

- Lapidot T, Sirard C, Vormoor J, et al. A cell initiating human acute myeloid leukaemia after transplantation into SCID mice. *Nature* 1994;367:645–648.
- Bonnet D, Dick JE. Human acute myeloid leukemia is organized as a hierarchy that originates from a primitive hematopoietic cell. *Nat Med* 1997;3:730–737.
- Buss EC, Ho AD. Leukemia stem cells. *Int J Cancer* 2011;129:2328–2336.
- Saito T, Chiba S, Ichikawa M, et al. Notch2 is preferentially expressed in mature B cells and indispensable for marginal zone B lineage development. *Immunity* 2003;18:675–685.
- Cozzio A, Passegue E, Ayton PM, et al. Similar MLL-associated leukemias arising from self-renewing stem cells and short-lived myeloid progenitors. *Genes Dev* 2003;17:3029–3035.
- Huntly BJ, Shigematsu H, Deguchi K, et al. MOZ-TIF2, but not BCR-ABL, confers properties of leukemic stem cells to committed murine hematopoietic progenitors. *Cancer Cell* 2004;6:587–596.
- Huntly BJ, Gilliland DG. Leukaemia stem cells and the evolution of cancer-stem-cell research. *Nat Rev Cancer* 2005;5:311–321.
- Jamieson CH, Ailles LE, Dylla SJ, et al. Granulocyte-macrophage progenitors as candidate leukemic stem cells in blast-crisis CML. *N Engl J Med* 2004;351:657–667.
- Speicher MR, Carter NP. The new cytogenetics: blurring the boundaries with molecular biology. *Nat Rev Genet* 2005;6:782–792.
- Feuk L, Carson AR, Scherer SW. Structural variation in the human genome. *Nat Rev Genet* 2006;7:85–97.
- International Cancer Genome Consortium, Hudson TJ, Anderson W, et al. International network of cancer genome projects. *Nature* 2010;464:993–998.
- Cancer Genome Atlas Research Network. Genomic and epigenomic landscapes of adult de novo acute myeloid leukemia. *N Engl J Med* 2013;368:2059–2074.
- Stratton MR, Campbell PJ, Futreal PA. The cancer genome. *Nature* 2009;458:719–724.
- Koschmieder S, Halmos B, Levantini E, et al. Dysregulation of the C/EBPalpha differentiation pathway in human cancer. *J Clin Oncol* 2009;27:619–628.
- Speck NA, Gilliland DG. Core-binding factors in haematopoiesis and leukaemia. *Nat Rev Cancer* 2002;2:502–513.
- Wang Q, Stacy T, Binder M, et al. Disruption of the Cbfa2 gene causes necrosis and hemorrhaging in the central nervous system and blocks definitive hematopoiesis. *Proc Natl Acad Sci U S A* 1996;93:3444–3449.
- Okuda T, van Deursen J, Hiebert SW, et al. AML1, the target of multiple chromosomal translocations in human leukemia, is essential for normal fetal liver hematopoiesis. *Cell* 1996;84:321–330.
- Goyama S, Mulloy JC. Molecular pathogenesis of core binding factor leukemia: current knowledge and future prospects. *Int J Hematol* 2011;94:126–133.
- Ichikawa M, Yoshimi A, Nakagawa M, et al. A role for RUNX1 in hematopoiesis and myeloid leukemia. *Int J Hematol* 2013;97:726–734.
- Vangala RK, Heiss-Neumann MS, Rangatia JS, et al. The myeloid master regulator transcription factor PU.1 is inactivated by AML1-ETO in t(8;21) myeloid leukemia. *Blood* 2003;101:270–277.
- Choi Y, Elagib KE, Delehanty LL, et al. Erythroid inhibition by the leukemic fusion AML1-ETO is associated with impaired acetylation of the major erythroid transcription factor GATA-1. *Cancer Res* 2006;66:2990–2996.
- Song WJ, Sullivan MG, Legare RD, et al. Haploinsufficiency of CBFA2 causes familial thrombocytopenia with propensity to develop acute myelogenous leukaemia. *Nat Genet* 1999;23:166–175.
- Michaud J, Wu F, Osato M, et al. In vitro analyses of known and novel RUNX1/AML1 mutations in dominant familial platelet disorder with predisposition to acute myelogenous leukemia: implications for mechanisms of pathogenesis. *Blood* 2002;99:1364–1372.
- Osato M, Asou N, Abdalla E, et al. Biallelic and heterozygous point mutations in the runt domain of the AML1/PEBP2alphaB gene associated with myeloblastic leukemias. *Blood* 1999;93:1817–1824.
- Yergeau DA, Hetherington CJ, Wang Q, et al. Embryonic lethality and impairment of haematopoiesis in mice heterozygous for an AML1-ETO fusion gene. *Nat Genet* 1997;15:303–306.
- Castilla LH, Garrett L, Adya N, et al. The fusion gene Cbfb-MYH11 blocks myeloid differentiation and predisposes mice to acute myelomonocytic leukaemia. *Nat Genet* 1999;23:144–146.
- Linggi B, Muller-Tidow C, van de Locht L, et al. The t(8;21) fusion protein, AML1 ETO, specifically represses the transcription of the p14(ARF) tumor suppressor in acute myeloid leukemia. *Nat Med* 2002;8:743–750.
- Markus J, Garin MT, Bies J, et al. Methylation-independent silencing of the tumor suppressor INK4b (p15) by CBFbeta-SMMHC in acute myelogenous leukemia with inv(16). *Cancer Res* 2007;67:992–1000.
- Alcalay M, Meani N, Gelmetti V, et al. Acute myeloid leukemia fusion proteins deregulate genes involved in stem cell maintenance and DNA repair. *J Clin Invest* 2003;112:1751–1761.
- Wang LC, Swat W, Fujiwara Y, et al. The TEL/ETV6 gene is required specifically for hematopoiesis in the bone marrow. *Genes Dev* 1998;12:2392–2402.
- Liu S, Shen T, Huynh L, et al. Interplay of RUNX1/MTG8 and DNA methyltransferase 1 in acute myeloid leukemia. *Cancer Res* 2005;65:1277–1284.
- Yan M, Ahn EY, Hiebert SW, et al. RUNX1/AML1 DNA-binding domain and ETO/MTG8 NHR2-dimerization domain are critical to AML1-ETO9a leukemogenesis. *Blood* 2009;113:883–886.
- Jiao B, Wu CF, Liang Y, et al. AML1-ETO9a is correlated with C-KIT over-expression/mutations and indicates poor disease outcome in t(8;21) acute myeloid leukemia-M2. *Leukemia* 2009;23:1598–1604.
- De Brackeleer E, Douet-Guilbert N, Morel F, et al. ETV6 fusion genes in hematological malignancies: a review. *Leuk Res* 2012;36:945–961.
- Mullighan CG. Genomic characterization of childhood acute lymphoblastic leukemia. *Semin Hematol* 2013;50:314–324.
- Wang LC, Kuo F, Fujiwara Y, et al. Yolk sac angiogenic defect and intra-embryonic apoptosis in mice lacking the Ets-related factor TEL. *Embo J* 1997;16:4374–4383.
- Tijchon E, Havinga J, van Leeuwen FN, et al. B-lineage transcription factors and cooperating gene lesions required for leukemia development. *Leukemia* 2013;27:541–552.
- Goddard AD, Borrow J, Freemont PS, et al. Characterization of a zinc finger gene disrupted by the t(15;17) in acute promyelocytic leukemia. *Science* 1991;254:1371–1374.
- Kakizuka A, Miller WH Jr, Umesono K, et al. Chromosomal translocation t(15;17) in human acute promyelocytic leukemia fuses RAR alpha with a novel putative transcription factor, PML. *Cell* 1991;66:663–674.
- de Thé H, Lavau C, Marchio A, et al. The PML-RAR alpha fusion mRNA generated by the t(15;17) translocation in acute promyelocytic leukemia encodes a functionally altered RAR. *Cell* 1991;66:675–684.
- Zelent A, Guidez F, Melnick A, et al. Translocations of the RARalpha gene in acute promyelocytic leukemia. *Oncogene* 2001;20:7186–7203.
- Li W, Rich T, Watson CJ. PML: a tumor suppressor that regulates cell fate in mammary gland. *Cell Cycle* 2009;8:2711–2717.
- Carracedo A, Ito K, Pandolfi PP. The nuclear bodies inside out: PML conquers the cytoplasm. *Curr Opin Cell Biol* 2011;23:360–366.
- Giorgi C, Ito K, Lin HK, et al. PML regulates apoptosis at endoplasmic reticulum by modulating calcium release. *Science* 2010;330:1247–1251.
- Ito K, Bernardi R, Morotti A, et al. PML targeting eradicates quiescent leukaemia-initiating cells. *Nature* 2008;453:1072–1078.
- Zhang XW, Yan XJ, Zhou ZR, et al. Arsenic trioxide controls the fate of the PML-RARalpha oncoprotein by directly binding PML. *Science* 2010;328:240–243.
- de Thé H, Chen Z. Acute promyelocytic leukaemia: novel insights into the mechanisms of cure. *Nat Rev Cancer* 2010;10:775–783.
- Martens JH, Brinkman AB, Simmer F, et al. PML-RARalpha/RXR Alters the Epigenetic Landscape in Acute Promyelocytic Leukemia. *Cancer Cell* 2010;17:173–185.
- Saeed S, Logie C, Stunnenberg HG, et al. Genome-wide functions of PML-RARalpha in acute promyelocytic leukaemia. *Br J Cancer* 2011;104:554–558.
- Grisolano JL, Wesselschmidt RL, Pelicci PG, et al. Altered myeloid development and acute leukemia in transgenic mice expressing PML-RAR alpha under control of cathepsin G regulatory sequences. *Blood* 1997;89:376–387.
- He LZ, Tribioli C, Rivi R, et al. Acute leukemia with promyelocytic features in PML/RARalpha transgenic mice. *Proc Natl Acad Sci U S A* 1997;94:5302–5307.
- Brown D, Kogan S, Lagasse E, et al. A PML/RARalpha transgene initiates murine acute promyelocytic leukemia. *Proc Natl Acad Sci U S A* 1997;94:2551–2556.
- Tallman MS, Nabhan C, Feusner JH, et al. Acute promyelocytic leukemia: evolving therapeutic strategies. *Blood* 2002;99:759–767.
- Alharbi RA, Pettengell R, Pandha HS, et al. The role of HOX genes in normal hematopoiesis and acute leukemia. *Leukemia* 2013;27:1000–1008.
- Abramovich C, Humphries RK. Hox regulation of normal and leukemic hematopoietic stem cells. *Curr Opin Hematol* 2005;12:210–216.
- Gough SM, Slape CI, Aplana PD. NUP98 gene fusions and hematopoietic malignancies: common themes and new biologic insights. *Blood* 2011;118:6247–6257.
- Kasper LH, Brindle PK, Schnabel CA, et al. CREB binding protein interacts with nucleoporin-specific FG repeats that activate transcription and mediate NUP98-HOX9 oncogenicity. *Mol Cell Biol* 1999;19:764–776.
- Bansal D, Scholl C, Frohling S, et al. Cdx4 dysregulates Hox gene expression and generates acute myeloid leukemia alone and in cooperation with Meis1a in a murine model. *Proc Natl Acad Sci U S A* 2006;103:16924–16929.
- Hatano M, Roberts CW, Minden M, et al. Deregulation of a homeobox gene, HOX11, by the t(10;14) in T cell leukemia. *Science* 1991;253:79–82.
- Rawat VP, Cusan M, Deshpande A, et al. Ectopic expression of the homeobox gene Cdx2 is the transforming event in a mouse model of t(12;13)(p13;q12) acute myeloid leukemia. *Proc Natl Acad Sci U S A* 2004;101:817–822.
- Pineault N, Buske C, Feuring-Buske M, et al. Induction of acute myeloid leukemia in mice by the human leukemia-specific fusion gene NUP98-HOXD13 in concert with Meis1. *Blood* 2003;101:4529–4538.
- Palmqvist L, Argiropoulos B, Pineault N, et al. The Flt3 receptor tyrosine kinase collaborates with NUP98-HOX fusions in acute myeloid leukemia. *Blood* 2006;108:1030–1036.
- Eguchi M, Eguchi-Ishimae M, Greaves M. Molecular pathogenesis of MLL-associated leukemias. *Int J Hematol* 2005;82:9–20.
- Slany RK. The molecular biology of mixed lineage leukemia. *Haematologica* 2009;94:984–993.
- Ng RK, Kong CT, So CC, et al. Epigenetic dysregulation of leukemic Hox code in MLL-rearranged leukemia mouse model. *J Pathol* 2014;232:65–74.

66. Yu BD, Hanson RD, Hess JL, et al. MLL, a mammalian trithorax-group gene, functions as a transcriptional maintenance factor in morphogenesis. *Proc Natl Acad Sci U S A* 1998;95:10632–10636.
67. Yokoyama A, Somerville TC, Smith KS, et al. The menin tumor suppressor protein is an essential oncogenic cofactor for MLL-associated leukemogenesis. *Cell* 2005;123:207–218.
68. Yokoyama A, Cleary ML. Menin critically links MLL proteins with LEDGF on cancer-associated target genes. *Cancer Cell* 2008;14:36–46.
69. Mohan M, Lin C, Guest E, et al. Licensed to elongate: a molecular mechanism for MLL-based leukaemogenesis. *Nat Rev Cancer* 2010;10:721–728.
70. Lin C, Smith ER, Takahashi H, et al. AFF4, a component of the ELL/P-TEFb elongation complex and a shared subunit of MLL chimeras, can link transcription elongation to leukemia. *Mol Cell* 2010;37:429–437.
71. Yeung J, Esposito MT, Gandillet A, et al. beta-Catenin mediates the establishment and drug resistance of MLL leukemic stem cells. *Cancer Cell* 2010;18:606–618.
72. Somerville TC, Cleary ML. Identification and characterization of leukemia stem cells in murine MLL-AF9 acute myeloid leukemia. *Cancer Cell* 2006;10:257–268.
73. Wei J, Wunderlich M, Fox C, et al. Microenvironment determines lineage fate in a human model of MLL-AF9 leukemia. *Cancer Cell* 2008;13:483–495.
74. Wang X, Scott E, Sawyers CL, et al. C/EBPalpha bypasses granulocyte colony-stimulating factor signals to rapidly induce PU.1 gene expression, stimulate granulocyte differentiation, and limit proliferation in 32D cl3 myeloblasts. *Blood* 1999;94:560–571.
75. Hackanson B, Bennett KL, Brena RM, et al. Epigenetic modification of CCAAT/enhancer binding protein alpha expression in acute myeloid leukemia. *Cancer Res* 2008;68:3142–3151.
76. Paz-Priel I, Friedman A. C/EBPalpha dysregulation in AML and ALL. *Crit Rev Oncog* 2011;16:93–102.
77. Mueller BU, Pabst T. C/EBPalpha and the pathophysiology of acute myeloid leukemia. *Curr Opin Hematol* 2006;13:7–14.
78. Schlenk RF, Dohner K, Krauter J, et al. Mutations and treatment outcome in cytogenetically normal acute myeloid leukemia. *N Engl J Med* 2008;358:1909–1918.
79. Chapiro E, Russell L, Radford-Weiss I, et al. Overexpression of CEBPA resulting from the translocation t(14;19)(q32;q13) of human precursor B acute lymphoblastic leukemia. *Blood* 2006;108:3560–3563.
80. Akasaka T, Balasas T, Russell LJ, et al. Five members of the CEBP transcription factor family are targeted by recurrent IGH translocations in B-cell precursor acute lymphoblastic leukemia (BCP-ALL). *Blood* 2007;109:3451–3461.
81. Khan I, Malinge S, Crispino J. Myeloid leukemia in Down syndrome. *Crit Rev Oncog* 2011;16:25–36.
82. Crispino JD. GATA1 mutations in Down syndrome: implications for biology and diagnosis of children with transient myeloproliferative disorder and acute megakaryoblastic leukemia. *Pediatr Blood Cancer* 2005;44:40–44.
83. Bresnick EH, Katsumura KR, Lee HY, et al. Master regulatory GATA transcription factors: mechanistic principles and emerging links to hematologic malignancies. *Nucleic Acids Res* 2012;40:5819–5831.
84. Wechsler J, Greene M, McDevitt MA, et al. Acquired mutations in GATA1 in the megakaryoblastic leukemia of Down syndrome. *Nat Genet* 2002;32:148–152.
85. Malinge S, Izraeli S, Crispino JD. Insights into the manifestations, outcomes, and mechanisms of leukemogenesis in Down syndrome. *Blood* 2009;113:2619–2628.
86. Taub JW, Mundschau G, Ge Y, et al. Prenatal origin of GATA1 mutations may be an initiating step in the development of megakaryocytic leukemia in Down syndrome. *Blood* 2004;104:1588–1589.
87. Kirsammer G, Jilani S, Liu H, et al. Highly penetrant myeloproliferative disease in the Ts65Dn mouse model of Down syndrome. *Blood* 2008;111:767–775.
88. Ma Z, Morris SW, Valentine V, et al. Fusion of two novel genes, RBM15 and MKL1, in the t(1;22)(p13;q13) of acute megakaryoblastic leukemia. *Nat Genet* 2001;28:220–221.
89. Mercher T, Busson-Le Coniat M, Khac FN, et al. Recurrence of OTT-MAL fusion in t(1;22) of infant AML-M7. *Genes Chromosomes Cancer* 2002;33:22–28.
90. Raffel GD, Mercher T, Shigematsu H, et al. Ott1(Rbm15) has pleiotropic roles in hematopoietic development. *Proc Natl Acad Sci U S A* 2007;104:6001–6006.
91. Xiao N, Jani K, Morgan K, et al. Hematopoietic stem cells lacking Ott1 display aspects associated with aging and are unable to maintain quiescence during proliferative stress. *Blood* 2012;119:4898–4907.
92. Miralles F, Posern G, Zaroymtidou AI, et al. Actin dynamics control SRF activity by regulation of its coactivator MAL. *Cell* 2003;113:329–342.
93. Smith EC, Teixeira AM, Chen RC, et al. Induction of megakaryocyte differentiation drives nuclear accumulation and transcriptional function of MKL1 via actin polymerization and RhoA activation. *Blood* 2013;121:1094–1101.
94. Mercher T, Raffel GD, Moore SA, et al. The OTT-MAL fusion oncogene activates RBPJ-mediated transcription and induces acute megakaryoblastic leukemia in a knockin mouse model. *J Clin Invest* 2009;119:852–864.
95. Taki T, Sako M, Tsuchida M, et al. The t(11;16)(q23;p13) translocation in myelodysplastic syndrome fuses the MLL gene to the CBP gene. *Blood* 1997;89:3945–3950.
96. Carapeti M, Aguiar RC, Goldman JM, et al. A novel fusion between MOZ and the nuclear receptor coactivator TIF2 in acute myeloid leukemia. *Blood* 1998;91:3127–3133.
97. Deguchi K, Ayton PM, Carapeti M, et al. MOZ-TIF2-induced acute myeloid leukemia requires the MOZ nucleosome binding motif and TIF2-mediated recruitment of CBP. *Cancer Cell* 2003;3:259–271.
98. Lavau C, Luo RT, Du C, et al. Retrovirus-mediated gene transfer of MLL-ELL transforms primary myeloid progenitors and causes acute myeloid leukemias in mice. *Proc Natl Acad Sci U S A* 2000;97:10984–10989.
99. Kung AL, Rebel VI, Bronson RT, et al. Gene dose-dependent control of hematopoiesis and hematologic tumor suppression by CBP. *Genes Dev* 2000;14:272–277.
100. Tefferi A. Novel mutations and their functional and clinical relevance in myeloproliferative neoplasms: JAK2, MPL, TET2, ASXL1, CBL, IDH and IKZF1. *Leukemia* 2010;24:1128–1138.
101. Patel JP, Gonen M, Figueroa ME, et al. Prognostic relevance of integrated genetic profiling in acute myeloid leukemia. *N Engl J Med* 2012;366:1079–1089.
102. Moran-Crusio K, Reavie L, Shih A, et al. Tet2 loss leads to increased hematopoietic stem cell self-renewal and myeloid transformation. *Cancer Cell* 2011;20:11–24.
103. Dang L, Jin S, Su SM. IDH mutations in glioma and acute myeloid leukemia. *Trends Mol Med* 2010;16:387–397.
104. Dang L, White DW, Gross S, et al. Cancer-associated IDH1 mutations produce 2-hydroxyglutarate. *Nature* 2009;462:739–744.
105. Ley TJ, Ding L, Walter MJ, et al. DNMT3A mutations in acute myeloid leukemia. *N Engl J Med* 2010;363:2424–2433.
106. Tadokoro Y, Ema H, Okano M, et al. De novo DNA methyltransferase is essential for self-renewal, but not for differentiation, in hematopoietic stem cells. *J Exp Med* 2007;204:715–722.
107. Tanaka S, Miyagi S, Sashida G, et al. Ezh2 augments leukemogenicity by reinforcing differentiation blockage in acute myeloid leukemia. *Blood* 2012;120:1107–1117.
108. Ernst T, Chase AJ, Score J, et al. Inactivating mutations of the histone methyltransferase gene EZH2 in myeloid disorders. *Nat Genet* 2010;42:722–726.
109. Delgado MD, Albajar M, Gomez-Casares MT, et al. MYC oncogene in myeloid neoplasias. *Clin Transl Oncol* 2013;15:87–94.
110. O'Neil J, Look AT. Mechanisms of transcription factor deregulation in lymphoid cell transformation. *Oncogene* 2007;26:6838–6849.
111. Dang CV. MYC on the path to cancer. *Cell* 2012;149:22–35.
112. Van Vlierberghe P, Ferrando A. The molecular basis of T cell acute lymphoblastic leukemia. *J Clin Invest* 2012;122:3398–3406.
113. Steelman LS, Franklin RA, Abrams SL, et al. Roles of the Ras/Raf/MEK/ERK pathway in leukemia therapy. *Leukemia* 2011;25:1080–1094.
114. Chung E, Kondo M. Role of Ras/Raf/MEK/ERK signaling in physiological hematopoiesis and leukemia development. *Immunol Res* 2011;49:248–268.
115. Takashima A, Faller DV. Targeting the RAS oncogene. *Expert Opin Ther Targets* 2013;17:507–531.
116. Lancet JE, Karp JE. Farnesyltransferase inhibitors in hematologic malignancies: new horizons in therapy. *Blood* 2003;102:3880–3889.
117. Braun BS, Shannon K. Targeting Ras in myeloid leukemias. *Clin Cancer Res* 2008;14:2249–2252.
118. Moorman AV, Harrison CJ, Buck GA, et al. Karyotype is an independent prognostic factor in adult acute lymphoblastic leukemia (ALL): analysis of cytogenetic data from patients treated on the Medical Research Council (MRC) UKALLXII/Eastern Cooperative Oncology Group (ECOG) 2993 trial. *Blood* 2007;109:3189–3197.
119. Jones LK, Saha V. Philadelphia positive acute lymphoblastic leukaemia of childhood. *Br J Haematol* 2005;130:489–500.
120. Nowell PC, Hungerford DA. Chromosome studies on normal and leukemic human leukocytes. *J Natl Cancer Inst* 1960;25:85–109.
121. Rowley JD. Letter: A new consistent chromosomal abnormality in chronic myelogenous leukaemia identified by quinacrine fluorescence and Giemsa staining. *Nature* 1973;243:290–293.
122. Hu Y, Liu Y, Pelletier S, et al. Requirement of Src kinases Lyn, Hck and Fgr for BCR-ABL1-induced B-lymphoblastic leukemia but not chronic myeloid leukemia. *Nat Genet* 2004;36:453–461.
123. Deininger M, Buchdunger E, Druker BJ. The development of imatinib as a therapeutic agent for chronic myeloid leukemia. *Blood* 2005;105:2640–2653.
124. Stirewalt DL, Radich JP. The role of FLT3 in haematopoietic malignancies. *Nat Rev Cancer* 2003;3:650–665.
125. Griffith J, Black J, Faerman C, et al. The structural basis for autoinhibition of FLT3 by the juxtamembrane domain. *Mol Cell* 2004;13:169–178.
126. Abu-Duhier FM, Goodeve AC, Wilson GA, et al. FLT3 internal tandem duplication mutations in adult acute myeloid leukaemia define a high-risk group. *Br J Haematol* 2000;111:190–195.
127. Kiyoi H, Naoe T, Nakano Y, et al. Prognostic implication of FLT3 and N-RAS gene mutations in acute myeloid leukemia. *Blood* 1999;93:3074–3080.
128. Meshinchi S, Woods WG, Stirewalt DL, et al. Prevalence and prognostic significance of FLT3 internal tandem duplication in pediatric acute myeloid leukemia. *Blood* 2001;97:89–94.
129. Griffith JD. Point mutations in the FLT3 gene in AML. *Blood* 2001;97:2193A–2193.
130. Kampa-Schittenhelm KM, Heinrich MC, Akmut F, et al. Quizartinib (AC220) is a potent second generation class III tyrosine kinase inhibitor that displays a distinct inhibition profile against mutant-FLT3, -PDGFRA and -KIT isoforms. *Mol Cancer* 2013;12:19.

131. Frohling S, Scholl C, Levine RL, et al. Identification of driver and passenger mutations of FLT3 by high-throughput DNA sequence analysis and functional assessment of candidate alleles. *Cancer Cell* 2007;12:501–513.
132. Pardanani AD, Levine RL, Lasho T, et al. MPLW515 mutations in myeloproliferative and other myeloid disorders: a study of 1182 patients. *Blood* 2006;108:3472–3476.
133. Hussein K, Bock O, Theophile K, et al. MPLW515L mutation in acute megakaryoblastic leukemia. *Leukemia* 2009;23:852–855.
134. Malinge S, Ragu C, Della-Valle V, et al. Activating mutations in human acute megakaryoblastic leukemia. *Blood* 2008;112:4220–4226.
135. Baker SJ, Rane SC, Reddy EP. Hematopoietic cytokine receptor signaling. *Oncogene* 2007;26:6724–6737.
136. Steensma DP, McClure RF, Karp JE, et al. JAK2 V617F is a rare finding in de novo acute myeloid leukemia, but STAT3 activation is common and remains unexplained. *Leukemia* 2006;20:971–978.
137. Frohling S, Lipka DB, Kayser S, et al. Rare occurrence of the JAK2 V617F mutation in AML subtypes M5, M6, and M7. *Blood* 2006;107:1242–1243.
138. Walters DK, Mercher T, Gu TL, et al. Activating alleles of JAK3 in acute megakaryoblastic leukemia. *Cancer Cell* 2006;10:65–75.
139. Mullighan CG, Zhang J, Harvey RC, et al. JAK mutations in high-risk childhood acute lymphoblastic leukemia. *Proc Natl Acad Sci U S A* 2009;106:9414–9418.
140. Benekli M, Xia Z, Donohue KA, et al. Constitutive activity of signal transducer and activator of transcription 3 protein in acute myeloid leukemia blasts is associated with short disease-free survival. *Blood* 2002;99:252–257.
141. Redell MS, Ruiz MJ, Gerbing RB, et al. FACS analysis of Stat3/5 signaling reveals sensitivity to G-CSF and IL-6 as a significant prognostic factor in pediatric AML: a Children's Oncology Group report. *Blood* 2013;121:1083–1093.
142. Palmi C, Vendramini E, Silvestri D, et al. Poor prognosis for P2RY8-CRLF2 fusion but not for CRLF2 over-expression in children with intermediate risk B-cell precursor acute lymphoblastic leukemia. *Leukemia* 2012;26:2245–2253.
143. Haber DA, Buckler AJ, Glaser T, et al. An internal deletion within an 11p13 zinc finger gene contributes to the development of Wilms' tumor. *Cell* 1990;61:1257–1269.
144. Hohenstein P, Hastie ND. The many facets of the Wilms' tumour gene, WT1. *Hum Mol Genet* 2006;15:R196–R201.
145. Baird PN, Simmons PJ. Expression of the Wilms' tumor gene (WT1) in normal hemopoiesis. *Exp Hematol* 1997;25:312–320.
146. Yang L, Han Y, Suarez Saiz F, et al. A tumor suppressor and oncogene: the WT1 story. *Leukemia* 2007;21:868–876.
147. Miyagi T, Ahuja H, Kubota T, et al. Expression of the candidate Wilm's tumor gene, WT1, in human leukemia cells. *Leukemia* 1993;7:970–977.
148. Miwa H, Beran M, Saunders GF. Expression of the Wilms' tumor gene (WT1) in human leukemias. *Leukemia* 1992;6:405–409.
149. Smith SI, Down M, Boyd AW, et al. Expression of the Wilms' tumor suppressor gene, WT1, reduces the tumorigenicity of the leukemic cell line M1 in C.B-17 scid/scid mice. *Cancer Res* 2000;60:808–814.
150. King-Underwood L, Renshaw J, Pritchard-Jones K. Mutations in the Wilms' tumor gene WT1 in leukemias. *Blood* 1996;87:2171–2179.
151. Summers K, Stevens J, Kakkas I, et al. Wilms' tumour 1 mutations are associated with FLT3-ITD and failure of standard induction chemotherapy in patients with normal karyotype AML. *Leukemia* 2007;21:550–551.
152. Virappane P, Gale R, Hills R, et al. Mutation of the Wilms' tumor 1 gene is a poor prognostic factor associated with chemotherapy resistance in normal karyotype acute myeloid leukemia: the United Kingdom Medical Research Council Adult Leukemia Working Party. *J Clin Oncol* 2008;26:5429–5435.
153. Paschka P, Marcucci G, Ruppert AS, et al. Wilms' tumor 1 gene mutations independently predict poor outcome in adults with cytogenetically normal acute myeloid leukemia: a cancer and leukemia group B study. *J Clin Oncol* 2008;26:4595–4602.
154. Gaidzik VI, Schlenk RF, Moschny S, et al. Prognostic impact of WT1 mutations in cytogenetically normal acute myeloid leukemia: a study of the German-Austrian AML Study Group. *Blood* 2009;113:4505–4511.
155. Vousden KH, Lu X. Live or let die: the cell's response to p53. *Nat Rev Cancer* 2002;2:594–604.
156. Nakai H, Misawa S, Taniwaki M, et al. Prognostic significance of loss of a chromosome 17p and p53 gene mutations in blast crisis of chronic myelogenous leukaemia. *Br J Haematol* 1994;87:425–427.
157. Dohner H, Fischer K, Bentz M, et al. p53 gene deletion predicts for poor survival and non-response to therapy with purine analogs in chronic B-cell leukemias. *Blood* 1995;85:1580–1589.
158. Sander CA, Yano T, Clark HM, et al. p53 mutation is associated with progression in follicular lymphomas. *Blood* 1993;82:1994–2004.
159. Venkatchalam S, Shi YP, Jones SN, et al. Retention of wild-type p53 in tumors from p53 heterozygous mice: reduction of p53 dosage can promote cancer formation. *Embo J* 1998;17:4657–4667.
160. Herzog G, Lu-Hesselmann J, Zimmermann Y, et al. Microsatellite instability and p53 mutations are characteristic of subgroups of acute myeloid leukemia but independent events. *Haematologica* 2005;90:693–695.
161. Fenaux P, Jonveaux P, Quiquandon I, et al. P53 gene mutations in acute myeloid leukemia with 17p monosomy. *Blood* 1991;78:1652–1657.
162. Watanabe T, Hotta T, Ichikawa A, et al. The MDM2 oncogene overexpression in chronic lymphocytic leukemia and low-grade lymphoma of B-cell origin. *Blood* 1994;84:3158–3165.
163. Haferlach C, Dicker F, Herholz H, et al. Mutations of the TP53 gene in acute myeloid leukemia are strongly associated with a complex aberrant karyotype. *Leukemia* 2008;22:1539–1541.
164. Schoch C, Kern W, Kohlmann A, et al. Acute myeloid leukemia with a complex aberrant karyotype is a distinct biological entity characterized by genomic imbalances and a specific gene expression profile. *Genes Chromosomes Cancer* 2005;43:227–238.
165. van der Holt B, Breems DA, Berna Beverloo H, et al. Various distinctive cytogenetic abnormalities in patients with acute myeloid leukaemia aged 60 years and older express adverse prognostic value: results from a prospective clinical trial. *Br J Haematol* 2007;136:96–105.
166. Seifert H, Mohr B, Thiede C, et al. The prognostic impact of 17p (p53) deletion in 2272 adults with acute myeloid leukemia. *Leukemia* 2009;23:656–663.
167. Fenaux P, Preudhomme C, Quiquandon I, et al. Mutations of the P53 gene in acute myeloid leukaemia. *Br J Haematol* 1992;80:178–183.
168. Lai JL, Preudhomme C, Zandecki M, et al. Myelodysplastic syndromes and acute myeloid leukemia with 17p deletion. An entity characterized by specific dysgranulopoiesis and a high incidence of P53 mutations. *Leukemia* 1995;9:370–381.
169. Nahi H, Selivanova G, Lehmann S, et al. Mutated and non-mutated TP53 as targets in the treatment of leukaemia. *Br J Haematol* 2008;141:445–453.
170. Schach M, Soucek S, Thiede C, et al. MDR1 and MRP1 gene expression are independent predictors for treatment outcome in adult acute myeloid leukaemia. *Br J Haematol* 2005;128:324–332.
171. Cavalcanti GB Jr, Vasconcelos FC, Pinto de Faria C, et al. Coexpression of p53 protein and MDR functional phenotype in leukemias: the predominant association in chronic myeloid leukemia. *Cytometry B Clin Cytom* 2004;61:1–8.
172. Radtke F, Wilson A, MacDonald HR. Notch signaling in hematopoiesis and lymphopoiesis: lessons from Drosophila. *Bioessays* 2005;27:1117–1128.
173. Pancewicz J, Nicot C. Current views on the role of Notch signaling and the pathogenesis of human leukemia. *BMC Cancer* 2011;11:502.
174. Weng AP, Ferrando AA, Lee W, et al. Activating mutations of NOTCH1 in human T cell acute lymphoblastic leukemia. *Science* 2004;306:269–271.
175. Thompson BJ, Buonamici S, Sulis ML, et al. The SCFFBW7 ubiquitin ligase complex as a tumor suppressor in T cell leukemia. *J Exp Med* 2007;204:1825–1835.
176. DeAngelo DJ, Stone JR, Silverman LB, et al. A phase I clinical Trial of the notch inhibitor MK-0752 in patients with T-cell acute lymphoblastic leukemia/lymphoma (T-ALL) and other leukemias. *ASCO Meeting Abstracts* 2006:6585.
177. Real PJ, Tosello V, Palomero T, et al. Gamma-secretase inhibitors reverse glucocorticoid resistance in T cell acute lymphoblastic leukemia. *Nat Med* 2005;15:50–58.
178. Federici L, Falini B. Nucleophosmin mutations in acute myeloid leukemia: a tale of protein unfolding and mislocalization. *Protein Sci* 2013;22:545–556.
179. Falini B, Mecucci C, Tiacci E, et al. Cytoplasmic nucleophosmin in acute myelogenous leukemia with a normal karyotype. *N Engl J Med* 2005;352:254–266.
180. Falini B, Nicoletti I, Martelli MF, et al. Acute myeloid leukemia carrying cytoplasmic/mutated nucleophosmin (NPMc+ AML): biologic and clinical features. *Blood* 2007;109:874–885.
181. Mullighan CG. Molecular genetics of B-precursor acute lymphoblastic leukemia. *J Clin Invest* 2012;122:3407–3415.
182. Mullighan CG, Goorha S, Radtke I, et al. Genome-wide analysis of genetic alterations in acute lymphoblastic leukaemia. *Nature* 2007;446:758–764.
183. Nutt SL, Heavey B, Rolink AG, et al. Commitment to the B-lymphoid lineage depends on the transcription factor Pax5. *Nature* 1999;401:556–562.
184. Kawamata N, Pennella MA, Woo JL, et al. Dominant-negative mechanism of leukemogenic PAX5 fusions. *Oncogene* 2012;31:966–977.
185. Mullighan CG, Su X, Zhang J, et al. Deletion of IKZF1 and prognosis in acute lymphoblastic leukemia. *N Engl J Med* 2009;360:470–480.
186. Georgopoulos K, Bigby M, Wang JH, et al. The Ikaros gene is required for the development of all lymphoid lineages. *Cell* 1994;79:143–156.
187. Merckenschlager M. Ikaros in immune receptor signaling, lymphocyte differentiation, and function. *FEBS Lett* 2010;584:4910–4914.
188. Bottardi S, Zmiri FA, Bourgoin V, et al. Ikaros interacts with P-TEFb and cooperates with GATA-1 to enhance transcription elongation. *Nucleic Acids Res* 2011;39:3505–3519.
189. Mullighan CG, Miller CB, Radtke I, et al. BCR-ABL1 lymphoblastic leukaemia is characterized by the deletion of Ikaros. *Nature* 2008;453:110–114.
190. Lu Q, Kamps MP. Heterodimerization of Hox proteins with Pbx1 and oncoprotein E2a-Pbx1 generates unique DNA-binding specificities at nucleotides predicted to contact the N-terminal arm of the Hox homeodomain—demonstration of Hox-dependent targeting of E2a-Pbx1 in vivo. *Oncogene* 1997;14:75–83.
191. Golub TR, Barker GF, Lovett M, et al. Fusion of PDGF receptor beta to a novel ets-like gene, tel, in chronic myelomonocytic leukemia with t(5;12) chromosomal translocation. *Cell* 1994;77:307–316.
192. Higuchi M, O'Brien D, Kumaravelu P, et al. Expression of a conditional AML1-ETO oncogene bypasses embryonic lethality and establishes a murine model of human t(8;21) acute myeloid leukemia. *Cancer Cell* 2002;1:63–74.

193. Wiemels JL, Cazzaniga G, Daniotti M, et al. Prenatal origin of acute lymphoblastic leukaemia in children. *Lancet* 1999;354:1499–1503.
194. Gilliland DC. Molecular genetics of human leukemias: new insights into therapy. *Semin Hematol* 2002;39:6–11.
195. Kelly LM, Liu Q, Kutok JL, et al. FLT3 internal tandem duplication mutations associated with human acute myeloid leukemias induce myeloproliferative disease in a murine bone marrow transplant model. *Blood* 2002;99:310–318.
196. Chan IT, Kutok JL, Williams IR, et al. Conditional expression of oncogenic K-ras from its endogenous promoter induces a myeloproliferative disease. *J Clin Invest* 2004;113:528–538.
197. Sanders MA, Valk PJ. The evolving molecular genetic landscape in acute myeloid leukaemia. *Curr Opin Hematol* 2013;20:79–85.
198. Welch JS, Ley TJ, Link DC, et al. The origin and evolution of mutations in acute myeloid leukemia. *Cell* 2012;150:264–278.