

References

1. Pollak, K. and E.A. Underwood, *The healers: the doctor, then and now.* 1968, London,: Nelson. x, 246 p.
2. Neill, C.A. and E.B. Clark, *Tetralogy of Fallot. The first 300 years.* Tex Heart Inst J, 1994. **21**(4): p. 272-9.
3. Maheshwari S, K.V., *Textbook of Cardiology (A Clinical & Historical Perspective)* N.C.N. H K Chopra Editor. 2012, Jaypee Brothers Medical Publishers. p. 270-282.
4. Robert E. Gross, M.D.J.P.H., M.D., *Surgical ligation of a patent ductus arteriosus report of first successful case.* JAMA, 1939. **112**(8): p. 729-731.
5. Rashkind, W.j., *Pediatric Cardiology: A Brief Historical Perspective*. Pediatr Cardiology, 1979. **1**: p. 63-71.
6. Baars, H.F., J.J.v.d. Smagt, and P.A. Doevedans, *Clinical cardiogenetics.* 2011, London: Springer. xv, 455 p.
7. Olley, P.M., F. Coceani, and E. Bodach, *E-type prostaglandins: a new emergency therapy for certain cyanotic congenital heart malformations.* Circulation, 1976. **53**(4): p. 728-31.
8. Laurenceau, J.L., et al., [Study of tetralogy of Fallot by echocardiography]. Arch Mal Coeur Vaiss, 1975. **68**(5): p. 505-12.
9. Ferencz, C.L., CA, Correa-Villasenor, Wilson,PD, *Genetic and Environmental Risk Factors of Major Cardiovascular Malformations, The Baltimore-Washington Infant Study, (1981-1989).* 1997: Perspectives in Pediatric Cardiology, vol.5. Armonk, N.Y: Futura Publishing Co.Inc.
10. !!! INVALID CITATION !!!
11. Gupta, V. and K.D. Poss, *Clonally dominant cardiomyocytes direct heart morphogenesis.* Nature, 2012. **484**(7395): p. 479-84.
12. Yelon, D., *Developmental biology: Heart under construction.* Nature, 2012. **484**(7395): p. 459-60.
13. van der Linde, D., et al., *Birth prevalence of congenital heart disease worldwide: a systematic review and meta-analysis.* J Am Coll Cardiol, 2011. **58**(21): p. 2241-7.
14. Fahed, A.C., et al., *Genetics of congenital heart disease: the glass half empty.* Circ Res, 2013. **112**(4): p. 707-20.
15. van der Bom, T., et al., *The changing epidemiology of congenital heart disease.* Nat Rev Cardiol, 2011. **8**(1): p. 50-60.
16. Brickner, M.E., L.D. Hillis, and R.A. Lange, *Congenital heart disease in adults. First of two parts.* N Engl J Med, 2000. **342**(4): p. 256-63.
17. Soulvie, M.A., et al., *Psychological Distress Experienced by Parents of Young Children With Congenital Heart Defects: A Comprehensive Review of Literature.* Journal of Social Service Research, 2012. **38**(4): p. 484-502.
18. Sadoh, W.E., D.U. Nwaneri, and A.C. Owobu, *The cost of out-patient management of chronic heart failure in children with congenital heart disease.* Niger J Clin Pract, 2011. **14**(1): p. 65-9.
19. Hoffman, J.I. and S. Kaplan, *The incidence of congenital heart disease.* J Am Coll Cardiol, 2002. **39**(12): p. 1890-900.

20. Bernier, P.L., et al., *The challenge of congenital heart disease worldwide: epidemiologic and demographic facts*. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu, 2010. **13**(1): p. 26-34.
21. Warnes, C.A., et al., *Task force 1: the changing profile of congenital heart disease in adult life*. J Am Coll Cardiol, 2001. **37**(5): p. 1170-5.
22. Marelli, A.J., et al., *Congenital heart disease in the general population: changing prevalence and age distribution*. Circulation, 2007. **115**(2): p. 163-72.
23. van der Velde, E.T., et al., *CONCOR, an initiative towards a national registry and DNA-bank of patients with congenital heart disease in the Netherlands: rationale, design, and first results*. Eur J Epidemiol, 2005. **20**(6): p. 549-57.
24. Nora, J.J. and A.H. Nora, *Maternal transmission of congenital heart diseases: new recurrence risk figures and the questions of cytoplasmic inheritance and vulnerability to teratogens*. Am J Cardiol, 1987. **59**(5): p. 459-63.
25. Nora, J.J. and A.H. Nora, *The evolution of specific genetic and environmental counseling in congenital heart diseases*. Circulation, 1978. **57**(2): p. 205-13.
26. Nora, J.J. and A.H. Nora, *Recurrence risks in children having one parent with a congenital heart disease*. Circulation, 1976. **53**(4): p. 701-2.
27. Nora, J.J., C.W. McGill, and D.G. McNamara, *Empiric recurrence risks in common and uncommon congenital heart lesions*. Teratology, 1970. **3**(4): p. 325-30.
28. Nora, J.J., *Multifactorial inheritance hypothesis for the etiology of congenital heart diseases. The genetic-environmental interaction*. Circulation, 1968. **38**(3): p. 604-17.
29. Burn, J., et al., *Recurrence risks in offspring of adults with major heart defects: results from first cohort of British collaborative study*. Lancet, 1998. **351**(9099): p. 311-6.
30. Burn, J. and G. Corney, *Congenital heart defects and twinning*. Acta Genet Med Gemellol (Roma), 1984. **33**(1): p. 61-9.
31. Fesslova, V., et al., *Recurrence of congenital heart disease in cases with familial risk screened prenatally by echocardiography*. J Pregnancy, 2011. **2011**: p. 368067.
32. Oyen, N., et al., *Recurrence of congenital heart defects in families*. Circulation, 2009. **120**(4): p. 295-301.
33. Hardin, J., et al., *Increased prevalence of cardiovascular defects among 56,709 California twin pairs*. Am J Med Genet A, 2009. **149A**(5): p. 877-86.
34. Lewin, M.B., et al., *Echocardiographic evaluation of asymptomatic parental and sibling cardiovascular anomalies associated with congenital left ventricular outflow tract lesions*. Pediatrics, 2004. **114**(3): p. 691-6.
35. Gill, H.K., et al., *Patterns of recurrence of congenital heart disease: an analysis of 6,640 consecutive pregnancies evaluated by detailed fetal echocardiography*. J Am Coll Cardiol, 2003. **42**(5): p. 923-9.
36. Shieh, J.T. and D. Srivastava, *Heart malformation: what are the chances it could happen again?* Circulation, 2009. **120**(4): p. 269-71.
37. Oyen, N., et al., *Recurrence of discordant congenital heart defects in families*. Circ Cardiovasc Genet, 2010. **3**(2): p. 122-8.
38. Hoffman, J.I., *Incidence of congenital heart disease: II. Prenatal incidence*. Pediatr Cardiol, 1995. **16**(4): p. 155-65.

39. Blue, G.M., et al., *Congenital heart disease: current knowledge about causes and inheritance*. Med J Aust, 2012. **197**(3): p. 155-9.
40. Talner, C.N., *Report of the New England Regional Infant Cardiac Program, by Donald C. Fyler, MD*, Pediatrics, 1980;65(suppl):375-461. Pediatrics, 1998. **102**(1 Pt 2): p. 258-9.
41. Chang, R.K., M. Gurvitz, and S. Rodriguez, *Missed diagnosis of critical congenital heart disease*. Arch Pediatr Adolesc Med, 2008. **162**(10): p. 969-74.
42. Hoffman, J.I., *It is time for routine neonatal screening by pulse oximetry*. Neonatology, 2011. **99**(1): p. 1-9.
43. Kemper, A.R., et al., *Strategies for implementing screening for critical congenital heart disease*. Pediatrics, 2011. **128**(5): p. e1259-67.
44. de-Wahl Granelli, A., et al., *Impact of pulse oximetry screening on the detection of duct dependent congenital heart disease: a Swedish prospective screening study in 39,821 newborns*. BMJ, 2009. **338**: p. a3037.
45. Chaturvedi, V. and A. Saxena, *Heart failure in children: clinical aspect and management*. Indian J Pediatr, 2009. **76**(2): p. 195-205.
46. Verheugt, C.L., et al., *Gender and outcome in adult congenital heart disease*. Circulation, 2008. **118**(1): p. 26-32.
47. Verheugt, C.L., et al., *Long-term prognosis of congenital heart defects: a systematic review*. Int J Cardiol, 2008. **131**(1): p. 25-32.
48. Walsh, E.P. and F. Cecchin, *Arrhythmias in adult patients with congenital heart disease*. Circulation, 2007. **115**(4): p. 534-45.
49. Rhodes, L.A., et al., *Arrhythmias and intracardiac conduction after the arterial switch operation*. J Thorac Cardiovasc Surg, 1995. **109**(2): p. 303-10.
50. van den Bosch, A.E., et al., *Long-term outcome and quality of life in adult patients after the Fontan operation*. Am J Cardiol, 2004. **93**(9): p. 1141-5.
51. Tleyjeh, I.M., et al., *Temporal trends in infective endocarditis: a population-based study in Olmsted County, Minnesota*. JAMA, 2005. **293**(24): p. 3022-8.
52. Niwa, K., et al., *Infective endocarditis in congenital heart disease: Japanese national collaboration study*. Heart, 2005. **91**(6): p. 795-800.
53. Di Filippo, S., et al., *Current patterns of infective endocarditis in congenital heart disease*. Heart, 2006. **92**(10): p. 1490-5.
54. Duffels, M.G., et al., *Pulmonary arterial hypertension in congenital heart disease: an epidemiologic perspective from a Dutch registry*. Int J Cardiol, 2007. **120**(2): p. 198-204.
55. Diller, G.P. and M.A. Gatzoulis, *Pulmonary vascular disease in adults with congenital heart disease*. Circulation, 2007. **115**(8): p. 1039-50.
56. Barst, R.J., et al., *Diagnosis and differential assessment of pulmonary arterial hypertension*. J Am Coll Cardiol, 2004. **43**(12 Suppl S): p. 40S-47S.
57. Vongpatanasin, W., et al., *The Eisenmenger syndrome in adults*. Ann Intern Med, 1998. **128**(9): p. 745-55.
58. Engelfriet, P.M., et al., *Pulmonary arterial hypertension in adults born with a heart septal defect: the Euro Heart Survey on adult congenital heart disease*. Heart, 2007. **93**(6): p. 682-7.

59. Organization, W.H. *ICD-10: International statistical classification of diseases and related health problems*. 2008; Available from: [sa9_thesis_corrected_3Jan2014.docx](#).
60. Leung, M.P., M.H. Tang, and A. Ghosh, *Prenatal diagnosis of congenital heart malformations: classification based on abnormalities detected by the four-chamber view*. Prenat Diagn, 1999. **19**(4): p. 305-13.
61. Knowles, R., et al., *Newborn screening for congenital heart defects: a systematic review and cost-effectiveness analysis*. Health Technol Assess, 2005. **9**(44): p. 1-152, iii-iv.
62. White, M.C., *Anaesthetic implications of congenital heart disease for children undergoing non-cardiac surgery*. Anaesthesia & Intensive Care Medicine, 2009. **10**(10): p. 504-509.
63. Connelly, M.S., et al., *Canadian Consensus Conference on Adult Congenital Heart Disease 1996*. Can J Cardiol, 1998. **14**(3): p. 395-452.
64. Lindinger, A., G. Schwedler, and H.W. Hense, *Prevalence of congenital heart defects in newborns in Germany: Results of the first registration year of the PAN Study (July 2006 to June 2007)*. Klin Padiatr, 2010. **222**(5): p. 321-6.
65. Marino, B. and M.C. Digilio, *Congenital heart disease and genetic syndromes: specific correlation between cardiac phenotype and genotype*. Cardiovasc Pathol, 2000. **9**(6): p. 303-15.
66. Clark, E.B., *Pathogenetic mechanisms of congenital cardiovascular malformations revisited*. Semin Perinatol, 1996. **20**(6): p. 465-72.
67. (NCS), N.C.S. *OPCS-4 Classification*. 2011; Available from: <http://www.connectingforhealth.nhs.uk/systemsandservices/data/clinicalcoding/codingstandards/opcs4/>.
68. Coding Committee of the Association for European Paediatric, C., *The European Paediatric Cardiac Code: the first revision*. Cardiol Young, 2002. **12 Suppl 2**: p. 1-211.
69. Vincent, S.D. and M.E. Buckingham, *How to make a heart: the origin and regulation of cardiac progenitor cells*. Curr Top Dev Biol, 2010. **90**: p. 1-41.
70. Epstein, J.A., *Franklin H. Epstein Lecture. Cardiac development and implications for heart disease*. N Engl J Med, 2010. **363**(17): p. 1638-47.
71. Yamagishi, H., et al., *Molecular embryology for an understanding of congenital heart diseases*. Anat Sci Int, 2009. **84**(3): p. 88-94.
72. Kelly, R.G., N.A. Brown, and M.E. Buckingham, *The arterial pole of the mouse heart forms from Fgf10-expressing cells in pharyngeal mesoderm*. Dev Cell, 2001. **1**(3): p. 435-40.
73. Buckingham, M., S. Meilhac, and S. Zaffran, *Building the mammalian heart from two sources of myocardial cells*. Nat Rev Genet, 2005. **6**(11): p. 826-35.
74. Srivastava, D. and E.N. Olson, *A genetic blueprint for cardiac development*. Nature, 2000. **407**(6801): p. 221-6.
75. Srivastava, D., *Making or breaking the heart: from lineage determination to morphogenesis*. Cell, 2006. **126**(6): p. 1037-48.
76. Hutson, M.R. and M.L. Kirby, *Model systems for the study of heart development and disease. Cardiac neural crest and conotruncal malformations*. Semin Cell Dev Biol, 2007. **18**(1): p. 101-10.

77. Waldo, K.L., et al., *Cardiac neural crest is necessary for normal addition of the myocardium to the arterial pole from the secondary heart field*. Dev Biol, 2005. **281**(1): p. 66-77.
78. Ward, C., et al., *Ablation of the secondary heart field leads to tetralogy of Fallot and pulmonary atresia*. Dev Biol, 2005. **284**(1): p. 72-83.
79. Mikawa, T. and R.G. Gourdie, *Pericardial mesoderm generates a population of coronary smooth muscle cells migrating into the heart along with ingrowth of the epicardial organ*. Dev Biol, 1996. **174**(2): p. 221-32.
80. Oostra, R.-J., G. Steding, and S. Virágh, *Steding's and Virágh's scanning electron microscopy atlas of the developing human heart*. 2007, New York: Springer. x, 211p.
81. Arraez-Aybar, L.A., A. Turrero-Nogues, and D.G. Marantos-Gamarra, *Embryonic cardiac morphometry in Carnegie stages 15-23, from the Complutense University of Madrid Institute of Embryology Human Embryo Collection*. Cells Tissues Organs, 2008. **187**(3): p. 211-20.
82. Sylva, M., M.J. van den Hoff, and A.F. Moorman, *Development of the Human Heart*. Am J Med Genet A, 2013: p. 0.
83. O'Rahilly, R., F. Müller, and G.L. Streeter, *Developmental stages in human embryos : including a revision of Streeter's "Horizons" and a survey of the Carnegie collection*. Publication / Carnegie Institution of Washington. 1987, Washington, D.C.: Carnegie Institution of Washington. 306 p., 1 leaf of plates.
84. Sommer, R.J., Z.M. Hijazi, and J.F. Rhodes, Jr., *Pathophysiology of congenital heart disease in the adult: part I: Shunt lesions*. Circulation, 2008. **117**(8): p. 1090-9.
85. Meissner, I., et al., *Patent foramen ovale: innocent or guilty? Evidence from a prospective population-based study*. J Am Coll Cardiol, 2006. **47**(2): p. 440-5.
86. Marie Valente, A. and J.F. Rhodes, *Current indications and contraindications for transcatheter atrial septal defect and patent foramen ovale device closure*. Am Heart J, 2007. **153**(4 Suppl): p. 81-4.
87. Heiden, K., *Congenital Heart Defects, Simplified* 2009: Midwest EchoSolutions.
88. Freed, M.D., et al., *Prostaglandin E1 infants with ductus arteriosus-dependent congenital heart disease*. Circulation, 1981. **64**(5): p. 899-905.
89. Audrey Marshall, M., *Hypoplastic left heart syndrome*. UpToDate.com, ed. D. Marion. 2013, Waltham, MA.
90. Jenkins, K.J., et al., *Noninherited risk factors and congenital cardiovascular defects: current knowledge: a scientific statement from the American Heart Association Council on Cardiovascular Disease in the Young: endorsed by the American Academy of Pediatrics*. Circulation, 2007. **115**(23): p. 2995-3014.
91. Wren, C., G. Birrell, and G. Hawthorne, *Cardiovascular malformations in infants of diabetic mothers*. Heart, 2003. **89**(10): p. 1217-20.
92. Cousins, L., *Etiology and prevention of congenital anomalies among infants of overt diabetic women*. Clin Obstet Gynecol, 1991. **34**(3): p. 481-93.
93. Levy, H.L., et al., *Congenital heart disease in maternal phenylketonuria: report from the Maternal PKU Collaborative Study*. Pediatr Res, 2001. **49**(5): p. 636-42.

94. Lenke, R.R. and H.L. Levy, *Maternal phenylketonuria and hyperphenylalaninemia. An international survey of the outcome of untreated and treated pregnancies.* N Engl J Med, 1980. **303**(21): p. 1202-8.
95. Botto, L.D., M.C. Lynberg, and J.D. Erickson, *Congenital heart defects, maternal febrile illness, and multivitamin use: a population-based study.* Epidemiology, 2001. **12**(5): p. 485-90.
96. Scanlon, K.S., et al., *Preconceptional folate intake and malformations of the cardiac outflow tract.* Baltimore-Washington Infant Study Group. Epidemiology, 1998. **9**(1): p. 95-8.
97. Stuckey, D., *Congenital heart defects following maternal rubella during pregnancy.* Br Heart J, 1956. **18**(4): p. 519-22.
98. Kelly, T.E., et al., *Teratogenicity of anticonvulsant drugs. II: A prospective study.* Am J Med Genet, 1984. **19**(3): p. 435-43.
99. Wilson, P.D., et al., *Attributable fraction for cardiac malformations.* Am J Epidemiol, 1998. **148**(5): p. 414-23.
100. Geiger, J.M., M. Baudin, and J.H. Saurat, *Teratogenic risk with etretinate and acitretin treatment.* Dermatology, 1994. **189**(2): p. 109-16.
101. Pierpont, M.E., et al., *Genetic basis for congenital heart defects: current knowledge: a scientific statement from the American Heart Association Congenital Cardiac Defects Committee, Council on Cardiovascular Disease in the Young: endorsed by the American Academy of Pediatrics.* Circulation, 2007. **115**(23): p. 3015-38.
102. Roos-Hesselink JW, K.-F.W., Meijboom FJ, Pieper PG., *Inheritance of congenital heart disease.* Neth Heart J 2005. **13:** 88-91.
103. Merscher, S., et al., *TBX1 is responsible for cardiovascular defects in velo-cardio-facial/DiGeorge syndrome.* Cell, 2001. **104**(4): p. 619-29.
104. Lange, A.W., J.D. Molkentin, and K.E. Yutzey, *DSCR1 gene expression is dependent on NFATc1 during cardiac valve formation and colocalizes with anomalous organ development in trisomy 16 mice.* Dev Biol, 2004. **266**(2): p. 346-60.
105. Arron, J.R., et al., *NFAT dysregulation by increased dosage of DSCR1 and DYRK1A on chromosome 21.* Nature, 2006. **441**(7093): p. 595-600.
106. Subramaniam, P., et al., *Diagnosis of Alagille syndrome-25 years of experience at King's College Hospital.* J Pediatr Gastroenterol Nutr, 2011. **52**(1): p. 84-9.
107. Warthen, D.M., et al., *Jagged1 (JAG1) mutations in Alagille syndrome: increasing the mutation detection rate.* Hum Mutat, 2006. **27**(5): p. 436-43.
108. Krantz, I.D., et al., *Deletions of 20p12 in Alagille syndrome: frequency and molecular characterization.* Am J Med Genet, 1997. **70**(1): p. 80-6.
109. Schott, J.J., et al., *Congenital heart disease caused by mutations in the transcription factor NKX2-5.* Science, 1998. **281**(5373): p. 108-11.
110. Garg, V., et al., *GATA4 mutations cause human congenital heart defects and reveal an interaction with TBX5.* Nature, 2003. **424**(6947): p. 443-7.
111. Wessels, M.W. and P.J. Willems, *Genetic factors in non-syndromic congenital heart malformations.* Clin Genet, 2010. **78**(2): p. 103-23.

112. Cordell, H.J., et al., *Genome-wide association study of multiple congenital heart disease phenotypes identifies a susceptibility locus for atrial septal defect at chromosome 4p16*. Nat Genet, 2013. **45**(7): p. 822-4.
113. Goodship, J.A., et al., *A common variant in the PTPN11 gene contributes to the risk of tetralogy of Fallot*. Circ Cardiovasc Genet, 2012. **5**(3): p. 287-92.
114. Hindorff, L.A., et al., *Potential etiologic and functional implications of genome-wide association loci for human diseases and traits*. Proc Natl Acad Sci U S A, 2009. **106**(23): p. 9362-7.
115. Hu, Z., et al., *A genome-wide association study identifies two risk loci for congenital heart malformations in Han Chinese populations*. Nat Genet, 2013. **45**(7): p. 818-21.
116. Reamon-Buettner, S.M. and J. Borlak, *Somatic NKX2-5 mutations as a novel mechanism of disease in complex congenital heart disease*. J Med Genet, 2004. **41**(9): p. 684-90.
117. Reamon-Buettner, S.M. and J. Borlak, *TBX5 mutations in non-Holt-Oram syndrome (HOS) malformed hearts*. Hum Mutat, 2004. **24**(1): p. 104.
118. Draus, J.M., Jr., et al., *Investigation of somatic NKX2-5 mutations in congenital heart disease*. J Med Genet, 2009. **46**(2): p. 115-22.
119. Cordes, K.R. and D. Srivastava, *MicroRNA regulation of cardiovascular development*. Circ Res, 2009. **104**(6): p. 724-32.
120. Liu, N. and E.N. Olson, *MicroRNA regulatory networks in cardiovascular development*. Dev Cell, 2010. **18**(4): p. 510-25.
121. Zhu, S., et al., *Identification of maternal serum microRNAs as novel non-invasive biomarkers for prenatal detection of fetal congenital heart defects*. Clin Chim Acta, 2013. **424C**: p. 66-72.
122. Soemedi, R., et al., *Contribution of global rare copy-number variants to the risk of sporadic congenital heart disease*. Am J Hum Genet, 2012. **91**(3): p. 489-501.
123. Zaidi, S., et al., *De novo mutations in histone-modifying genes in congenital heart disease*. Nature, 2013. **498**(7453): p. 220-3.
124. Bentham, J. and S. Bhattacharya, *Genetic mechanisms controlling cardiovascular development*. Ann N Y Acad Sci, 2008. **1123**: p. 10-9.
125. Hutchison, C.A., 3rd, *DNA sequencing: bench to bedside and beyond*. Nucleic Acids Res, 2007. **35**(18): p. 6227-37.
126. International Human Genome Sequencing, C., *Finishing the euchromatic sequence of the human genome*. Nature, 2004. **431**(7011): p. 931-45.
127. Margulies, M., et al., *Genome sequencing in microfabricated high-density picolitre reactors*. Nature, 2005. **437**(7057): p. 376-80.
128. Shendure, J., et al., *Accurate multiplex polony sequencing of an evolved bacterial genome*. Science, 2005. **309**(5741): p. 1728-32.
129. Schuster, S.C., *Next-generation sequencing transforms today's biology*. Nat Methods, 2008. **5**(1): p. 16-8.
130. Blazej, R.G., P. Kumaresan, and R.A. Mathies, *Microfabricated bioprocessor for integrated nanoliter-scale Sanger DNA sequencing*. Proc Natl Acad Sci U S A, 2006. **103**(19): p. 7240-5.
131. Gresham, D., M.J. Dunham, and D. Botstein, *Comparing whole genomes using DNA microarrays*. Nat Rev Genet, 2008. **9**(4): p. 291-302.
132. Healy, K., *Nanopore-based single-molecule DNA analysis*. Nanomedicine (Lond), 2007. **2**(4): p. 459-81.

133. Soni, G.V. and A. Meller, *Progress toward ultrafast DNA sequencing using solid-state nanopores*. Clin Chem, 2007. **53**(11): p. 1996-2001.
134. Mitra, R.D. and G.M. Church, *In situ localized amplification and contact replication of many individual DNA molecules*. Nucleic Acids Res, 1999. **27**(24): p. e34.
135. Metzker, M.L., *Sequencing technologies - the next generation*. Nat Rev Genet, 2010. **11**(1): p. 31-46.
136. Shendure, J. and H. Ji, *Next-generation DNA sequencing*. Nat Biotechnol, 2008. **26**(10): p. 1135-45.
137. Pabinger, S., et al., *A survey of tools for variant analysis of next-generation genome sequencing data*. Brief Bioinform, 2013.
138. Knierim, E., et al., *Systematic comparison of three methods for fragmentation of long-range PCR products for next generation sequencing*. PLoS One, 2011. **6**(11): p. e28240.
139. Glenn, T.C., *Field guide to next-generation DNA sequencers*. Mol Ecol Resour, 2011. **11**(5): p. 759-69.
140. Quail, M.A., et al., *A tale of three next generation sequencing platforms: comparison of Ion Torrent, Pacific Biosciences and Illumina MiSeq sequencers*. BMC Genomics, 2012. **13**: p. 341.
141. Glenn, T. *2013 NGS Field Guide*. 2013; Available from: <http://www.molecularecologist.com/next-gen-fieldguide-2013/>.
142. Cock, P.J., et al., *The Sanger FASTQ file format for sequences with quality scores, and the Solexa/Illumina FASTQ variants*. Nucleic Acids Res, 2010. **38**(6): p. 1767-71.
143. Nielsen, R., et al., *Genotype and SNP calling from next-generation sequencing data*. Nat Rev Genet, 2011. **12**(6): p. 443-51.
144. Dai, M., et al., *NGSQC: cross-platform quality analysis pipeline for deep sequencing data*. BMC Genomics, 2010. **11 Suppl 4**: p. S7.
145. Li, H. and N. Homer, *A survey of sequence alignment algorithms for next-generation sequencing*. Brief Bioinform, 2010. **11**(5): p. 473-83.
146. Ruffalo, M., T. LaFramboise, and M. Koyuturk, *Comparative analysis of algorithms for next-generation sequencing read alignment*. Bioinformatics, 2011. **27**(20): p. 2790-6.
147. Kent, W.J., *BLAT--the BLAST-like alignment tool*. Genome Res, 2002. **12**(4): p. 656-64.
148. Ning, Z., A.J. Cox, and J.C. Mullikin, *SSAHA: a fast search method for large DNA databases*. Genome Res, 2001. **11**(10): p. 1725-9.
149. Li, H. and R. Durbin, *Fast and accurate short read alignment with Burrows-Wheeler transform*. Bioinformatics, 2009. **25**(14): p. 1754-60.
150. Langmead, B., et al., *Ultrafast and memory-efficient alignment of short DNA sequences to the human genome*. Genome Biol, 2009. **10**(3): p. R25.
151. Malhis, N., et al., *Slider--maximum use of probability information for alignment of short sequence reads and SNP detection*. Bioinformatics, 2009. **25**(1): p. 6-13.
152. Li, H., et al., *The Sequence Alignment/Map format and SAMtools*. Bioinformatics, 2009. **25**(16): p. 2078-9.
153. McKenna, A., et al., *The Genome Analysis Toolkit: a MapReduce framework for analyzing next-generation DNA sequencing data*. Genome Res, 2010. **20**(9): p. 1297-303.

154. DePristo, M.A., et al., *A framework for variation discovery and genotyping using next-generation DNA sequencing data*. Nat Genet, 2011. **43**(5): p. 491-8.
155. Genomes Project, C., et al., *An integrated map of genetic variation from 1,092 human genomes*. Nature, 2012. **491**(7422): p. 56-65.
156. Kim, S.Y. and T.P. Speed, *Comparing somatic mutation-callers: beyond Venn diagrams*. BMC Bioinformatics, 2013. **14**: p. 189.
157. Duan, J., et al., *Comparative studies of copy number variation detection methods for next-generation sequencing technologies*. PLoS One, 2013. **8**(3): p. e59128.
158. Albers, C.A., et al., *Dindel: accurate indel calls from short-read data*. Genome Res, 2011. **21**(6): p. 961-73.
159. Ye, K., et al., *Pindel: a pattern growth approach to detect break points of large deletions and medium sized insertions from paired-end short reads*. Bioinformatics, 2009. **25**(21): p. 2865-71.
160. Neuman, J.A., O. Isakov, and N. Shomron, *Analysis of insertion-deletion from deep-sequencing data: software evaluation for optimal detection*. Brief Bioinform, 2013. **14**(1): p. 46-55.
161. Danecek, P., et al., *The variant call format and VCFtools*. Bioinformatics, 2011. **27**(15): p. 2156-8.
162. Li, H., *Tabix: fast retrieval of sequence features from generic TAB-delimited files*. Bioinformatics, 2011. **27**(5): p. 718-9.
163. Tennessen, J.A., et al., *Evolution and functional impact of rare coding variation from deep sequencing of human exomes*. Science, 2012. **337**(6090): p. 64-9.
164. Davydov, E.V., et al., *Identifying a high fraction of the human genome to be under selective constraint using GERP++*. PLoS Comput Biol, 2010. **6**(12): p. e1001025.
165. Cooper, G.M., et al., *Distribution and intensity of constraint in mammalian genomic sequence*. Genome Res, 2005. **15**(7): p. 901-13.
166. Siepel, A., et al., *Evolutionarily conserved elements in vertebrate, insect, worm, and yeast genomes*. Genome Res, 2005. **15**(8): p. 1034-50.
167. Pollard, K.S., et al., *Detection of nonneutral substitution rates on mammalian phylogenies*. Genome Res, 2010. **20**(1): p. 110-21.
168. Stenson, P.D., et al., *The Human Gene Mutation Database (HGMD) and its exploitation in the fields of personalized genomics and molecular evolution*. Curr Protoc Bioinformatics, 2012. **Chapter 1**: p. Unit1 13.
169. Cingolani, P., et al., *A program for annotating and predicting the effects of single nucleotide polymorphisms, SnpEff: SNPs in the genome of Drosophila melanogaster strain w1118; iso-2; iso-3*. Fly (Austin), 2012. **6**(2): p. 80-92.
170. McLaren, W., et al., *Deriving the consequences of genomic variants with the Ensembl API and SNP Effect Predictor*. Bioinformatics, 2010. **26**(16): p. 2069-70.
171. Adzhubei, I.A., et al., *A method and server for predicting damaging missense mutations*. Nat Methods, 2010. **7**(4): p. 248-9.
172. Kumar, P., S. Henikoff, and P.C. Ng, *Predicting the effects of coding non-synonymous variants on protein function using the SIFT algorithm*. Nat Protoc, 2009. **4**(7): p. 1073-81.

173. Gonzalez-Perez, A. and N. Lopez-Bigas, *Improving the assessment of the outcome of nonsynonymous SNVs with a consensus deleteriousness score*, *Condel. Am J Hum Genet*, 2011. **88**(4): p. 440-9.
174. Ng, S.B., et al., *Exome sequencing identifies the cause of a mendelian disorder*. *Nat Genet*, 2010. **42**(1): p. 30-5.
175. Dewey, F.E., et al., *DNA sequencing: clinical applications of new DNA sequencing technologies*. *Circulation*, 2012. **125**(7): p. 931-44.
176. Johnson, J.O., et al., *Exome sequencing reveals VCP mutations as a cause of familial ALS*. *Neuron*, 2010. **68**(5): p. 857-64.
177. Bonnefond, A., et al., *Molecular diagnosis of neonatal diabetes mellitus using next-generation sequencing of the whole exome*. *PLoS One*, 2010. **5**(10): p. e13630.
178. Ostergaard, P., et al., *Rapid identification of mutations in GJC2 in primary lymphoedema using whole exome sequencing combined with linkage analysis with delineation of the phenotype*. *J Med Genet*, 2011. **48**(4): p. 251-5.
179. Wang, J.L., et al., *TGM6 identified as a novel causative gene of spinocerebellar ataxias using exome sequencing*. *Brain*, 2010. **133**(Pt 12): p. 3510-8.
180. Sirmaci, A., et al., *MASP1 mutations in patients with facial, umbilical, coccygeal, and auditory findings of Carnevale, Malpuech, OSA, and Michels syndromes*. *Am J Hum Genet*, 2010. **87**(5): p. 679-86.
181. Montenegro, G., et al., *Exome sequencing allows for rapid gene identification in a Charcot-Marie-Tooth family*. *Ann Neurol*, 2011. **69**(3): p. 464-70.
182. Choi, M., et al., *Genetic diagnosis by whole exome capture and massively parallel DNA sequencing*. *Proc Natl Acad Sci U S A*, 2009. **106**(45): p. 19096-101.
183. Bolze, A., et al., *Whole-exome-sequencing-based discovery of human FADD deficiency*. *Am J Hum Genet*, 2010. **87**(6): p. 873-81.
184. Musunuru, K., et al., *Exome sequencing, ANGPTL3 mutations, and familial combined hypolipidemia*. *N Engl J Med*, 2010. **363**(23): p. 2220-7.
185. Lalonde, E., et al., *Unexpected allelic heterogeneity and spectrum of mutations in Fowler syndrome revealed by next-generation exome sequencing*. *Hum Mutat*, 2010. **31**(8): p. 918-23.
186. Edvardson, S., et al., *Joubert syndrome 2 (JBTS2) in Ashkenazi Jews is associated with a TMEM216 mutation*. *Am J Hum Genet*, 2010. **86**(1): p. 93-7.
187. Caliskan, M., et al., *Exome sequencing reveals a novel mutation for autosomal recessive non-syndromic mental retardation in the TECR gene on chromosome 19p13*. *Hum Mol Genet*, 2011. **20**(7): p. 1285-9.
188. Walsh, T., et al., *Whole exome sequencing and homozygosity mapping identify mutation in the cell polarity protein GPSM2 as the cause of nonsyndromic hearing loss DFNB82*. *Am J Hum Genet*, 2010. **87**(1): p. 90-4.
189. Kalay, E., et al., *CEP152 is a genome maintenance protein disrupted in Seckel syndrome*. *Nat Genet*, 2011. **43**(1): p. 23-6.
190. Vissers, L.E., et al., *A de novo paradigm for mental retardation*. *Nat Genet*, 2010. **42**(12): p. 1109-12.

191. Hoischen, A., et al., *De novo mutations of SETBP1 cause Schinzel-Giedion syndrome*. Nat Genet, 2010. **42**(6): p. 483-5.
192. Worthey, E.A., et al., *Making a definitive diagnosis: successful clinical application of whole exome sequencing in a child with intractable inflammatory bowel disease*. Genet Med, 2011. **13**(3): p. 255-62.
193. Sobreira, N.L., et al., *Whole-genome sequencing of a single proband together with linkage analysis identifies a Mendelian disease gene*. PLoS Genet, 2010. **6**(6): p. e1000991.
194. Lupski, J.R., et al., *Whole-genome sequencing in a patient with Charcot-Marie-Tooth neuropathy*. N Engl J Med, 2010. **362**(13): p. 1181-91.
195. Roach, J.C., et al., *Analysis of genetic inheritance in a family quartet by whole-genome sequencing*. Science, 2010. **328**(5978): p. 636-9.
196. Rios, J., et al., *Identification by whole-genome resequencing of gene defect responsible for severe hypercholesterolemia*. Hum Mol Genet, 2010. **19**(22): p. 4313-8.
197. Genomes Project, C., et al., *A map of human genome variation from population-scale sequencing*. Nature, 2010. **467**(7319): p. 1061-73.
198. Durbin, R.M., et al., *A map of human genome variation from population-scale sequencing*. Nature, 2010. **467**(7319): p. 1061-73.
199. Fu, W., et al., *Analysis of 6,515 exomes reveals the recent origin of most human protein-coding variants*. Nature, 2013. **493**(7431): p. 216-20.
200. International HapMap, C., et al., *Integrating common and rare genetic variation in diverse human populations*. Nature, 2010. **467**(7311): p. 52-8.
201. Sherry, S.T., et al., *dbSNP: the NCBI database of genetic variation*. Nucleic Acids Res, 2001. **29**(1): p. 308-11.
202. Boycott, K.M., et al., *Rare-disease genetics in the era of next-generation sequencing: discovery to translation*. Nat Rev Genet, 2013.
203. Schuurs-Hoeijmakers, J.H., et al., *Mutations in DDHD2, encoding an intracellular phospholipase A(1), cause a recessive form of complex hereditary spastic paraparesis*. Am J Hum Genet, 2012. **91**(6): p. 1073-81.
204. Kalsoom, U.E., et al., *Whole exome sequencing identified a novel zinc-finger gene ZNF141 associated with autosomal recessive postaxial polydactyly type A*. J Med Genet, 2013. **50**(1): p. 47-53.
205. Sankaran, V.G., et al., *Exome sequencing identifies GATA1 mutations resulting in Diamond-Blackfan anemia*. J Clin Invest, 2012. **122**(7): p. 2439-43.
206. Fiskerstrand, T., et al., *Familial diarrhea syndrome caused by an activating GUCY2C mutation*. N Engl J Med, 2012. **366**(17): p. 1586-95.
207. Gibson, W.T., et al., *Mutations in EZH2 cause Weaver syndrome*. Am J Hum Genet, 2012. **90**(1): p. 110-8.
208. Boyd, S.D., *Diagnostic applications of high-throughput DNA sequencing*. Annu Rev Pathol, 2013. **8**: p. 381-410.
209. Pleasance, E.D., et al., *A comprehensive catalogue of somatic mutations from a human cancer genome*. Nature, 2010. **463**(7278): p. 191-6.
210. Campbell, P.J., et al., *Identification of somatically acquired rearrangements in cancer using genome-wide massively parallel paired-end sequencing*. Nat Genet, 2008. **40**(6): p. 722-9.
211. Pleasance, E.D., et al., *A small-cell lung cancer genome with complex signatures of tobacco exposure*. Nature, 2010. **463**(7278): p. 184-90.

212. Stephens, P.J., et al., *Complex landscapes of somatic rearrangement in human breast cancer genomes*. Nature, 2009. **462**(7276): p. 1005-10.
213. Ley, T.J., et al., *DNMT3A mutations in acute myeloid leukemia*. N Engl J Med, 2010. **363**(25): p. 2424-33.
214. Logan, A.C., et al., *High-throughput VDJ sequencing for quantification of minimal residual disease in chronic lymphocytic leukemia and immune reconstitution assessment*. Proc Natl Acad Sci U S A, 2011. **108**(52): p. 21194-9.
215. Boyd, S.D., et al., *Measurement and clinical monitoring of human lymphocyte clonality by massively parallel VDJ pyrosequencing*. Sci Transl Med, 2009. **1**(12): p. 12ra23.
216. Cohorts for, H., et al., *Whole-genome sequence-based analysis of high-density lipoprotein cholesterol*. Nat Genet, 2013. **45**(8): p. 899-901.
217. Chin, C.S., et al., *The origin of the Haitian cholera outbreak strain*. N Engl J Med, 2011. **364**(1): p. 33-42.
218. Rasko, D.A., et al., *Origins of the E. coli strain causing an outbreak of hemolytic-uremic syndrome in Germany*. N Engl J Med, 2011. **365**(8): p. 709-17.
219. Assiri, A., et al., *Hospital Outbreak of Middle East Respiratory Syndrome Coronavirus*. N Engl J Med, 2013.
220. Snyder, T.M., et al., *Universal noninvasive detection of solid organ transplant rejection*. Proc Natl Acad Sci U S A, 2011. **108**(15): p. 6229-34.
221. Fan, H.C., et al., *Noninvasive diagnosis of fetal aneuploidy by shotgun sequencing DNA from maternal blood*. Proc Natl Acad Sci U S A, 2008. **105**(42): p. 16266-71.
222. Chiu, R.W., et al., *Non-invasive prenatal assessment of trisomy 21 by multiplexed maternal plasma DNA sequencing: large scale validity study*. BMJ, 2011. **342**: p. c7401.
223. Bornman, D.M., et al., *Short-read, high-throughput sequencing technology for STR genotyping*. Biotechniques, 2012. **0**(0): p. 1-6.
224. Warshauer, D.H., et al., *STRait Razor: A length-based forensic STR allele-calling tool for use with second generation sequencing data*. Forensic Sci Int Genet, 2013. **7**(4): p. 409-17.
225. Consortium, E.P., et al., *An integrated encyclopedia of DNA elements in the human genome*. Nature, 2012. **489**(7414): p. 57-74.
226. Soon, W.W., M. Hariharan, and M.P. Snyder, *High-throughput sequencing for biology and medicine*. Mol Syst Biol, 2013. **9**: p. 640.
227. Waern, K., U. Nagalakshmi, and M. Snyder, *RNA sequencing*. Methods Mol Biol, 2011. **759**: p. 125-32.
228. Kodzius, R., et al., *CAGE: cap analysis of gene expression*. Nat Methods, 2006. **3**(3): p. 211-22.
229. Fullwood, M.J., et al., *Next-generation DNA sequencing of paired-end tags (PET) for transcriptome and genome analyses*. Genome Res, 2009. **19**(4): p. 521-32.
230. Chu, C., et al., *Genomic maps of long noncoding RNA occupancy reveal principles of RNA-chromatin interactions*. Mol Cell, 2011. **44**(4): p. 667-78.
231. Core, L.J., J.J. Waterfall, and J.T. Lis, *Nascent RNA sequencing reveals widespread pausing and divergent initiation at human promoters*. Science, 2008. **322**(5909): p. 1845-8.

232. Churchman, L.S. and J.S. Weissman, *Nascent transcript sequencing visualizes transcription at nucleotide resolution*. Nature, 2011. **469**(7330): p. 368-73.
233. Ingolia, N.T., et al., *Genome-wide analysis in vivo of translation with nucleotide resolution using ribosome profiling*. Science, 2009. **324**(5924): p. 218-23.
234. Robertson, G., et al., *Genome-wide profiles of STAT1 DNA association using chromatin immunoprecipitation and massively parallel sequencing*. Nat Methods, 2007. **4**(8): p. 651-7.
235. Hesselberth, J.R., et al., *Global mapping of protein-DNA interactions in vivo by digital genomic footprinting*. Nat Methods, 2009. **6**(4): p. 283-9.
236. Crawford, G.E., et al., *Genome-wide mapping of DNase hypersensitive sites using massively parallel signature sequencing (MPSS)*. Genome Res, 2006. **16**(1): p. 123-31.
237. Giresi, P.G., et al., *FAIRE (Formaldehyde-Assisted Isolation of Regulatory Elements) isolates active regulatory elements from human chromatin*. Genome Res, 2007. **17**(6): p. 877-85.
238. Wang, Z., et al., *Genome-wide mapping of HATs and HDACs reveals distinct functions in active and inactive genes*. Cell, 2009. **138**(5): p. 1019-31.
239. Smith, Z.D., et al., *High-throughput bisulfite sequencing in mammalian genomes*. Methods, 2009. **48**(3): p. 226-32.
240. Dostie, J., et al., *Chromosome Conformation Capture Carbon Copy (5C): a massively parallel solution for mapping interactions between genomic elements*. Genome Res, 2006. **16**(10): p. 1299-309.
241. Fullwood, M.J., et al., *An oestrogen-receptor-alpha-bound human chromatin interactome*. Nature, 2009. **462**(7269): p. 58-64.
242. Stein, L.D., *The case for cloud computing in genome informatics*. Genome Biol, 2010. **11**(5): p. 207.
243. Lin, Z., A.B. Owen, and R.B. Altman, *Genetics. Genomic research and human subject privacy*. Science, 2004. **305**(5681): p. 183.
244. Homer, N., et al., *Resolving individuals contributing trace amounts of DNA to highly complex mixtures using high-density SNP genotyping microarrays*. PLoS Genet, 2008. **4**(8): p. e1000167.
245. Greenbaum, D., et al., *Genomics and privacy: implications of the new reality of closed data for the field*. PLoS Comput Biol, 2011. **7**(12): p. e1002278.
246. Rehm, H.L., *Disease-targeted sequencing: a cornerstone in the clinic*. Nat Rev Genet, 2013. **14**(4): p. 295-300.
247. Green, R.C., et al., *Exploring concordance and discordance for return of incidental findings from clinical sequencing*. Genet Med, 2012. **14**(4): p. 405-10.
248. Makrythanasis, P. and S.E. Antonarakis, *High-throughput sequencing and rare genetic diseases*. Mol Syndromol, 2012. **3**(5): p. 197-203.
249. Stevenson, D.A. and J.C. Carey, *Contribution of malformations and genetic disorders to mortality in a children's hospital*. Am J Med Genet A, 2004. **126A**(4): p. 393-7.
250. Yoon, P.W., et al., *Contribution of birth defects and genetic diseases to pediatric hospitalizations. A population-based study*. Arch Pediatr Adolesc Med, 1997. **151**(11): p. 1096-103.

251. Kumar, P., et al., *Prevalence and patterns of presentation of genetic disorders in a pediatric emergency department*. Mayo Clin Proc, 2001. **76**(8): p. 777-83.
252. Barroso, I., et al., *Dominant negative mutations in human PPARgamma associated with severe insulin resistance, diabetes mellitus and hypertension*. Nature, 1999. **402**(6764): p. 880-3.
253. Amberger, J., et al., *McKusick's Online Mendelian Inheritance in Man (OMIM)*. Nucleic Acids Res, 2009. **37**(Database issue): p. D793-6.
254. Rabbani, B., et al., *Next-generation sequencing: impact of exome sequencing in characterizing Mendelian disorders*. J Hum Genet, 2012. **57**(10): p. 621-32.
255. Kaasinen, E., et al., *Recessively inherited right atrial isomerism caused by mutations in growth/differentiation factor 1 (GDF1)*. Hum Mol Genet, 2010. **19**(14): p. 2747-53.
256. Zaidi, S., et al., *De novo mutations in histone-modifying genes in congenital heart disease*. Nature, 2013.
257. Cordell, H.J., et al., *Genome-wide association study identifies loci on 12q24 and 13q32 associated with Tetralogy of Fallot*. Hum Mol Genet, 2013.
258. Olander, E., et al., *Third Prader-Willi syndrome phenotype due to maternal uniparental disomy 15 with mosaic trisomy 15*. Am J Med Genet, 2000. **93**(3): p. 215-8.
259. Wang, W., et al., *MTHFR C677T polymorphism and risk of congenital heart defects: evidence from 29 case-control and TDT studies*. PLoS One, 2013. **8**(3): p. e58041.
260. Firth, H.V., C.F. Wright, and D.D.D. Study, *The Deciphering Developmental Disorders (DDD) study*. Dev Med Child Neurol, 2011. **53**(8): p. 702-3.
261. Ge, D., et al., *SVA: software for annotating and visualizing sequenced human genomes*. Bioinformatics, 2011. **27**(14): p. 1998-2000.
262. Coutant, S., et al., *EVA: Exome Variation Analyzer, an efficient and versatile tool for filtering strategies in medical genomics*. BMC Bioinformatics, 2012. **13 Suppl 14**: p. S9.
263. Teer, J.K., et al., *VarSifter: visualizing and analyzing exome-scale sequence variation data on a desktop computer*. Bioinformatics, 2012. **28**(4): p. 599-600.
264. UK10K. *UK10K*. 2013; Available from: <http://www.uk10k.org>.
265. Conrad, D.F., et al., *Variation in genome-wide mutation rates within and between human families*. Nat Genet, 2011. **43**(7): p. 712-4.
266. Ramu, A., et al., *DeNovoGear: de novo indel and point mutation discovery and phasing*. Nat Methods, 2013.
267. Sanders, S.J., et al., *De novo mutations revealed by whole-exome sequencing are strongly associated with autism*. Nature, 2012. **485**(7397): p. 237-41.
268. O'Roak, B.J., et al., *Sporadic autism exomes reveal a highly interconnected protein network of de novo mutations*. Nature, 2012. **485**(7397): p. 246-50.
269. Iossifov, I., et al., *De novo gene disruptions in children on the autistic spectrum*. Neuron, 2012. **74**(2): p. 285-99.
270. Neale, B.M., et al., *Patterns and rates of exonic de novo mutations in autism spectrum disorders*. Nature, 2012. **485**(7397): p. 242-5.

271. Rauch, A., et al., *Range of genetic mutations associated with severe non-syndromic sporadic intellectual disability: an exome sequencing study.* Lancet, 2012. **380**(9854): p. 1674-82.
272. Li, H., et al., *The Sequence Alignment/Map format and SAMtools.* Bioinformatics, 2009. **25**(16): p. 2078-9.
273. Huang, N., et al., *Characterising and predicting haploinsufficiency in the human genome.* PLoS Genet, 2010. **6**(10): p. e1001154.
274. Stenson, P.D., et al., *Human Gene Mutation Database (HGMD): 2003 update.* Hum Mutat, 2003. **21**(6): p. 577-81.
275. GATK Technical Documentation. 2013 GATK version 2.7-2-g701cd16 built at 2013/08/28 16:38:05.; Available from: http://www.broadinstitute.org/gatk/gatkdocs/org_broadinstitute_sting_gatk_walkers_annotation_QualByDepth.html.
276. Albers, C.A., et al., *Dindel: Accurate indel calls from short-read data.* Genome Res, 2010.
277. Ahn, S.J., J. Costa, and J.R. Emanuel, *PicoGreen quantitation of DNA: effective evaluation of samples pre- or post-PCR.* Nucleic Acids Res, 1996. **24**(13): p. 2623-5.
278. Frazer, K.A., et al., *Human genetic variation and its contribution to complex traits.* Nat Rev Genet, 2009. **10**(4): p. 241-51.
279. Dick, K.J., et al., *Refinement of the locus for distal hereditary motor neuronopathy VII (dHMN-VII) and exclusion of candidate genes.* Genome, 2008. **51**(11): p. 959-62.
280. McEntagart, M., et al., *Localization of the gene for distal hereditary motor neuronopathy VII (dHMN-VII) to chromosome 2q14.* Am J Hum Genet, 2001. **68**(5): p. 1270-6.
281. Barwick, K.E., et al., *Defective presynaptic choline transport underlies hereditary motor neuropathy.* Am J Hum Genet, 2012. **91**(6): p. 1103-7.
282. Baple, E.L., et al., *Mutations in KPTN Cause Macrocephaly, Neurodevelopmental Delay, and Seizures.* Am J Hum Genet, 2013.
283. Harlalka, G.V., et al., *Mutations in B4GALNT1 (GM2 synthase) underlie a new disorder of ganglioside biosynthesis.* Brain, 2013. **136**(Pt 12): p. 3618-24.
284. Asai, K., et al., *Isolation of novel human cDNA (hGMF-gamma) homologous to Glia Maturation Factor-beta gene.* Biochim Biophys Acta, 1998. **1396**(3): p. 242-4.
285. Ikeda, K., et al., *Glia maturation factor-gamma is preferentially expressed in microvascular endothelial and inflammatory cells and modulates actin cytoskeleton reorganization.* Circ Res, 2006. **99**(4): p. 424-33.
286. Walker, M.G., *Gene expression versus sequence for predicting function: Glia Maturation Factor gamma is not a glia maturation factor.* Genomics Proteomics Bioinformatics, 2003. **1**(1): p. 52-7.
287. Sleep, E., et al., *Transcriptomics approach to investigate zebrafish heart regeneration.* J Cardiovasc Med (Hagerstown), 2010. **11**(5): p. 369-80.
288. Eppig, J.T., et al., *The Mouse Genome Database (MGD): comprehensive resource for genetics and genomics of the laboratory mouse.* Nucleic Acids Res, 2012. **40**(Database issue): p. D881-6.

289. Merveille, A.C., et al., *CCDC39 is required for assembly of inner dynein arms and the dynein regulatory complex and for normal ciliary motility in humans and dogs*. Nat Genet, 2011. **43**(1): p. 72-8.
290. Olbrich, H., et al., *Recessive HYDIN mutations cause primary ciliary dyskinesia without randomization of left-right body asymmetry*. Am J Hum Genet, 2012. **91**(4): p. 672-84.
291. McInerney-Leo, A.M., et al., *Short-Rib Polydactyly and Jeune Syndromes Are Caused by Mutations in WDR60*. Am J Hum Genet, 2013.
292. Schmidts, M., et al., *Combined NGS approaches identify mutations in the intraflagellar transport gene IFT140 in skeletal ciliopathies with early progressive kidney Disease*. Hum Mutat, 2013. **34**(5): p. 714-24.
293. Fallot, E.L.A., *Contribution à l'anatomie pathologique de la maladie bleue* Marseille médical, 1888. **25: 77-93, 138-158, 207-223, 341-354, 370-386, 403-420**.
294. M. Cristina Digilio, B.D., Bruno Marino, *The right ventricle in adults with tetralogy of fallot*, ed. A.G. Massimo Chessa. 2012, New York: Springer.
295. Abbott ME, D.W., *The clinical classification of congenital heart disease, with remarks upon its pathological anatomy, diagnosis and treatment*. Int Clin, 1924. **4:156-188**.
296. Abbott, M.E., *Atlas of congenital cardiac disease*. 1936, New York, N.Y.: The American heart association. x, 62 p. incl. front. (5 port.) illus., diagrs.
297. Ferencz, C., Rubin, JD, Loffredo, CA, Magee, CM., *The Epidemiology of Congenital Heart Disease, The Baltimore-Washington Infant Study (1981-1989)*. Perspectives in Pediatric Cardiology. Vol. vol.4.. 1993: Futura Publishing Co.Inc.
298. Anderson RH, M.F., Shinebourne EA, *Fallot's Tetralogy*. In: *Paediatric Cardiology*, ed. T. M. 2002: London: Churchill Livingstone.
299. Jenkins, K.J., et al., *Noninherited risk factors and congenital cardiovascular defects: current knowledge: a scientific statement from the American Heart Association Council on Cardiovascular Disease in the Young: endorsed by the American Academy of Pediatrics*. Circulation, 2007. **115**(23): p. 2995-3014.
300. Correa-Villasenor, A., et al., *White-black differences in cardiovascular malformations in infancy and socioeconomic factors. The Baltimore-Washington Infant Study Group*. Am J Epidemiol, 1991. **134**(4): p. 393-402.
301. Digilio, M.C., et al., *Recurrence risk figures for isolated tetralogy of Fallot after screening for 22q11 microdeletion*. J Med Genet, 1997. **34**(3): p. 188-90.
302. Bailliard, F. and R.H. Anderson, *Tetralogy of Fallot*. Orphanet J Rare Dis, 2009. **4**: p. 2.
303. Hansen, J.T. and F.H. Netter, *Netter's clinical anatomy*. 2nd ed. 2010, Philadelphia: Saunders/Elsevier. xviii, 470 p.
304. Anderson, R.H. and P.M. Weinberg, *The clinical anatomy of tetralogy of fallot*. Cardiol Young, 2005. **15 Suppl 1**: p. 38-47.
305. Jiang, X., et al., *Fate of the mammalian cardiac neural crest*. Development, 2000. **127**(8): p. 1607-16.

306. Anderson, R.H., et al., *Development of the heart: (3) formation of the ventricular outflow tracts, arterial valves, and intrapericardial arterial trunks*. Heart, 2003. **89**(9): p. 1110-8.
307. Lin, C.J., et al., *Partitioning the heart: mechanisms of cardiac septation and valve development*. Development, 2012. **139**(18): p. 3277-99.
308. Changela, V., C. John, and S. Maheshwari, *Unusual cardiac associations with Tetralogy of Fallot-a descriptive study*. Pediatr Cardiol, 2010. **31**(6): p. 785-91.
309. Gilboa, S.M., et al., *Relation between ambient air quality and selected birth defects, seven county study, Texas, 1997-2000*. Am J Epidemiol, 2005. **162**(3): p. 238-52.
310. Digilio, M.C., et al., *Comparison of occurrence of genetic syndromes in ventricular septal defect with pulmonic stenosis (classic tetralogy of Fallot) versus ventricular septal defect with pulmonic atresia*. Am J Cardiol, 1996. **77**(15): p. 1375-6.
311. Freeman, S.B., et al., *Ethnicity, sex, and the incidence of congenital heart defects: a report from the National Down Syndrome Project*. Genet Med, 2008. **10**(3): p. 173-80.
312. Karr, S.S., et al., *Tetralogy of Fallot. The spectrum of severity in a regional study, 1981-1985*. Am J Dis Child, 1992. **146**(1): p. 121-4.
313. Musewe, N.N., et al., *Echocardiographic evaluation of the spectrum of cardiac anomalies associated with trisomy 13 and trisomy 18*. J Am Coll Cardiol, 1990. **15**(3): p. 673-7.
314. McDonald-McGinn, D.M., et al., *The Philadelphia story: the 22q11.2 deletion: report on 250 patients*. Genet Couns, 1999. **10**(1): p. 11-24.
315. Ryan, A.K., et al., *Spectrum of clinical features associated with interstitial chromosome 22q11 deletions: a European collaborative study*. J Med Genet, 1997. **34**(10): p. 798-804.
316. Lindsay, E.A., et al., *Tbx1 haploinsufficiency in the DiGeorge syndrome region causes aortic arch defects in mice*. Nature, 2001. **410**(6824): p. 97-101.
317. McElhinney, D.B., et al., *Analysis of cardiovascular phenotype and genotype-phenotype correlation in individuals with a JAG1 mutation and/or Alagille syndrome*. Circulation, 2002. **106**(20): p. 2567-74.
318. Emerick, K.M., et al., *Features of Alagille syndrome in 92 patients: frequency and relation to prognosis*. Hepatology, 1999. **29**(3): p. 822-9.
319. Spinner, N.B., L.D. Leonard, and I.D. Krantz, *Alagille Syndrome*, in *GeneReviews*, R.A. Pagon, et al., Editors. 1993: Seattle (WA).
320. Crosnier, C., et al., *Mutations in JAGGED1 gene are predominantly sporadic in Alagille syndrome*. Gastroenterology, 1999. **116**(5): p. 1141-8.
321. Bauer, R.C., et al., *Jagged1 (JAG1) mutations in patients with tetralogy of Fallot or pulmonic stenosis*. Hum Mutat, 2010. **31**(5): p. 594-601.
322. Rauch, R., et al., *Comprehensive genotype-phenotype analysis in 230 patients with tetralogy of Fallot*. J Med Genet, 2010. **47**(5): p. 321-31.
323. Eldadah, Z.A., et al., *Familial Tetralogy of Fallot caused by mutation in the jagged1 gene*. Hum Mol Genet, 2001. **10**(2): p. 163-9.
324. Krantz, I.D., et al., *Spectrum and frequency of jagged1 (JAG1) mutations in Alagille syndrome patients and their families*. Am J Hum Genet, 1998. **62**(6): p. 1361-9.

325. Lu, F., J.J. Morrissette, and N.B. Spinner, *Conditional JAG1 mutation shows the developing heart is more sensitive than developing liver to JAG1 dosage*. Am J Hum Genet, 2003. **72**(4): p. 1065-70.
326. Majewski, J., et al., *Mutations in NOTCH2 in families with Hajdu-Cheney syndrome*. Hum Mutat, 2011. **32**(10): p. 1114-7.
327. Zanotti, S. and E. Canalis, *Notch and the skeleton*. Mol Cell Biol, 2010. **30**(4): p. 886-96.
328. Penton, A.L., L.D. Leonard, and N.B. Spinner, *Notch signaling in human development and disease*. Semin Cell Dev Biol, 2012. **23**(4): p. 450-7.
329. Blake, K.D. and C. Prasad, *CHARGE syndrome*. Orphanet J Rare Dis, 2006. **1**: p. 34.
330. Jay, P.Y., et al., *Nkx2-5 mutation causes anatomic hypoplasia of the cardiac conduction system*. J Clin Invest, 2004. **113**(8): p. 1130-7.
331. McElhinney, D.B., et al., *NKX2.5 mutations in patients with congenital heart disease*. J Am Coll Cardiol, 2003. **42**(9): p. 1650-5.
332. Goldmuntz, E., E. Geiger, and D.W. Benson, *NKX2.5 mutations in patients with tetralogy of fallot*. Circulation, 2001. **104**(21): p. 2565-8.
333. Pizzuti, A., et al., *Mutations of ZFPM2/FOG2 gene in sporadic cases of tetralogy of Fallot*. Hum Mutat, 2003. **22**(5): p. 372-7.
334. Sperling, S., et al., *Identification and functional analysis of CITED2 mutations in patients with congenital heart defects*. Hum Mutat, 2005. **26**(6): p. 575-82.
335. Roessler, E., et al., *Reduced NODAL signaling strength via mutation of several pathway members including FOXH1 is linked to human heart defects and holoprosencephaly*. Am J Hum Genet, 2008. **83**(1): p. 18-29.
336. Guida, V., et al., *Novel and recurrent JAG1 mutations in patients with tetralogy of Fallot*. Clin Genet, 2011. **80**(6): p. 591-4.
337. Griffin, H.R., et al., *Systematic survey of variants in TBX1 in non-syndromic tetralogy of Fallot identifies a novel 57 base pair deletion that reduces transcriptional activity but finds no evidence for association with common variants*. Heart, 2010. **96**(20): p. 1651-5.
338. A Töpf, H.R.G., D H Hall, E Glen, B D Keavney, J A Goodship, The Change Study Collaborators, *Gene screening of the secondary heart field network in tetralogy of fallot patients*. Heart, 2011.
339. Guida, V., et al., *A variant in the carboxyl-terminus of connexin 40 alters GAP junctions and increases risk for tetralogy of Fallot*. Eur J Hum Genet, 2013. **21**(1): p. 69-75.
340. Silversides, C.K., et al., *Rare copy number variations in adults with tetralogy of Fallot implicate novel risk gene pathways*. PLoS Genet, 2012. **8**(8): p. e1002843.
341. Greenway, S.C., et al., *De novo copy number variants identify new genes and loci in isolated sporadic tetralogy of Fallot*. Nat Genet, 2009. **41**(8): p. 931-5.
342. Schork, N.J., et al., *Common vs. rare allele hypotheses for complex diseases*. Curr Opin Genet Dev, 2009. **19**(3): p. 212-9.
343. Pritchard, J.K. and N.J. Cox, *The allelic architecture of human disease genes: common disease-common variant...or not?* Hum Mol Genet, 2002. **11**(20): p. 2417-23.

344. Cordell, H.J., et al., *Genome-wide association study identifies loci on 12q24 and 13q32 associated with tetralogy of Fallot*. Hum Mol Genet, 2013. **22**(7): p. 1473-81.
345. Smyth, D.J., et al., *Shared and distinct genetic variants in type 1 diabetes and celiac disease*. N Engl J Med, 2008. **359**(26): p. 2767-77.
346. Soranzo, N., et al., *A genome-wide meta-analysis identifies 22 loci associated with eight hematological parameters in the HaemGen consortium*. Nat Genet, 2009. **41**(11): p. 1182-90.
347. Stahl, E.A., et al., *Genome-wide association study meta-analysis identifies seven new rheumatoid arthritis risk loci*. Nat Genet, 2010. **42**(6): p. 508-14.
348. Tartaglia, M., et al., *Mutations in PTPN11, encoding the protein tyrosine phosphatase SHP-2, cause Noonan syndrome*. Nat Genet, 2001. **29**(4): p. 465-8.
349. Filmus, J., M. Capurro, and J. Rast, *Glypicans*. Genome Biol, 2008. **9**(5): p. 224.
350. E., D.-G., *Hypothèses de dimérisation et de non-pénétrance*. Acta genet, 1962. **12**: p. 65-96
- .
351. Schaffer, A.A., *Digenic inheritance in medical genetics*. J Med Genet, 2013.
352. Kajiwara, K., E.L. Benson, and T.P. Dryja, *Digenic retinitis pigmentosa due to mutations at the unlinked peripherin/RDS and ROM1 loci*. Science, 1994. **264**(5165): p. 1604-8.
353. Lemmers, R.J., et al., *Digenic inheritance of an SMCHD1 mutation and an FSHD-permissive D4Z4 allele causes facioscapulohumeral muscular dystrophy type 2*. Nat Genet, 2012. **44**(12): p. 1370-4.
354. Margolin, D.H., et al., *Ataxia, dementia, and hypogonadotropism caused by disordered ubiquitination*. N Engl J Med, 2013. **368**(21): p. 1992-2003.
355. You, F.M., et al., *BatchPrimer3: a high throughput web application for PCR and sequencing primer design*. BMC Bioinformatics, 2008. **9**: p. 253.
356. Geneious Biomatters.
357. Kryukov, G.V., L.A. Pennacchio, and S.R. Sunyaev, *Most rare missense alleles are deleterious in humans: implications for complex disease and association studies*. Am J Hum Genet, 2007. **80**(4): p. 727-39.
358. Bray, S.J., *Notch signalling: a simple pathway becomes complex*. Nat Rev Mol Cell Biol, 2006. **7**(9): p. 678-89.
359. McBride, K.L., et al., *NOTCH1 mutations in individuals with left ventricular outflow tract malformations reduce ligand-induced signaling*. Hum Mol Genet, 2008. **17**(18): p. 2886-93.
360. Mohamed, S.A., et al., *Novel missense mutations (p.T596M and p.P1797H) in NOTCH1 in patients with bicuspid aortic valve*. Biochem Biophys Res Commun, 2006. **345**(4): p. 1460-5.
361. Garg, V., et al., *Mutations in NOTCH1 cause aortic valve disease*. Nature, 2005. **437**(7056): p. 270-4.
362. Mao, Y., et al., *Characterization of a Dchs1 mutant mouse reveals requirements for Dchs1-Fat4 signaling during mammalian development*. Development, 2011. **138**(5): p. 947-57.
363. Kuroda, K., et al., *Regulation of marginal zone B cell development by MINT, a suppressor of Notch/RBP-J signaling pathway*. Immunity, 2003. **18**(2): p. 301-12.

364. Gocke, C.B. and H. Yu, *ZNF198 stabilizes the LSD1-CoREST-HDAC1 complex on chromatin through its MYM-type zinc fingers*. PLoS One, 2008. **3**(9): p. e3255.
365. Xiao, S., et al., *FGFR1 is fused with a novel zinc-finger gene, ZNF198, in the t(8;13) leukaemia/lymphoma syndrome*. Nat Genet, 1998. **18**(1): p. 84-7.
366. Ren, M. and J.K. Cowell, *Constitutive Notch pathway activation in murine ZMYM2-FGFR1-induced T-cell lymphomas associated with atypical myeloproliferative disease*. Blood, 2011. **117**(25): p. 6837-47.
367. Puck, J.M. and H.F. Willard, *X inactivation in females with X-linked disease*. N Engl J Med, 1998. **338**(5): p. 325-8.
368. Kawagoe, T., et al., *Sequential control of Toll-like receptor-dependent responses by IRAK1 and IRAK2*. Nat Immunol, 2008. **9**(6): p. 684-91.
369. Ramalingam, T.R., et al., *Unique functions of the type II interleukin 4 receptor identified in mice lacking the interleukin 13 receptor alpha1 chain*. Nat Immunol, 2008. **9**(1): p. 25-33.
370. Christensen, S.R., et al., *Toll-like receptor 7 and TLR9 dictate autoantibody specificity and have opposing inflammatory and regulatory roles in a murine model of lupus*. Immunity, 2006. **25**(3): p. 417-28.
371. Lugtenberg, D., et al., *ZNF674: a new kruppel-associated box-containing zinc-finger gene involved in nonsyndromic X-linked mental retardation*. Am J Hum Genet, 2006. **78**(2): p. 265-78.
372. Hurles, P.V.a.M. *CoNVex*. 2013; Available from: /nfs/users/nfs_p/pv1/ConvexPackage/CoNVex_0.5.tar.gz.
373. Grozinger, C.M., C.A. Hassig, and S.L. Schreiber, *Three proteins define a class of human histone deacetylases related to yeast Hda1p*. Proc Natl Acad Sci U S A, 1999. **96**(9): p. 4868-73.
374. Vega, R.B., et al., *Histone deacetylase 4 controls chondrocyte hypertrophy during skeletogenesis*. Cell, 2004. **119**(4): p. 555-66.
375. Aldred, M.A., et al., *Molecular analysis of 20 patients with 2q37.3 monosomy: definition of minimum deletion intervals for key phenotypes*. J Med Genet, 2004. **41**(6): p. 433-9.
376. Williams, S.R., et al., *Haploinsufficiency of HDAC4 causes brachydactyly mental retardation syndrome, with brachydactyly type E, developmental delays, and behavioral problems*. Am J Hum Genet, 2010. **87**(2): p. 219-28.
377. Karamboulas, C., et al., *HDAC activity regulates entry of mesoderm cells into the cardiac muscle lineage*. J Cell Sci, 2006. **119**(Pt 20): p. 4305-14.
378. Yi, W., et al., *Phosphofructokinase 1 glycosylation regulates cell growth and metabolism*. Science, 2012. **337**(6097): p. 975-80.
379. Town, L., et al., *The metalloendopeptidase gene Pitrm1 is regulated by hedgehog signaling in the developing mouse limb and is expressed in muscle progenitors*. Dev Dyn, 2009. **238**(12): p. 3175-84.
380. Mittaz, L., et al., *Localization of a novel human RNA-editing deaminase (hRED2 or ADARB2) to chromosome 10p15*. Hum Genet, 1997. **100**(3-4): p. 398-400.
381. Sasman, A., et al., *Generation of conditional alleles for Foxc1 and Foxc2 in mice*. Genesis, 2012. **50**(10): p. 766-74.
382. Winnier, G.E., et al., *Roles for the winged helix transcription factors MF1 and MFH1 in cardiovascular development revealed by nonallelic noncomplementation of null alleles*. Dev Biol, 1999. **213**(2): p. 418-31.

383. Fuse, N., et al., *Novel mutations in the FOXC1 gene in Japanese patients with Axenfeld-Rieger syndrome*. Mol Vis, 2007. **13**: p. 1005-9.
384. Schouten, J.P., et al., *Relative quantification of 40 nucleic acid sequences by multiplex ligation-dependent probe amplification*. Nucleic Acids Res, 2002. **30**(12): p. e57.
385. Hofmann, J.J., et al., *Endothelial deletion of murine Jag1 leads to valve calcification and congenital heart defects associated with Alagille syndrome*. Development, 2012. **139**(23): p. 4449-60.
386. Krantz, I.D., et al., *Jagged1 mutations in patients ascertained with isolated congenital heart defects*. Am J Med Genet, 1999. **84**(1): p. 56-60.
387. Damert, A., et al., *Insufficient VEGFA activity in yolk sac endoderm compromises haematopoietic and endothelial differentiation*. Development, 2002. **129**(8): p. 1881-92.
388. Ferrara, N., et al., *Heterozygous embryonic lethality induced by targeted inactivation of the VEGF gene*. Nature, 1996. **380**(6573): p. 439-42.
389. Lambrechts, D., et al., *Low expression VEGF haplotype increases the risk for tetralogy of Fallot: a family based association study*. J Med Genet, 2005. **42**(6): p. 519-22.
390. Lui, T.T., et al., *The ubiquitin-specific protease USP34 regulates axin stability and Wnt/beta-catenin signaling*. Mol Cell Biol, 2011. **31**(10): p. 2053-65.
391. Chia, I.V., et al., *Both the RGS domain and the six C-terminal amino acids of mouse Axin are required for normal embryogenesis*. Genetics, 2009. **181**(4): p. 1359-68.
392. Hurlstone, A.F., et al., *The Wnt/beta-catenin pathway regulates cardiac valve formation*. Nature, 2003. **425**(6958): p. 633-7.
393. Lissitzky, J.C., et al., *Endoproteolytic processing of integrin pro-alpha subunits involves the redundant function of furin and proprotein convertase (PC) 5A, but not paired basic amino acid converting enzyme (PACE) 4, PC5B or PC7*. Biochem J, 2000. **346 Pt 1**: p. 133-8.
394. Szumska, D., et al., *VACTERL/caudal regression/Currarino syndrome-like malformations in mice with mutation in the proprotein convertase Pcsk5*. Genes Dev, 2008. **22**(11): p. 1465-77.
395. Pytela, R. and G. Wiche, *High molecular weight polypeptides (270,000-340,000) from cultured cells are related to hog brain microtubule-associated proteins but copurify with intermediate filaments*. Proc Natl Acad Sci U S A, 1980. **77**(8): p. 4808-12.
396. Natsuga, K., et al., *Plectin expression patterns determine two distinct subtypes of epidermolysis bullosa simplex*. Hum Mutat, 2010. **31**(3): p. 308-16.
397. Gundesli, H., et al., *Mutation in exon 1f of PLEC, leading to disruption of plectin isoform 1f, causes autosomal-recessive limb-girdle muscular dystrophy*. Am J Hum Genet, 2010. **87**(6): p. 834-41.
398. Konieczny, P., et al., *Myofiber integrity depends on desmin network targeting to Z-disks and costameres via distinct plectin isoforms*. J Cell Biol, 2008. **181**(4): p. 667-81.
399. Fukuda, M., et al., *Cloning of cDNAs encoding human lysosomal membrane glycoproteins, h-lamp-1 and h-lamp-2. Comparison of their deduced amino acid sequences*. J Biol Chem, 1988. **263**(35): p. 18920-8.

400. Nishino, I., et al., *Primary LAMP-2 deficiency causes X-linked vacuolar cardiomyopathy and myopathy (Danon disease)*. Nature, 2000. **406**(6798): p. 906-10.
401. Arad, M., et al., *Glycogen storage diseases presenting as hypertrophic cardiomyopathy*. N Engl J Med, 2005. **352**(4): p. 362-72.
402. Charron, P., et al., *Danon's disease as a cause of hypertrophic cardiomyopathy: a systematic survey*. Heart, 2004. **90**(8): p. 842-6.
403. Tanaka, Y., et al., *Accumulation of autophagic vacuoles and cardiomyopathy in LAMP-2-deficient mice*. Nature, 2000. **406**(6798): p. 902-6.
404. Spielman, R.S., R.E. McGinnis, and W.J. Ewens, *Transmission test for linkage disequilibrium: the insulin gene region and insulin-dependent diabetes mellitus (IDDM)*. Am J Hum Genet, 1993. **52**(3): p. 506-16.
405. Lewis, C.M., *Genetic association studies: design, analysis and interpretation*. Brief Bioinform, 2002. **3**(2): p. 146-53.
406. Ewens, W.J. and R.S. Spielman, *What is the significance of a significant TDT?* Hum Hered, 2005. **60**(4): p. 206-10.
407. LeClerc, S., et al., *Molecular cloning and characterization of a factor that binds the human glucocorticoid receptor gene and represses its expression*. J Biol Chem, 1991. **266**(26): p. 17333-40.
408. Brouns, M.R., et al., *The adhesion signaling molecule p190 RhoGAP is required for morphogenetic processes in neural development*. Development, 2000. **127**(22): p. 4891-903.
409. Arthur, W.T. and K. Burridge, *RhoA inactivation by p190RhoGAP regulates cell spreading and migration by promoting membrane protrusion and polarity*. Mol Biol Cell, 2001. **12**(9): p. 2711-20.
410. Kshitz, et al., *Matrix rigidity controls endothelial differentiation and morphogenesis of cardiac precursors*. Sci Signal, 2012. **5**(227): p. ra41.
411. Goldenberg, I. and A.J. Moss, *Long QT syndrome*. J Am Coll Cardiol, 2008. **51**(24): p. 2291-300.
412. Westenskow, P., et al., *Compound mutations: a common cause of severe long-QT syndrome*. Circulation, 2004. **109**(15): p. 1834-41.
413. Tester, D.J., et al., *Compendium of cardiac channel mutations in 541 consecutive unrelated patients referred for long QT syndrome genetic testing*. Heart Rhythm, 2005. **2**(5): p. 507-17.
414. Millat, G., et al., *Spectrum of pathogenic mutations and associated polymorphisms in a cohort of 44 unrelated patients with long QT syndrome*. Clin Genet, 2006. **70**(3): p. 214-27.
415. Morimoto, S., *Sarcomeric proteins and inherited cardiomyopathies*. Cardiovasc Res, 2008. **77**(4): p. 659-66.
416. Martinsson, T., et al., *Autosomal dominant myopathy: missense mutation (Glu-706 --> Lys) in the myosin heavy chain IIa gene*. Proc Natl Acad Sci U S A, 2000. **97**(26): p. 14614-9.
417. Rutland, C.S., et al., *Knockdown of embryonic myosin heavy chain reveals an essential role in the morphology and function of the developing heart*. Development, 2011. **138**(18): p. 3955-66.
418. Kontogianni-Konstantopoulos, A., et al., *Obscurin regulates the organization of myosin into A bands*. Am J Physiol Cell Physiol, 2004. **287**(1): p. C209-17.

419. Konstantopoulos, M.A.A.a.A.K.-. *Cardiomyopathies*, J.M.a.G. Ambrosio, Editor. 2013, InTech.
420. Svensson, E.C., et al., *Molecular cloning of FOG-2: a modulator of transcription factor GATA-4 in cardiomyocytes*. Proc Natl Acad Sci U S A, 1999. **96**(3): p. 956-61.
421. Tevosian, S.G., et al., *FOG-2, a cofactor for GATA transcription factors, is essential for heart morphogenesis and development of coronary vessels from epicardium*. Cell, 2000. **101**(7): p. 729-39.
422. Svensson, E.C., et al., *A syndrome of tricuspid atresia in mice with a targeted mutation of the gene encoding Fog-2*. Nat Genet, 2000. **25**(3): p. 353-6.
423. Hildebrand, J.D. and P. Soriano, *Overlapping and unique roles for C-terminal binding protein 1 (CtBP1) and CtBP2 during mouse development*. Mol Cell Biol, 2002. **22**(15): p. 5296-307.
424. Chen, J.D. and R.M. Evans, *A transcriptional co-repressor that interacts with nuclear hormone receptors*. Nature, 1995. **377**(6548): p. 454-7.
425. Jepsen, K., et al., *SMRT-mediated repression of an H3K27 demethylase in progression from neural stem cell to neuron*. Nature, 2007. **450**(7168): p. 415-9.
426. Vidal, O., et al., *Estrogen receptor specificity in the regulation of skeletal growth and maturation in male mice*. Proc Natl Acad Sci U S A, 2000. **97**(10): p. 5474-9.
427. Arevalo, M.A., et al., *Estradiol meets notch signaling in developing neurons*. Front Endocrinol (Lausanne), 2011. **2**: p. 21.
428. Laherty, C.D., et al., *SAP30, a component of the mSin3 corepressor complex involved in N-CoR-mediated repression by specific transcription factors*. Mol Cell, 1998. **2**(1): p. 33-42.
429. Kanehisa, M., et al., *KEGG for integration and interpretation of large-scale molecular data sets*. Nucleic Acids Res, 2012. **40**(Database issue): p. D109-14.
430. UniProt, C., *Update on activities at the Universal Protein Resource (UniProt) in 2013*. Nucleic Acids Res, 2013. **41**(Database issue): p. D43-7.
431. Yuan, S., S. Zaidi, and M. Brueckner, *Congenital heart disease: emerging themes linking genetics and development*. Curr Opin Genet Dev, 2013. **23**(3): p. 352-9.
432. Gale, R.E., et al., *Acquired skewing of X-chromosome inactivation patterns in myeloid cells of the elderly suggests stochastic clonal loss with age*. Br J Haematol, 1997. **98**(3): p. 512-9.
433. McKellar, S.H., et al., *Novel NOTCH1 mutations in patients with bicuspid aortic valve disease and thoracic aortic aneurysms*. J Thorac Cardiovasc Surg, 2007. **134**(2): p. 290-6.
434. *Echocardiography in Pediatric and Adult Congenital Heart Disease*. 2012.
435. Craig E Fleishman, M.A.T., MD, *Clinical manifestations, pathophysiology, and diagnosis of atrioventricular (AV) canal defects*. UpToDate, ed. D.S. Basow. 2013: Waltham, MA.
436. Allen HD, S.R., Driscoll DJ, Feltes Moss and Adams' *Heart Disease in Infants, Children, and Adolescents Including the Fetus and Young Adult*. 2007, Lippincott Williams & Wilkins.

437. Rastelli, G., J.W. Kirklin, and J.L. Titus, *Anatomic observations on complete form of persistent common atrioventricular canal with special reference to atrioventricular valves*. Mayo Clin Proc, 1966. **41**(5): p. 296-308.
438. Reller, M.D., et al., *Prevalence of congenital heart defects in metropolitan Atlanta, 1998-2005*. J Pediatr, 2008. **153**(6): p. 807-13.
439. Hoffman, J.I., *Incidence of congenital heart disease: I. Postnatal incidence*. Pediatr Cardiol, 1995. **16**(3): p. 103-13.
440. Allan, L.D., et al., *Prospective diagnosis of 1,006 consecutive cases of congenital heart disease in the fetus*. J Am Coll Cardiol, 1994. **23**(6): p. 1452-8.
441. Peoples, W.M., J.H. Moller, and J.E. Edwards, *Polysplenia: a review of 146 cases*. Pediatr Cardiol, 1983. **4**(2): p. 129-37.
442. Services, T.D.o.S.H. *Texas Birth Defects Epidemiology and Surveillance*. 2011 [20 July 2013]; Available from: <http://www.dshs.state.tx.us/birthdefects/>.
443. Agopian, A.J., et al., *Descriptive epidemiology of non-syndromic complete atrioventricular canal defects*. Paediatr Perinat Epidemiol, 2012. **26**(6): p. 515-24.
444. Rosenthal, G.L., et al., *Birth weight and cardiovascular malformations: a population-based study. The Baltimore-Washington Infant Study*. Am J Epidemiol, 1991. **133**(12): p. 1273-81.
445. Craig, B., *Atrioventricular septal defect: from fetus to adult*. Heart, 2006. **92**(12): p. 1879-85.
446. Calabro, R. and G. Limongelli, *Complete atrioventricular canal*. Orphanet J Rare Dis, 2006. **1**: p. 8.
447. Berger, T.J., et al., *Survival and probability of cure without and with operation in complete atrioventricular canal*. Ann Thorac Surg, 1979. **27**(2): p. 104-11.
448. Aubert, S., et al., *Atypical forms of isolated partial atrioventricular septal defect increase the risk of initial valve replacement and reoperation*. Eur J Cardiothorac Surg, 2005. **28**(2): p. 223-8.
449. Studer, M., et al., *Determinants of early and late results of repair of atrioventricular septal (canal) defects*. J Thorac Cardiovasc Surg, 1982. **84**(4): p. 523-42.
450. Abuhamad, A. and R. Chaoui, *A practical guide to fetal echocardiography : normal and abnormal hearts*. 2nd ed. 2010, Philadelphia, PA: Wolters Kluwer Health/Lippincott Williams & Wilkins. vii, 379 p.
451. Eisenberg, L.M. and R.R. Markwald, *Molecular regulation of atrioventricular valvuloseptal morphogenesis*. Circ Res, 1995. **77**(1): p. 1-6.
452. Webb, S., N.A. Brown, and R.H. Anderson, *Formation of the atrioventricular septal structures in the normal mouse*. Circ Res, 1998. **82**(6): p. 645-56.
453. Snarr, B.S., C.B. Kern, and A. Wessels, *Origin and fate of cardiac mesenchyme*. Dev Dyn, 2008. **237**(10): p. 2804-19.
454. Snarr, B.S., et al., *Isl1 expression at the venous pole identifies a novel role for the second heart field in cardiac development*. Circ Res, 2007. **101**(10): p. 971-4.
455. Anderson, R.H., et al., *Development of the heart: (2) Septation of the atriums and ventricles*. Heart, 2003. **89**(8): p. 949-58.

456. Moorman, A., et al., *Development of the heart: (1) formation of the cardiac chambers and arterial trunks*. Heart, 2003. **89**(7): p. 806-14.
457. Patel, S.S., *Non-Syndromic atrioventricular septal defects: a refined definition, associated risk factors, and prognostic factors for left atrioventricular valve replacement following primary repair*, 2010, University of Iowa.
458. Carmi, R., J.A. Boughman, and C. Ferencz, *Endocardial cushion defect: further studies of "isolated" versus "syndromic" occurrence*. Am J Med Genet, 1992. **43**(3): p. 569-75.
459. Ferencz, C., et al., *Congenital cardiovascular malformations: questions on inheritance*. Baltimore-Washington Infant Study Group. J Am Coll Cardiol, 1989. **14**(3): p. 756-63.
460. Nemer, A.C.F.a.G.M., *Genetic Causes of Syndromic and Non-Syndromic Congenital Heart Disease*, in *Mutations in Human Genetic Disease*, P.D. Cooper, Editor. 2012, InTech.
461. Barlow, G.M., et al., *Down syndrome congenital heart disease: a narrowed region and a candidate gene*. Genet Med, 2001. **3**(2): p. 91-101.
462. Casas, C., et al., *Dscr1, a novel endogenous inhibitor of calcineurin signaling, is expressed in the primitive ventricle of the heart and during neurogenesis*. Mech Dev, 2001. **101**(1-2): p. 289-92.
463. Ackerman, C., et al., *An excess of deleterious variants in VEGF-A pathway genes in Down-syndrome-associated atrioventricular septal defects*. Am J Hum Genet, 2012. **91**(4): p. 646-59.
464. Green, E.K., et al., *Detailed mapping of a congenital heart disease gene in chromosome 3p25*. J Med Genet, 2000. **37**(8): p. 581-7.
465. Digilio, M.C., et al., *Atrioventricular canal and 8p- syndrome*. Am J Med Genet, 1993. **47**(3): p. 437-8.
466. Marino, B., et al., *Nonrandom association of atrioventricular canal and del (8p) syndrome*. Am J Med Genet, 1992. **42**(4): p. 424-7.
467. Mohapatra, B., et al., *Identification and functional characterization of NODAL rare variants in heterotaxy and isolated cardiovascular malformations*. Hum Mol Genet, 2009. **18**(5): p. 861-71.
468. Maslen, C.L., *Molecular genetics of atrioventricular septal defects*. Curr Opin Cardiol, 2004. **19**(3): p. 205-10.
469. O'Nuallain, S., J.G. Hall, and S.J. Stamm, *Autosomal dominant inheritance of endocardial cushion defect*. Birth Defects Orig Artic Ser, 1977. **13**(3A): p. 143-7.
470. Emanuel, R., et al., *Evidence of congenital heart disease in the offspring of parents with atrioventricular defects*. Br Heart J, 1983. **49**(2): p. 144-7.
471. Wilson, L., et al., *A large, dominant pedigree of atrioventricular septal defect (AVSD): exclusion from the Down syndrome critical region on chromosome 21*. Am J Hum Genet, 1993. **53**(6): p. 1262-8.
472. Kumar, A., C.A. Williams, and B.E. Victorica, *Familial atrioventricular septal defect: possible genetic mechanisms*. Br Heart J, 1994. **71**(1): p. 79-81.
473. Amati, F., et al., *Two pedigrees of autosomal dominant atrioventricular canal defect (AVCD): exclusion from the critical region on 8p*. Am J Med Genet, 1995. **57**(3): p. 483-8.

474. Cousineau, A.J., et al., *Linkage analysis of autosomal dominant atrioventricular canal defects: exclusion of chromosome 21*. Hum Genet, 1994. **93**(2): p. 103-8.
475. Robinson, S.W., et al., *Missense mutations in CRELD1 are associated with cardiac atrioventricular septal defects*. Am J Hum Genet, 2003. **72**(4): p. 1047-52.
476. Sheffield, V.C., et al., *Identification of a complex congenital heart defect susceptibility locus by using DNA pooling and shared segment analysis*. Hum Mol Genet, 1997. **6**(1): p. 117-21.
477. Phipps, M.E., et al., *Molecular genetic analysis of the 3p- syndrome*. Hum Mol Genet, 1994. **3**(6): p. 903-8.
478. Drumheller, T., et al., *Precise localisation of 3p25 breakpoints in four patients with the 3p-syndrome*. J Med Genet, 1996. **33**(10): p. 842-7.
479. Rupp, P.A., et al., *Identification, genomic organization and mRNA expression of CRELD1, the founding member of a unique family of matricellular proteins*. Gene, 2002. **293**(1-2): p. 47-57.
480. Guo, Y., et al., *Novel CRELD1 gene mutations in patients with atrioventricular septal defect*. World J Pediatr, 2010. **6**(4): p. 348-52.
481. Sarkozy, A., et al., *CRELD1 and GATA4 gene analysis in patients with nonsyndromic atrioventricular canal defects*. Am J Med Genet A, 2005. **139**(3): p. 236-8.
482. Zatyka, M., et al., *Analysis of CRELD1 as a candidate 3p25 atrioventricular septal defect locus (AVSD2)*. Clin Genet, 2005. **67**(6): p. 526-8.
483. Smith, K.A., et al., *Dominant-negative ALK2 allele associates with congenital heart defects*. Circulation, 2009. **119**(24): p. 3062-9.
484. Rajagopal, S.K., et al., *Spectrum of heart disease associated with murine and human GATA4 mutation*. J Mol Cell Cardiol, 2007. **43**(6): p. 677-85.
485. Zhang, W., et al., *GATA4 mutations in 486 Chinese patients with congenital heart disease*. Eur J Med Genet, 2008. **51**(6): p. 527-35.
486. Maitra, M., et al., *Identification of GATA6 sequence variants in patients with congenital heart defects*. Pediatr Res, 2010. **68**(4): p. 281-5.
487. Stefansson, H., et al., *Large recurrent microdeletions associated with schizophrenia*. Nature, 2008. **455**(7210): p. 232-6.
488. Jun, G., et al., *Detecting and estimating contamination of human DNA samples in sequencing and array-based genotype data*. Am J Hum Genet, 2012. **91**(5): p. 839-48.
489. Pearson, T.A. and T.A. Manolio, *How to interpret a genome-wide association study*. JAMA, 2008. **299**(11): p. 1335-44.
490. Benson, G., *Tandem repeats finder: a program to analyze DNA sequences*. Nucleic Acids Res, 1999. **27**(2): p. 573-80.
491. Bailey, J.A., et al., *Recent segmental duplications in the human genome*. Science, 2002. **297**(5583): p. 1003-7.
492. Kent, W.J., et al., *The human genome browser at UCSC*. Genome Res, 2002. **12**(6): p. 996-1006.
493. Zhang, K., et al., *Molecular cloning and characterization of three novel lysozyme-like genes, predominantly expressed in the male reproductive system of humans, belonging to the c-type lysozyme/alpha-lactalbumin family*. Biol Reprod, 2005. **73**(5): p. 1064-71.

494. Richardson, L., et al., *EMAGE mouse embryo spatial gene expression database: 2010 update*. Nucleic Acids Res, 2010. **38**(Database issue): p. D703-9.
495. Hirano, S., et al., *Identification of a neural alpha-catenin as a key regulator of cadherin function and multicellular organization*. Cell, 1992. **70**(2): p. 293-301.
496. Cook, S.A., et al., *Cerebellar deficient folia (cdf): a new mutation on mouse chromosome 6*. Mamm Genome, 1997. **8**(2): p. 108-12.
497. Futterer, A., et al., *Ablation of Dido3 compromises lineage commitment of stem cells in vitro and during early embryonic development*. Cell Death Differ, 2012. **19**(1): p. 132-43.
498. Gronda, M., et al., *Hematopoietic protein tyrosine phosphatase suppresses extracellular stimulus-regulated kinase activation*. Mol Cell Biol, 2001. **21**(20): p. 6851-8.
499. Hentschke, M. and U. Borgmeyer, *Identification of PNRC2 and TLE1 as activation function-1 cofactors of the orphan nuclear receptor ERRgamma*. Biochem Biophys Res Commun, 2003. **312**(4): p. 975-82.
500. Fossey, S.C., et al., *Identification and characterization of PRKCBP1, a candidate RACK-like protein*. Mamm Genome, 2000. **11**(10): p. 919-25.
501. Lin, F.J., et al., *Endocardial cushion morphogenesis and coronary vessel development require chicken ovalbumin upstream promoter-transcription factor II*. Arterioscler Thromb Vasc Biol, 2012. **32**(11): p. e135-46.
502. Kruse, S.W., et al., *Identification of COUP-TFII orphan nuclear receptor as a retinoic acid-activated receptor*. PLoS Biol, 2008. **6**(9): p. e227.
503. Tsai, S.Y. and M.J. Tsai, *Chick ovalbumin upstream promoter-transcription factors (COUP-TFs): coming of age*. Endocr Rev, 1997. **18**(2): p. 229-40.
504. Winston, J.B., et al., *Heterogeneity of genetic modifiers ensures normal cardiac development*. Circulation, 2010. **121**(11): p. 1313-21.
505. Hardenbol, P., et al., *Multiplexed genotyping with sequence-tagged molecular inversion probes*. Nat Biotechnol, 2003. **21**(6): p. 673-8.
506. Schippers, A., et al., *Mucosal addressin cell-adhesion molecule-1 controls plasma-cell migration and function in the small intestine of mice*. Gastroenterology, 2009. **137**(3): p. 924-33.
507. de la Pompa, J.L., et al., *Role of the NF-ATc transcription factor in morphogenesis of cardiac valves and septum*. Nature, 1998. **392**(6672): p. 182-6.
508. Dor, Y., et al., *A novel role for VEGF in endocardial cushion formation and its potential contribution to congenital heart defects*. Development, 2001. **128**(9): p. 1531-8.
509. Digilio, M.C., et al., *Cardiac malformations in patients with oral-facial-skeletal syndromes: clinical similarities with heterotaxia*. Am J Med Genet, 1999. **84**(4): p. 350-6.
510. Ruiz-Perez, V.L., et al., *Evc is a positive mediator of Ihh-regulated bone growth that localises at the base of chondrocyte cilia*. Development, 2007. **134**(16): p. 2903-12.
511. Sund, K.L., et al., *Analysis of Ellis van Creveld syndrome gene products: implications for cardiovascular development and disease*. Hum Mol Genet, 2009. **18**(10): p. 1813-24.

512. Lin, F.J., et al., *Coup d'Etat: an orphan takes control*. Endocr Rev, 2011. **32**(3): p. 404-21.
513. Pereira, F.A., et al., *The orphan nuclear receptor COUP-TFII is required for angiogenesis and heart development*. Genes Dev, 1999. **13**(8): p. 1037-49.
514. Correa, A., et al., *Diabetes mellitus and birth defects*. Am J Obstet Gynecol, 2008. **199**(3): p. 237 e1-9.
515. Botto, L.D., et al., *Vitamin A and cardiac outflow tract defects*. Epidemiology, 2001. **12**(5): p. 491-6.
516. Perilhou, A., et al., *The transcription factor COUP-TFII is negatively regulated by insulin and glucose via Foxo1- and ChREBP-controlled pathways*. Mol Cell Biol, 2008. **28**(21): p. 6568-79.
517. Vilhais-Neto, G.C., et al., *Rere controls retinoic acid signalling and somite bilateral symmetry*. Nature, 2010. **463**(7283): p. 953-7.
518. Nakamura, E., et al., *5.78 Mb terminal deletion of chromosome 15q in a girl, evaluation of NR2F2 as candidate gene for congenital heart defects*. Eur J Med Genet, 2011. **54**(3): p. 354-6.
519. Zollner, S. and J.K. Pritchard, *Overcoming the winner's curse: estimating penetrance parameters from case-control data*. Am J Hum Genet, 2007. **80**(4): p. 605-15.
520. Ulucan, H., et al., *Extending the spectrum of Ellis van Creveld syndrome: a large family with a mild mutation in the EVC gene*. BMC Med Genet, 2008. **9**: p. 92.
521. Langheinrich, U., et al., *Zebrafish as a model organism for the identification and characterization of drugs and genes affecting p53 signaling*. Curr Biol, 2002. **12**(23): p. 2023-8.
522. Robu, M.E., et al., *p53 activation by knockdown technologies*. PLoS Genet, 2007. **3**(5): p. e78.
523. Bill, B.R., et al., *A primer for morpholino use in zebrafish*. Zebrafish, 2009. **6**(1): p. 69-77.
524. Staudt, D. and D. Stainier, *Uncovering the molecular and cellular mechanisms of heart development using the zebrafish*. Annu Rev Genet, 2012. **46**: p. 397-418.
525. Bakkers, J., *Zebrafish as a model to study cardiac development and human cardiac disease*. Cardiovasc Res, 2011. **91**(2): p. 279-88.
526. Shaner, N.C., et al., *Improved monomeric red, orange and yellow fluorescent proteins derived from Discosoma sp. red fluorescent protein*. Nat Biotechnol, 2004. **22**(12): p. 1567-72.
527. Pipaon, C., S.Y. Tsai, and M.J. Tsai, *COUP-TF upregulates NGFI-A gene expression through an Sp1 binding site*. Mol Cell Biol, 1999. **19**(4): p. 2734-45.
528. Achatz, G., et al., *Functional domains of the human orphan receptor ARP-1/COUP-TFII involved in active repression and transrepression*. Mol Cell Biol, 1997. **17**(9): p. 4914-32.