
563. Vinograd-Byk H, Sapir T, Cantarero L, Lazo PA, Zeligson S, Lev D, et al. The spinal muscular atrophy with pontocerebellar hypoplasia gene VRK1 regulates neuronal migration through an amyloid-beta precursor protein-dependent mechanism. *The Journal of neuroscience : the official journal of the Society for Neuroscience*. 2015;35(3):936-42.
564. Gonzaga-Jauregui C, Lotze T, Jamal L, Penney S, Campbell IM, Pehlivan D, et al. Mutations in VRK1 associated with complex motor and sensory axonal neuropathy plus microcephaly. *JAMA Neurol*. 2013;70(12):1491-8.
565. Salzano M, Vazquez-Cedeira M, Sanz-Garcia M, Valbuena A, Blanco S, Fernandez IF, et al. Vaccinia-related kinase 1 (VRK1) confers resistance to DNA-damaging agents in human breast cancer by affecting DNA damage response. *Oncotarget*. 2014;5(7):1770-8.
566. Sanz-Garcia M, Monsalve DM, Sevilla A, Lazo PA. Vaccinia-related kinase 1 (VRK1) is an upstream nucleosomal kinase required for the assembly of 53BP1 foci in response to ionizing radiation-induced DNA damage. *The Journal of biological chemistry*. 2012;287(28):23757-68.
567. Salzano M, Sanz-Garcia M, Monsalve DM, Moura DS, Lazo PA. VRK1 chromatin kinase phosphorylates H2AX and is required for foci formation induced by DNA damage. *Epigenetics*. 2015;10(5):373-83.
568. Monsalve DM, Campillo-Marcos I, Salzano M, Sanz-Garcia M, Cantarero L, Lazo PA. VRK1 phosphorylates and protects NBS1 from ubiquitination and proteasomal degradation in response to DNA damage. *Biochimica et biophysica acta*. 2016;1863(4):760-9.
569. Kettunen J, Tukiainen T, Sarin AP, Ortega-Alonso A, Tikkanen E, Lyytikäinen LP, et al. Genome-wide association study identifies multiple loci influencing human serum metabolite levels. *Nature genetics*. 2012;44(3):269-76.
570. Comuzzie AG, Cole SA, Laston SL, Voruganti VS, Haack K, Gibbs RA, et al. Novel genetic loci identified for the pathophysiology of childhood obesity in the Hispanic population. *PloS one*. 2012;7(12):e51954.
571. Sanchez J, Priego T, Pico C, Ahrens W, De Henauw S, Fraterman A, et al. Blood cells as a source of transcriptional biomarkers of childhood obesity and its related metabolic alterations: results of the IDEFICS study. *J Clin Endocrinol Metab*. 2012;97(4):E648-52.
572. Saunders CL, Chiodini BD, Sham P, Lewis CM, Abkevich V, Adeyemo AA, et al. Meta-analysis of genome-wide linkage studies in BMI and obesity. *Obesity*. 2007;15(9):2263-75.

573. Collins SA, Sinclair G, McIntosh S, Bamforth F, Thompson R, Sobol I, et al. Carnitine palmitoyltransferase 1A (CPT1A) P479L prevalence in live newborns in Yukon, Northwest Territories, and Nunavut. *Molecular genetics and metabolism*. 2010;101(2-3):200-4.
574. Collins SA, Surmala P, Osborne G, Greenberg C, Bathory LW, Edmunds-Potvin S, et al. Causes and risk factors for infant mortality in Nunavut, Canada 1999-2011. *BMC pediatrics*. 2012;12:190.
575. Sinclair GB, Collins S, Popescu O, McFadden D, Arbour L, Vallance HD. Carnitine palmitoyltransferase I and sudden unexpected infant death in British Columbia First Nations. *Pediatrics*. 2012;130(5):e1162-9.
576. Brown NF, Mullur RS, Subramanian I, Esser V, Bennett MJ, Saudubray JM, et al. Molecular characterization of L-CPT I deficiency in six patients: insights into function of the native enzyme. *Journal of lipid research*. 2001;42(7):1134-42.
577. Akkaoui M, Cohen I, Esnous C, Lenoir V, Sournac M, Girard J, et al. Modulation of the hepatic malonyl-CoA-carnitine palmitoyltransferase 1A partnership creates a metabolic switch allowing oxidation of de novo fatty acids. *Biochem J*. 2009;420(3):429-38.
578. Greenberg CR, Dilling LA, Thompson GR, Seargeant LE, Haworth JC, Phillips S, et al. The paradox of the carnitine palmitoyltransferase type Ia P479L variant in Canadian Aboriginal populations. *Molecular genetics and metabolism*. 2009;96(4):201-7.
579. Gessner BD, Gillingham MB, Wood T, Koeller DM. Association of a genetic variant of carnitine palmitoyltransferase 1A with infections in Alaska Native children. *J Pediatr*. 2013;163(6):1716-21.
580. Gillingham MB, Hirschfeld M, Lowe S, Matern D, Shoemaker J, Lambert WE, et al. Impaired fasting tolerance among Alaska native children with a common carnitine palmitoyltransferase 1A sequence variant. *Molecular genetics and metabolism*. 2011;104(3):261-4.
581. Rajakumar C, Ban MR, Cao H, Young TK, Bjerregaard P, Hegele RA. Carnitine palmitoyltransferase IA polymorphism P479L is common in Greenland Inuit and is associated with elevated plasma apolipoprotein A-I. *Journal of lipid research*. 2009;50(6):1223-8.
582. Gessner BD, Gillingham MB, Johnson MA, Richards CS, Lambert WE, Sesser D, et al. Prevalence and distribution of the c.1436C-->T sequence variant of carnitine palmitoyltransferase 1A among Alaska Native infants. *J Pediatr*. 2011;158(1):124-9.
583. Lemas DJ, Wiener HW, O'Brien DM, Hopkins S, Stanhope KL, Havel PJ, et al. Genetic polymorphisms in carnitine palmitoyltransferase 1A gene are associated with variation in body composition and fasting lipid traits in Yup'ik Eskimos. *Journal of lipid research*. 2012;53(1):175-84.
584. Madsen L, Rustan AC, Vaagenes H, Berge K, Dyroy E, Berge RK. Eicosapentaenoic and docosahexaenoic acid affect mitochondrial and peroxisomal fatty acid oxidation in relation to substrate preference. *Lipids*. 1999;34(9):951-63.
585. Andersen MK, Jorsboe E, Sandholt CH, Grarup N, Jorgensen ME, Faergeman NJ, et al. Identification of Novel Genetic Determinants of Erythrocyte Membrane Fatty Acid Composition among Greenlanders. *PLoS genetics*. 2016;12(6):e1006119.

586. Reynes B, Garcia-Ruiz E, Oliver P, Palou A. Gene expression of peripheral blood mononuclear cells is affected by cold exposure. *Am J Physiol Regul Integr Comp Physiol*. 2015;309(8):R824-34.
587. Nyman LR, Cox KB, Hoppel CL, Kerner J, Barnoski BL, Hamm DA, et al. Homozygous carnitine palmitoyltransferase 1a (liver isoform) deficiency is lethal in the mouse. *Molecular genetics and metabolism*. 2005;86(1-2):179-87.
588. Ahmed ZM, Riazuddin S, Aye S, Ali RA, Venselaar H, Anwar S, et al. Gene structure and mutant alleles of PCDH15: nonsyndromic deafness DFNB23 and type 1 Usher syndrome. *Human genetics*. 2008;124(3):215-23.
589. Alagramam KN, Murcia CL, Kwon HY, Pawlowski KS, Wright CG, Woychik RP. The mouse Ames waltzer hearing-loss mutant is caused by mutation of *Pcdh15*, a novel protocadherin gene. *Nature genetics*. 2001;27(1):99-102.
590. Ahmed ZM, Riazuddin S, Ahmad J, Bernstein SL, Guo Y, Sabar MF, et al. PCDH15 is expressed in the neurosensory epithelium of the eye and ear and mutant alleles are responsible for both USH1F and DFNB23. *Human molecular genetics*. 2003;12(24):3215-23.
591. Ahmed ZM, Goodyear R, Riazuddin S, Lagziel A, Legan PK, Behra M, et al. The tip-link antigen, a protein associated with the transduction complex of sensory hair cells, is protocadherin-15. *The Journal of neuroscience : the official journal of the Society for Neuroscience*. 2006;26(26):7022-34.
592. Kazmierczak P, Sakaguchi H, Tokita J, Wilson-Kubalek EM, Milligan RA, Muller U, et al. Cadherin 23 and protocadherin 15 interact to form tip-link filaments in sensory hair cells. *Nature*. 2007;449(7158):87-91.
593. Geng R, Sotomayor M, Kinder KJ, Gopal SR, Gerka-Stuyt J, Chen DH, et al. Noddy, a mouse harboring a missense mutation in protocadherin-15, reveals the impact of disrupting a critical interaction site between tip-link cadherins in inner ear hair cells. *The Journal of neuroscience : the official journal of the Society for Neuroscience*. 2013;33(10):4395-404.
594. Zheng QY, Yan D, Ouyang XM, Du LL, Yu H, Chang B, et al. Digenic inheritance of deafness caused by mutations in genes encoding cadherin 23 and protocadherin 15 in mice and humans. *Human molecular genetics*. 2005;14(1):103-11.
595. Naoi K, Kuramoto T, Kuwamura Y, Gohma H, Kuwamura M, Serikawa T. Characterization of the Kyoto circling (KCI) rat carrying a spontaneous nonsense mutation in the protocadherin 15 (*Pcdh15*) gene. *Experimental animals / Japanese Association for Laboratory Animal Science*. 2009;58(1):1-10.
596. Hampton LL, Wright CG, Alagramam KN, Battey JF, Noben-Trauth K. A new spontaneous mutation in the mouse Ames waltzer gene, *Pcdh15*. *Hearing research*. 2003;180(1-2):67-75.
597. Webb SW, Grillet N, Andrade LR, Xiong W, Swarthout L, Della Santina CC, et al. Regulation of PCDH15 function in mechanosensory hair cells by alternative splicing of the cytoplasmic domain. *Development*. 2011;138(8):1607-17.
598. Rouget-Quermalet V, Giustiniani J, Marie-Cardine A, Beaud G, Besnard F, Loyaux D, et al. Protocadherin 15 (PCDH15): a new secreted isoform and a potential marker for NK/T cell lymphomas. *Oncogene*. 2006;25(19):2807-11.

599. Oki NO, Motsinger-Reif AA, Antas PR, Levy S, Holland SM, Sterling TR. Novel human genetic variants associated with extrapulmonary tuberculosis: a pilot genome wide association study. *BMC research notes*. 2011;4:28.
600. Grupe A, Li Y, Rowland C, Nowotny P, Hinrichs AL, Smemo S, et al. A scan of chromosome 10 identifies a novel locus showing strong association with late-onset Alzheimer disease. *American journal of human genetics*. 2006;78(1):78-88.
601. Ovsyannikova IG, Kennedy RB, O'Byrne M, Jacobson RM, Pankratz VS, Poland GA. Genome-wide association study of antibody response to smallpox vaccine. *Vaccine*. 2012;30(28):4182-9.
602. Croteau-Chonka DC, Marvelle AF, Lange EM, Lee NR, Adair LS, Lange LA, et al. Genome-wide association study of anthropometric traits and evidence of interactions with age and study year in Filipino women. *Obesity*. 2011;19(5):1019-27.
603. Huertas-Vazquez A, Plaisier CL, Geng R, Haas BE, Lee J, Greevenbroek MM, et al. A nonsynonymous SNP within PCDH15 is associated with lipid traits in familial combined hyperlipidemia. *Human genetics*. 2010;127(1):83-9.
604. Yasunaga S, Grati M, Chardenoux S, Smith TN, Friedman TB, Lalwani AK, et al. OTOF encodes multiple long and short isoforms: genetic evidence that the long ones underlie recessive deafness DFNB9. *American journal of human genetics*. 2000;67(3):591-600.
605. Yasunaga S, Grati M, Cohen-Salmon M, El-Amraoui A, Mustapha M, Salem N, et al. A mutation in OTOF, encoding otoferlin, a FER-1-like protein, causes DFNB9, a nonsyndromic form of deafness. *Nature genetics*. 1999;21(4):363-9.
606. Rouillon I, Marcolla A, Roux I, Marlin S, Feldmann D, Couderc R, et al. Results of cochlear implantation in two children with mutations in the OTOF gene. *Int J Pediatr Otorhinolaryngol*. 2006;70(4):689-96.
607. Pangrsic T, Reisinger E, Moser T. Otoferlin: a multi-C2 domain protein essential for hearing. *Trends Neurosci*. 2012;35(11):671-80.
608. Roux I, Safieddine S, Nouvian R, Grati M, Simmler MC, Bahloul A, et al. Otoferlin, defective in a human deafness form, is essential for exocytosis at the auditory ribbon synapse. *Cell*. 2006;127(2):277-89.
609. Lek A, Evesson FJ, Sutton RB, North KN, Cooper ST. Ferlins: regulators of vesicle fusion for auditory neurotransmission, receptor trafficking and membrane repair. *Traffic*. 2012;13(2):185-94.
610. Dulon D, Safieddine S, Jones SM, Petit C. Otoferlin is critical for a highly sensitive and linear calcium-dependent exocytosis at vestibular hair cell ribbon synapses. *The Journal of neuroscience : the official journal of the Society for Neuroscience*. 2009;29(34):10474-87.
611. Beurq M, Safieddine S, Roux I, Bouleau Y, Petit C, Dulon D. Calcium- and otoferlin-dependent exocytosis by immature outer hair cells. *The Journal of neuroscience : the official journal of the Society for Neuroscience*. 2008;28(8):1798-803.
612. Beurq M, Michalski N, Safieddine S, Bouleau Y, Schneggenburger R, Chapman ER, et al. Control of exocytosis by synaptotagmins and otoferlin in auditory hair cells. *The Journal of neuroscience : the official journal of the Society for Neuroscience*. 2010;30(40):13281-90.

613. Mahdieh N, Shirkavand A, Rabbani B, Tekin M, Akbari B, Akbari MT, et al. Screening of OTOF mutations in Iran: a novel mutation and review. *Int J Pediatr Otorhinolaryngol.* 2012;76(11):1610-5.
614. Zhang Q, Lan L, Shi W, Yu L, Xie LY, Xiong F, et al. Temperature sensitive auditory neuropathy. *Hearing research.* 2016;335:53-63.
615. Starr A, Sininger Y, Winter M, Derebery MJ, Oba S, Michalewski HJ. Transient deafness due to temperature-sensitive auditory neuropathy. *Ear Hear.* 1998;19(3):169-79.
616. Marlin S, Feldmann D, Nguyen Y, Rouillon I, Loundon N, Jonard L, et al. Temperature-sensitive auditory neuropathy associated with an otoferlin mutation: Deafening fever! *Biochemical and biophysical research communications.* 2010;394(3):737-42.
617. Longo-Guess C, Gagnon LH, Bergstrom DE, Johnson KR. A missense mutation in the conserved C2B domain of otoferlin causes deafness in a new mouse model of DFNB9. *Hearing research.* 2007;234(1-2):21-8.
618. Hudson NJ, Baker ML, Hart NS, Wynne JW, Gu Q, Huang Z, et al. Sensory rewiring in an echolocator: genome-wide modification of retinogenic and auditory genes in the bat *Myotis davidii*. *G3 (Bethesda).* 2014;4(10):1825-35.
619. Shen YY, Liang L, Li GS, Murphy RW, Zhang YP. Parallel evolution of auditory genes for echolocation in bats and toothed whales. *PLoS genetics.* 2012;8(6):e1002788.
620. Akey JM, Swanson WJ, Madeoy J, Eberle M, Shriver MD. TRPV6 exhibits unusual patterns of polymorphism and divergence in worldwide populations. *Human molecular genetics.* 2006;15(13):2106-13.
621. Hughes DA, Tang K, Strotmann R, Schoneberg T, Prenen J, Nilius B, et al. Parallel selection on TRPV6 in human populations. *PloS one.* 2008;3(2):e1686.
622. Field Y, Boyle EA, Telis N, Gao Z, Gaulton KJ, Golan D, et al. Detection of human adaptation during the past 2000 years. *Science.* 2016;354(6313):760-4.
623. Bulik-Sullivan BK, Loh PR, Finucane HK, Ripke S, Yang J, Schizophrenia Working Group of the Psychiatric Genomics C, et al. LD Score regression distinguishes confounding from polygenicity in genome-wide association studies. *Nature genetics.* 2015;47(3):291-5.
624. Matthews PM, Sudlow C. The UK Biobank. *Brain.* 2015;138(Pt 12):3463-5.
625. Sudlow C, Gallacher J, Allen N, Beral V, Burton P, Danesh J, et al. UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. *PLoS Med.* 2015;12(3):e1001779.
626. Zhen Y, Andolfatto P. Methods to detect selection on noncoding DNA. *Methods Mol Biol.* 2012;856:141-59.
627. Kudaravalli S, Veyrieras JB, Stranger BE, Dermitzakis ET, Pritchard JK. Gene expression levels are a target of recent natural selection in the human genome. *Molecular biology and evolution.* 2009;26(3):649-58.
628. Chen J, Shishkin AA, Zhu X, Kadri S, Maza I, Guttman M, et al. Evolutionary analysis across mammals reveals distinct classes of long non-coding RNAs. *Genome biology.* 2016;17:19.
629. Wiberg RA, Halligan DL, Ness RW, Necsulea A, Kaessmann H, Keightley PD. Assessing Recent Selection and Functionality at Long Noncoding RNA Loci in the Mouse Genome. *Genome Biol Evol.* 2015;7(8):2432-44.



630. Sudmant PH, Mallick S, Nelson BJ, Hormozdiari F, Krumm N, Huddleston J, et al. Global diversity, population stratification, and selection of human copy-number variation. *Science*. 2015;349(6253):aab3761.
631. Perry GH, Dominy NJ, Claw KG, Lee AS, Fiegler H, Redon R, et al. Diet and the evolution of human amylase gene copy number variation. *Nature genetics*. 2007;39(10):1256-60.
632. Hardwick RJ, Menard A, Sironi M, Milet J, Garcia A, Sese C, et al. Haptoglobin (HP) and Haptoglobin-related protein (HPR) copy number variation, natural selection, and trypanosomiasis. *Human genetics*. 2014;133(1):69-83.
633. Xue Y, Sun D, Daly A, Yang F, Zhou X, Zhao M, et al. Adaptive evolution of UGT2B17 copy-number variation. *American journal of human genetics*. 2008;83(3):337-46.
634. Marian AJ. Elements of 'missing heritability'. *Curr Opin Cardiol*. 2012;27(3):197-201.
635. Pai AA, Pritchard JK, Gilad Y. The genetic and mechanistic basis for variation in gene regulation. *PLoS genetics*. 2015;11(1):e1004857.
636. Schubeler D. Function and information content of DNA methylation. *Nature*. 2015;517(7534):321-6.
637. Illingworth RS, Bird AP. CpG islands--'a rough guide'. *FEBS letters*. 2009;583(11):1713-20.
638. Banovich NE, Lan X, McVicker G, van de Geijn B, Degner JF, Blischak JD, et al. Methylation QTLs are associated with coordinated changes in transcription factor binding, histone modifications, and gene expression levels. *PLoS genetics*. 2014;10(9):e1004663.
639. Boks MP, Derks EM, Weisenberger DJ, Strengman E, Janson E, Sommer IE, et al. The relationship of DNA methylation with age, gender and genotype in twins and healthy controls. *PloS one*. 2009;4(8):e6767.
640. Kaminsky ZA, Tang T, Wang SC, Ptak C, Oh GH, Wong AH, et al. DNA methylation profiles in monozygotic and dizygotic twins. *Nature genetics*. 2009;41(2):240-5.
641. Zhang D, Cheng L, Badner JA, Chen C, Chen Q, Luo W, et al. Genetic control of individual differences in gene-specific methylation in human brain. *American journal of human genetics*. 2010;86(3):411-9.
642. Gibbs JR, van der Brug MP, Hernandez DG, Traynor BJ, Nalls MA, Lai SL, et al. Abundant quantitative trait loci exist for DNA methylation and gene expression in human brain. *PLoS genetics*. 2010;6(5):e1000952.
643. Bell JT, Pai AA, Pickrell JK, Gaffney DJ, Pique-Regi R, Degner JF, et al. DNA methylation patterns associate with genetic and gene expression variation in HapMap cell lines. *Genome biology*. 2011;12(1):R10.
644. Ziller MJ, Gu H, Muller F, Donaghey J, Tsai LT, Kohlbacher O, et al. Charting a dynamic DNA methylation landscape of the human genome. *Nature*. 2013;500(7463):477-81.
645. Fraser HB, Lam LL, Neumann SM, Kobor MS. Population-specificity of human DNA methylation. *Genome biology*. 2012;13(2):R8.
646. Heyn H, Moran S, Hernando-Herraez I, Sayols S, Gomez A, Sandoval J, et al. DNA methylation contributes to natural human variation. *Genome research*. 2013;23(9):1363-72.
647. Moen EL, Zhang X, Mu W, Delaney SM, Wing C, McQuade J, et al. Genome-wide variation of cytosine modifications between European and African

- populations and the implications for complex traits. *Genetics*. 2013;194(4):987-96.
648. Fagny M, Patin E, Maclsaac JL, Rotival M, Flutre T, Jones MJ, et al. The epigenomic landscape of African rainforest hunter-gatherers and farmers. *Nature communications*. 2015;6:10047.