

CHAPTER 5

REFERENCES

1. Irons RD, Stillman WS: The process of leukemogenesis. *Environ Health Perspect* 1996, 104 Suppl (December):1239–46.
2. Kennedy JA, Barabé F: Investigating human leukemogenesis: from cell lines to in vivo models of human leukemia. *Leukemia* 2008, 22:2029–40.
3. Leary AG, Zeng HQ, Clark SC, Ogawa M: Growth factor requirements for survival in G0 and entry into the cell cycle of primitive human hemopoietic progenitors. *Proc Natl Acad Sci U S A* 1992, 89:4013–7.
4. Misaghian N, Ligresti G, Steelman LS, Bertrand FE, Bäsecke J, Libra M, Nicoletti F, Stivala F, Milella M, Tafuri A, Cervello M, Martelli a M, McCubrey JA: Targeting the leukemic stem cell: the Holy Grail of leukemia therapy. *Leukemia* 2009, 23:25–42.
5. Haidar C, Pharm D, Pauley JL, Bickert B, Semla TP, Thompson MA: Pediatric Leukemias. *PSAP* .
6. Kantarjian EH, Estey SH, Faderl HM: *Acute Leukemias*. Springer; 2008.
7. Schindler JW, Van Buren D, Foudi A, Krejci O, Qin J, Orkin SH, Hock H: TEL-AML1 corrupts hematopoietic stem cells to persist in the bone marrow and initiate leukemia. *Cell Stem Cell* 2009, 5:43–53.
8. Rizzari C, Sala A, Chiesa R, Citterio M, Biondi A: Acute Lymphoblastic Leukemia. *Orphanet Encycl* 2004, 350:1–13.
9. Gökbuget N, Hoelzer D: Recent approaches in acute lymphoblastic leukemia in adults. *Rev Clin Exp Hematol* 2002, 6.2:114–141.
10. Ching-Hon Pui: Childhood leukemias. *N Engl J Med* 1995, 332:1618–1630.
11. Uckun FM, Gaynon PS, Sensel MG, Nachman J, Trigg ME, Steinherz PG, Hutchinson R, Bostrom BC, Sather HN, Reaman GH: Clinical features and treatment outcome of childhood T-lineage acute lymphoblastic leukemia according to the apparent maturational stage of T-lineage leukemic blasts: a Children’s Cancer Group study. *J Clin Oncol* 1997, 15:2214–2221.
12. Pui C-H, Evans WE: Treatment of acute lymphoblastic leukemia. *N Engl J Med* 2006, 354:166–78.
13. Silverman LB, Gelber RD, Dalton VK, Asselin BL, Barr RD, Clavell LA, Hurwitz CA, Moghrabi A, Samson Y, Schorin MA, Arkin S, Declerck L, Cohen HJ, Sallan SE: Improved outcome for children with acute lymphoblastic leukemia: results of Dana-Farber Consortium Protocol 91-01. *Blood* 2001, 97:1211–1218.

14. Morrison SJ, Spradling AC: Stem cells and niches: mechanisms that promote stem cell maintenance throughout life. *Cell* 2008, 132:598–611.
15. Jude CD, Gaudet J, Speck N, Ernst P: Leukemia and Hematopoietic Stem Cells: Balancing Proliferation and Quiescence. 2010, 7:586–591.
16. Wang LC, Swat W, Fujiwara Y, Davidson L, Visvader J, Kuo F, Alt FW, Gilliland DG, Golub TR, Orkin SH: The TEL/ETV6 gene is required specifically for hematopoiesis in the bone marrow. *Genes Dev* 1998, 12:2392–2402.
17. Fiedler K, Brunner C: *Mechanisms Controlling Hematopoiesis*. March 2012. In Tech; 2012.
18. Crans HN, Sakamoto KM: Transcription factors and translocations in lymphoid and myeloid leukemia. *Leukemia* 2001, 15:313–331.
19. Orkin SH, Zon LI: Hematopoiesis: an evolving paradigm for stem cell biology. *Cell* 2008, 132:631–44.
20. Kim SI, Bresnick EH: Transcriptional control of erythropoiesis: emerging mechanisms and principles. *Oncogene* 2007, 26:6777–94.
21. Nutt SL, Kee BL: The transcriptional regulation of B cell lineage commitment. *Immunity* 2007, 26:715–25.
22. Blom B, Spits H: Development of human lymphoid cells. *Annu Rev Immunol* 2006, 24:287–320.
23. O’Neil J, Look A: Mechanisms of transcription factor deregulation in lymphoid cell transformation. *Oncogene* 2007, 26:6838–49.
24. Look AT: Oncogenic Transcription Factors in the Human Acute Leukemias. *Science (80-)* 1997, 278:1059–1064.
25. Jeha S, Pei D, Raimondi SC, Onciu M, Campana D, Sandlund JT, Ribeiro RC, Rubnitz JE, Howard SC, Downing R, Evans WE, Relling MV, Pui C: Increased Risk for CNS Relapse in Pre-B Cell Leukemia with the t (1;19)/TCF3-PBX1. *Leukemia* 2010, 23:1406–1409.
26. Weng AP, Millholland JM, Yashiro-Ohtani Y, Arcangeli ML, Lau A, Wai C, Del Bianco C, Rodriguez CG, Sai H, Tobias J, Li Y, Wolfe MS, Shachaf C, Felsher D, Blacklow SC, Pear WS, Aster JC: c-Myc is an important direct target of Notch1 in T-cell acute lymphoblastic leukemia/lymphoma. *Genes Dev* 2006, 20:2096–109.
27. Ramirez O, Linares A, Trujillo ML CJ: WT1 mRNA in cerebrospinal fluid associated with relapse in pediatric lymphoblastic leukemia. *J Pediatr Hematol Oncol* 2003, 25:453–8.
28. Heesch S, Goekbuget N, Stroux A, Tancher JO, Schlee C, Burmeister T, Schwartz S, Blau O, Keilholz U, Busse A, Hoelzer D, Thiel E, Hofmann WK, Baldus CD: Prognostic implications of mutations and expression of the Wilms tumor 1 (WT1) gene in adult acute T-lymphoblastic leukemia. *Haematologica* 2010, 95:942–9.

29. De Jong D, Voetdijk BM, Beverstock GC, van Ommen GJ, Willemze R KP: Activation of the c-myc oncogene in a precursor-B-cell blast crisis of follicular lymphoma, presenting as composite lymphoma. *N Engl J Med* 1988, 318:1373–8.
30. Williams MT, Yousafzai Y, Cox C, Blair A, Carmody R, Sai S, Chapman KE, McAndrew R, Thomas A, Spence A, Gibson B, Graham GJ HC: Interleukin-15 enhances cellular proliferation and upregulates CNS homing molecules in pre-B acute lymphoblastic leukemia. *Blood* 2014, 123.
31. Baldus CD, Burmeister T, Martus P, Schwartz S, Gökbuget N, Bloomfield CD, Hoelzer D, Thiel E, Hofmann WK: High expression of the ETS transcription factor ERG predicts adverse outcome in acute T-lymphoblastic leukemia in adults. *J Clin Oncol* 2006, 24:4714–20.
32. Nardi NB, Alegre P: The hematopoietic stroma. *Braz J Med Biol Res* 1999, 32:601–609.
33. Yoshihara H, Arai F, Hosokawa K, Hagiwara T, Takubo K, Nakamura Y, Gomei Y, Iwasaki H, Matsuoka S, Miyamoto K, Miyazaki H, Takahashi T, Suda T: Thrombopoietin/MPL signaling regulates hematopoietic stem cell quiescence and interaction with the osteoblastic niche. *Cell Stem Cell* 2007, 1:685–97.
34. Carmichael CL, Metcalf D, Henley KJ, Kruse EA, Di Rago L, Mifsud S, Alexander WS, Kile BT: Hematopoietic overexpression of the transcription factor Erg induces lymphoid and erythro-megakaryocytic leukemia. *Proc Natl Acad Sci U S A* 2012, 109:15437–42.
35. Zhu J, Emerson SG: Hematopoietic cytokines, transcription factors and lineage commitment. *Oncogene* 2002, 21:3295–3313.
36. Metcalf D: Hematopoietic cytokines. *Blood* 2007, 111:485–491.
37. Kaushansky K: Hematopoietic growth factors, signaling and the chronic myeloproliferative disorders. *Cytokine Growth Factor Rev* 2006, 17:423–430.
38. Rizo A, Vellenga E, de Haan G, Schuringa JJ: Signaling pathways in self-renewing hematopoietic and leukemic stem cells: do all stem cells need a niche? *Hum Mol Genet* 2006, 15:210–9.
39. Ivanovic Z: Interleukin-3 and ex vivo maintenance of hematopoietic stem cells: facts and controversies. *Eur Cytokine Netw* 2004, 15:6–13.
40. Edward Allan R Sison & Patrick Brown: The bone marrow microenvironment and leukemia: biology and therapeutic targeting. *Expert Rev Hematol* 2011, 4:271–283.
41. Luis TC, Killmann NMB, Staal FJT: Signal transduction pathways regulating hematopoietic stem cell biology: introduction to a series of Spotlight Reviews. *Leukemia* 2012, 26:86–90.
42. Khan NI, Bendall LJ: Role of WNT signaling in normal and malignant hematopoiesis. *Histol Histopathol* 2006, 21:761–74.

43. Huelsken J, Behrens J: The Wnt signalling pathway. *J Cell Sci* 2002, 115:3977–3978.
44. Reya T, Duncan AW, Ailles L, Domen J, Scherer DC, Willert K, Hintz L, Nusse RWI: A role for Wnt signalling in self-renewal of haematopoietic stem cells. *Nature* 2003, 423:409–14.
45. Rawadi G, Vayssière B, Dunn F, Baron R RRS: BMP-2 controls alkaline phosphatase expression and osteoblast mineralization by a Wnt autocrine loop. *J Bone Min Res* 2003, 18:1842–53.
46. Weber BN, Chi AW-S, Chavez A, Yashiro-Ohtani Y, Yang Q, Shestova O, Bhandoola A: A critical role for TCF-1 in T-lineage specification and differentiation. *Nature* 2011, 476:63–8.
47. Ge X, Wang X: Role of Wnt canonical pathway in hematological malignancies. *J Hematol Oncol* 2010, 3:33–38.
48. McWhirter JR, Neuteboom ST, Wancewicz E V, Monia BP, Downing JR, Murre C: Oncogenic homeodomain transcription factor E2A-Pbx1 activates a novel WNT gene in pre-B acute lymphoblastoid leukemia. *Proc Natl Acad Sci U S A* 1999, 96:11464–9.
49. Román-Gómez J, Cordeu L, Agirre X, Jiménez-Velasco A, San José-Eneriz E, Garate L, Calasanz MJ, Heiniger A, Torres A, Prosper F: Epigenetic regulation of Wnt-signaling pathway in acute lymphoblastic leukemia. *Blood* 2007, 109:3462–9.
50. Khan N, Bradstock K, Bendall L: Activation of Wnt/beta-catenin pathway mediates growth and survival in B-cell progenitor acute lymphoblastic leukaemia. *Br J Haematol* 2007, 138:338–48.
51. Hogan LE, Meyer J a, Yang J, Wang J, Wong N, Yang W, Condos G, Hunger SP, Raetz E, Saffery R, Relling M V, Bhojwani D, Morrison DJ, Carroll WL: Integrated genomic analysis of relapsed childhood acute lymphoblastic leukemia reveals therapeutic strategies. *Blood* 2011, 118:5218–26.
52. Burke MJ, Bhatla T: Epigenetic Modifications in Pediatric Acute Lymphoblastic Leukemia. *Front Pediatr* 2014, 2(May):42.
53. Aithal MGS, Rajeswari N: Role of Notch signalling pathway in cancer and its association with DNA methylation. *J Genet* 2013, 92:667–75.
54. Schwanbeck R, Just U: The Notch signaling pathway in hematopoiesis and hematologic malignancies. *Haematologica* 2011, 96:1735–7.
55. Weber JM, Calvi LM: Notch Signaling and the Bone Marrow Hematopoietic Stem Cell Niche. *Bone* 2010, 46:281–285.
56. Warr MR, Pietras EM, Passegué E: Mechanisms controlling hematopoietic stem cell functions during normal hematopoiesis and hematological malignancies. *Wiley Interdiscip Rev Syst Biol Med* 2011, 3:681–701.

57. Zweidler-McKay PA, He Y, Xu L, Rodriguez CG, Karnell FG, Carpenter AC, Aster JC, Allman D, Pear WS: Notch signaling is a potent inducer of growth arrest and apoptosis in a wide range of B-cell malignancies. *Blood* 2005, 106:3898–906.
58. Leong KG, Karsan A: Recent insights into the role of Notch signaling in tumorigenesis. *Blood* 2006, 107:2223–33.
59. Buonamici S, Trimarchi T, Ruocco MG, Reavie L, Cathelin S, Mar BG, Klinakis A, Lukyanov Y, Tseng JC, Sen F, Gehrie E, Li M, Newcomb E, Zavadil J, Meruelo D, Lipp M, Ibrahim S, Efstratiadis A, Zagzag D, Bromberg JS, Dustin ML, Aifantis I: CCR7 signalling as an essential regulator of CNS infiltration in T-cell leukaemia. *Nature* 2009, 459:1000–4.
60. Lim Y: Hedgehog Signaling in Hematopoiesis. *Crit Rev Eukaryot Gene Expr* 2010, 20:129–139.
61. Irvine DA, Copland M: Targeting hedgehog in hematologic malignancy. *Blood* 2012, 119:2196–204.
62. Lin TL, Wang QH, Brown P, Peacock C, Merchant AA, Brennan S, Jones E, McGovern K, Watkins DN, Sakamoto KM, Matsui W: Self-renewal of acute lymphocytic leukemia cells is limited by the Hedgehog pathway inhibitors cyclopamine and IPI-926. *PLoS One* 2010, 5:e15262.
63. Feng S, Huang Y CZ: Does VEGF secreted by leukemic cells increase the permeability of blood-brain barrier by disrupting tight-junction proteins in central nervous system leukemia? *Med Hypotheses* 2011, 76:618–21.
64. Steelman LS, Franklin RA, Abrams SL, Chappell W, Kempf CR, Bäsecke J, Stivala F, Donia M, Fagone P, Nicoletti F, Libra M, Ruvolo P, Ruvolo V, Evangelisti C, Martelli AM MJ: Roles of the Ras/Raf/MEK/ERK pathway in leukemia therapy. *Leukemia* 2011, 25:1080–94.
65. Avellino R, Romano S, Parasole R, Bisogni R, Lamberti A, Poggi V, Venuta S, Romano MF: Rapamycin stimulates apoptosis of childhood acute lymphoblastic leukemia cells. *Blood* 2005, 106:1400–6.
66. Jotta PY, Ganazza MA, Silva A, Viana MB, da Silva MJ, Zambaldi LJG, Barata JT, Brandalise SR, Yunes JA: Negative prognostic impact of PTEN mutation in pediatric T-cell acute lymphoblastic leukemia. *Leukemia* 2010, 24:239–42.
67. Levitzki A, Klein S: Signal transduction therapy of cancer. *Mol Aspects Med* 2010, 31:287–329.
68. Amir T, Fathi, Steven Grant JEK: Exploiting Cellular Pathways to Develop New Treatment Strategies for AML. *Cancer Treat Rev* 2010, 36:142–150.
69. Zhao WL: Targeted therapy in T-cell malignancies: dysregulation of the cellular signaling pathways. *Leukemia* 2010, 24:13–21.

70. Okumura N, Yoshida H, Kitagishi Y, Murakami M, Nishimura Y, Matsuda S: PI3K/AKT/PTEN Signaling as a Molecular Target in Leukemia Angiogenesis. *Adv Hematol* 2012, 2012:843085.
71. Case M, Matheson E, Minto L, Hassan R, Harrison CJ, Bown N, Bailey S, Vormoor J, Hall AG, Irving JAE: Mutation of genes affecting the RAS pathway is common in childhood acute lymphoblastic leukemia. *Cancer Res* 2008, 68:6803–9.
72. Chappell WH, Linda S Steelman, Abrams SL, Donia M, Paolo Fagone, Graziella Malaponte Mazzarino MC, Nicoletti F, Libra M, Maksimovic-Ivanic D, Mijatovic S, Montalto G, Cervello M, Laidler P, Milella M, Tafuri A, Bonati A, Evangelisti C, Cocco L, Martelli A, McCubrey JA: Ras/Raf/MEK/ERK and PI3K/PTEN/Akt/mTOR Inhibitors: Rationale and Importance to Inhibiting These Pathways in Human Health. *Oncotarget* 2011, 2:135–164.
73. Vainchenker W C, Onstantinescu S: JAK/STAT signaling in hematological malignancies. *Oncogene* 2013, 32:2601–13.
74. Quintás-Cardama A, Verstovsek S: Molecular Pathways:Jak/STAT pathway: mutations, inhibitors, and resistance. *Clin Cancer Res* 2013, 19:1933–40.
75. Kim SJ, Letterio J: Transforming growth factor-beta signaling in normal and malignant hematopoiesis. *Leukemia* 2003, 17:1731–7.
76. Dong M, Blobel GC: Review in translational hematology Role of transforming growth factor- β in hematologic malignancies. *Blood* 2006, 107:4589–4596.
77. Kubiczakova L, Sedlarikova L, Hajek R, Sevcikova S: TGF- β - an excellent servant but a bad master. *J Transl Med* 2012, 10:183.
78. Ross ME, Zhou X, Song G, Shurtleff S a, Girtman K, Williams WK, Liu HC, Mahfouz R, Raimondi SC, Lenny N, Patel A, Downing JR: Classification of pediatric acute lymphoblastic leukemia by gene expression profiling. *Blood* 2003, 102:2951–9.
79. Chiaretti A, Ruggiero A, Coccia P, Antonelli A, Pierri F, Barone G, Attinà G, Iuvone L, Maurizi P, Riccardi R: Expression of liquoral neuroprotection markers in children with acute lymphoblastic leukemia. *Leuk Res* 2011, 35:1467–71.
80. Chiaretti S, Li X, Gentleman R, Vitale A, Wang KS, Mandelli F, Foà R, Ritz J: Gene expression profiles of B-lineage adult acute lymphocytic leukemia reveal genetic patterns that identify lineage derivation and distinct mechanisms of transformation. *Clin Cancer Res* 2005, 11:7209–19.
81. Juric D, Lacayo NJ, Ramsey MC, Racevskis J, Wiernik PH, Rowe JM, Goldstone AH, O'Dwyer PJ, Paietta E, Sikic BI: Differential gene expression patterns and interaction networks in BCR-ABL-positive and -negative adult acute lymphoblastic leukemias. *J Clin Oncol* 2007, 25:1341–9.

82. Stam RW, Schneider P, Hagelstein JAP, van der Linden MH, Stumpel DJPM, de Menezes RX, de Lorenzo P, Valsecchi MG, Pieters R: Gene expression profiling-based dissection of MLL translocated and MLL germline acute lymphoblastic leukemia in infants. *Blood* 2010, 115:2835–44.
83. Tsutsumi S, Taketani T, Nishimura K: Two Distinct Gene Expression Signatures in Pediatric Acute Lymphoblastic Leukemia with MLL Rearrangements Two Distinct Gene Expression Signatures in Pediatric Acute Lymphoblastic. *Cancer Res* 2006, 63:4882–4887.
84. Bhojwani D, Kang H, Moskowitz NP, Min DJ, Lee H, Potter JW, Davidson G, Willman CL, Borowitz MJ, Belitskaya-Levy I, Hunger SP, Raetz EA, Carroll WL: Biologic pathways associated with relapse in childhood acute lymphoblastic leukemia: a Children's Oncology Group study. *Blood* 2006, 108:711–7.
85. Mullighan CG, Phillips LA, Su X, Ma J, Miller CB, Shurtleff SA, Downing JR: Genomic analysis of the clonal origins of relapsed acute lymphoblastic leukemia. *Science* 2008, 322:1377–80.
86. Rivera GK, Zhou Y, Hancock ML, Gajjar A, Rubnitz J, Ribeiro RC, Sandlund JT, Hudson M, Relling M, Evans WE, Pui CH: Bone marrow recurrence after initial intensive treatment for childhood acute lymphoblastic leukemia. *Cancer* 2005, 103:368–76.
87. Einsiedel HG, Von Stackelberg A, Hartmann R, Fengler R, Schrappe M, Janka-Schaub G, Mann G, Hähnel K, Göbel U, Klingebiel T, Ludwig WD, Henze G: Long-term outcome in children with relapsed ALL by risk-stratified salvage therapy: results of trial acute lymphoblastic leukemia-relapse study of the Berlin-Frankfurt-Münster Group 87. *J Clin Oncol* 2005, 23:7942–7950.
88. Armstrong SA, Look AT: Molecular genetics of acute lymphoblastic leukemia. *J Clin Oncol* 2005, 23:6306–15.
89. Alastair J.J. Wood M.: Biologic characterization of leukemic cells. *Drug Ther (NY)* 1998, 339:605–615.
90. Landau H, Lamanna N: Clinical manifestations and treatment of newly diagnosed acute lymphoblastic leukemia in adults. *Curr Hematol Malig Rep* 2006, 1:171–179.
91. Butturini AM, Dorey FJ, Lange BJ, Henry DW, Gaynon PS, Fu C, Franklin J, Siegel SE, Seibel NL, Rogers PC, Sather H, Trigg M, Bleyer WA, Carroll WL: Obesity and outcome in pediatric acute lymphoblastic leukemia. *J Clin Oncol* 2007, 25:2063–9.
92. Hijiya N, Panetta JC, Zhou Y, Kyzer EP, Howard SC, Jeha S, Razzouk BI, Ribeiro RC, Rubnitz JE, Hudson MM, Sandlund JT, Pui CH, Relling M V: Body mass index does not influence pharmacokinetics or outcome of treatment in children with acute lymphoblastic leukemia. *Blood* 2006, 108:3997–4002.
93. Sallan SE, Ritz J, Pesando J, Gelber R, O'Brien C, Hitchcock S, Coral F, Schlossman SF: Cell surface antigens: prognostic implications in childhood acute lymphoblastic leukemia. *Blood* 1980, 55:395–402.

94. Pui C, Relling MV, Downing JR: Acute Lymphoblastic Leukemia. *N Engl J Med* 2004, 350:1535–48.
95. Zelent A, Greaves M, Enver T: Role of the TEL-AML1 fusion gene in the molecular pathogenesis of childhood acute lymphoblastic leukaemia. *Oncogene* 2004, 23:4275–4283.
96. Ren R: Mechanisms of BCR-ABL in the pathogenesis of chronic myelogenous leukaemia. *Nat Rev Cancer* 2005, 5:172–183.
97. Druker BJ: Imatinib as a paradigm of targeted therapies. *Adv Cancer Res* 2004, 91:1–30.
98. Faderl S, Kantarjian HM, Talpaz M, Estrov Z: Clinical significance of cytogenetic abnormalities in adult acute lymphoblastic leukemia. *Blood* 1998, 91:3995–4019.
99. Pui CH, Gaynon PS, Boyett JM, Chessells JM, Baruchel A, Kamps W, Silverman LB, Biondi A, Harms DO, Vilmer E, Schrappe M, Camitta B: Outcome of treatment in childhood acute lymphoblastic leukaemia with rearrangements of the 11q23 chromosomal region. *Lancet* 2002, 359:1909–1915.
100. Weng AP, Ferrando AA, Lee W, Morris JP, Silverman LB, Sanchez-Irizarry C, Blacklow SC, Look AT, Aster JC: Activating mutations of NOTCH1 in human T cell acute lymphoblastic leukemia. *Science (80-)* 2004, 306:269–271.
101. Demarest RM, Ratti F, Capobianco AJ: It's T-ALL about Notch. *Oncogene* 2008, 27:5082–5091.
102. Graux C, Cools J, Melotte C, Quentmeier H, Ferrando A, Levine R, Vermeesch JR, Stul M, Dutta B, Boeckx N, Bosly A, Heimann P, Uyttebroeck A, Mentens N, Somers R, MacLeod RAF, Drexler HG, Look AT, Gilliland DG, Michaux L, Vandenberghe P, Wlodarska I, Marynen P, Hagemeijer A: Fusion of NUP214 to ABL1 on amplified episomes in T-cell acute lymphoblastic leukemia. *Nat Genet* 2004, 36:1084–1089.
103. Su XY, Busson M, Della Valle V, Ballerini P, Dastugue N, Talmant P, Ferrando AA, Baudry-Bluteau D, Romana S, Berger R: Various types of rearrangements target TLX3 locus in T-cell acute lymphoblastic leukemia. *Genes Chromosom cancer* 2004, 41:243–249.
104. Flex E, Petrangeli V, Stella L, Chiaretti S, Hornakova T, Knoops L, Ariola C, Fodale V, Clappier E, Paoloni F, Martinelli S, Fragale A, Sanchez M, Tavolaro S, Messina M, Cazzaniga G, Camera A, Pizzolo G, Tornesello A, Vignetti M, Battistini A, Cavé H, Gelb BD, Renauld J-C, Biondi A, Constantinescu SN, Foà R, Tartaglia M: Somatically acquired JAK1 mutations in adult acute lymphoblastic leukemia. *J Exp Med* 2008, 205:751–8.
105. Mullighan CG, Goorha S, Radtke I, Miller CB, Coustan-Smith E, Dalton JD, Girtman K, Mathew S, Ma J, Pounds SB, Su X, Pui C-H, Relling M V, Evans WE, Shurtleff S a, Downing JR: Genome-wide analysis of genetic alterations in acute lymphoblastic leukaemia. *Nature* 2007, 446:758–64.
106. Pui CH, Relling MV, Downing JR: Acute lymphoblastic leukemia. *N Engl J Med* 2004, 350:1535–48.

107. Raimondi SC, Roberson PK, Pui CH, Behm FG, Rivera GK: Hyperdiploid (47-50) acute lymphoblastic leukemia in children. *Blood* 1992, 79:3245–3252.
108. Ankathil R, Geetha N, Remani P, Gangadharan VP, Pillai GR, Nair MK: Clinical implications of cytogenetic classification in adult acute lymphoblastic leukaemia patients. *J Cancer Res Clin Oncol* 1996, 122:370–373.
109. Garcia-Manero G, Bueso-Ramos C, Daniel J, Williamson J, Kantarjian HM IJ: DNA methylation patterns at relapse in adult acute lymphocytic leukemia. *Clin Cancer Res* 2002, 8:1897–1903.
110. Shen L, Toyota M, Kondo Y, Obata T, Daniel S, Pierce S, Imai K, Kantarjian HM, Issa JPJ, Garcia-Manero G: Aberrant DNA methylation of p57KIP2 identifies a cell-cycle regulatory pathway with prognostic impact in adult acute lymphocytic leukemia. *Blood* 2003, 101:4131–4136.
111. Roman-Gomez J, Jimenez-Velasco A, Castillejo JA, Agirre X, Barrios M, Navarro G, Molina FJ, Calasanz MJ, Prosper F, Heiniger A, Torres A: Promoter hypermethylation of cancer-related genes: a strong independent prognostic factor in acute lymphoblastic leukemia. *Blood* 2004, 104:2492–8.
112. Moorman A V, Harrison CJ, Buck GAN, Richards SM, Secker-Walker LM, Martineau M, Vance GH, Cherry AM, Higgins RR, Fielding AK, Foroni L, Paietta E, Tallman MS, Litzow MR, Wiernik PH, Rowe JM, Goldstone AH, Dewald GW: 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, 109:3189–97.
113. Nachman JB, Heerema NA, Sather H, Camitta B, Forestier E, Harrison CJ, Dastugue N, Schrappe M, Pui CH, Basso G, Silverman LB, Janka-Schaub GE: Outcome of treatment in children with hypodiploid acute lymphoblastic leukemia. *Blood* 2007, 110:1112–1115.
114. Zhu YM, Zhao WL, Fu JF, Shi JY, Pan Q, Hu J, Gao XD, Chen B, Li JM, Xiong SM, Gu LJ, Tang JY, Liang H, Jiang H, Xue YQ, Shen ZX, Chen Z, Chen SJ: NOTCH1 mutations in T-cell acute lymphoblastic leukemia: prognostic significance and implication in multifactorial leukemogenesis. *Clin Cancer Res* 2006, 12:3043–3049.
115. Lanciotti M, Dufour C, Corral L, Di Michele P, Pigullo S, De Rossi G, Basso G, Leszl A, Luciani M, Lo Nigro L, Micalizzi C, Valsecchi MG, Biondi A, Haupt R: Genetic polymorphism of NAD(P)H:quinone oxidoreductase is associated with an increased risk of infant acute lymphoblastic leukemia without MLL gene rearrangements. *Leukemia* 2005, 19:214–6.
116. Heim S, Mitelman F: Proliferation-specific and differentiation-associated chromosomal breakpoints in human neoplasia - a unifying model. 1986, 312:307–312.
117. Damm-Welk C, Fuchs U, Wössmann W, Borkhardt A: Targeting oncogenic fusion genes in leukemias and lymphomas by RNA interference. *Semin Cancer Biol* 2003, 13:283–292.

118. Schrauder A, Reiter A, Gadner H, Niethammer D, Klingebiel T, Kremens B, Peters C, Ebell W, Zimmermann M, Niggli F, Ludwig WD, Riehm H, Welte K, Schrappe M: Superiority of allogeneic hematopoietic stem-cell transplantation compared with chemotherapy alone in high-risk childhood T-cell acute lymphoblastic leukemia: results from ALL-BFM 90 and 95. *J Clin Oncol* 2006, 24:5742–5749.
119. Vey N, Thomas X, Picard C, Kovascovicz T, Charin C, Cayuela JM, Dombret H, Dastugue N, Huguet F, Bastard C, Stamatoulas a, Giollant M, Tournilhac O, Macintyre E, Buzyn a, Bories D, Kuentz M, Dreyfus F, Delannoy A, Raynaud S, Gratecos N, Bordessoule D, de Botton S, Preudhomme C, Reman O, Troussard X, Pigneux a, Bilhou C, Vernant JP, Boucheix C, et al.: Allogeneic stem cell transplantation improves the outcome of adults with t(1;19)/E2A-PBX1 and t(4;11)/MLL-AF4 positive B-cell acute lymphoblastic leukemia: results of the prospective multicenter LALA-94 study. *Leukemia* 2006, 20:2155–61.
120. Pui CH, Campana D, Evans WE: Childhood acute lymphoblastic leukaemia--current status and future perspectives. *Lancet Oncol* 2001, 2:597–607.
121. Coustan-Smith E, Sancho J, Behm FG, Hancock ML, Razzouk BI, Ribeiro RC, Rivera GK, Rubnitz JE, Sandlund JT, Pui CH, Campana D: Prognostic importance of measuring early clearance of leukemic cells by flow cytometry in childhood acute lymphoblastic leukemia. *Blood* 2002, 100:52–58.
122. Dworzak MN, Fröschl G, Printz D, Mann G, Pötschger U, Mühlegger N, Fritsch G, Gadner H: Prognostic significance and modalities of flow cytometric minimal residual disease detection in childhood acute lymphoblastic leukemia. *Blood* 2002, 99:1952–1958.
123. Zhou J, Goldwasser MA, Li A, Dahlberg SE, Neuberg D, Wang H, Dalton V, McBride KD, Sallan SE, Silverman LB, Gribben JG: Quantitative analysis of minimal residual disease predicts relapse in children with B-lineage acute lymphoblastic leukemia in DFCI ALL Consortium Protocol 95-01. *Blood* 2007, 110:1607–11.
124. Neale GAM, Coustan-Smith E, Stow P, Pan Q, Chen X, Pui CH, Campana D: Comparative analysis of flow cytometry and polymerase chain reaction for the detection of minimal residual disease in childhood acute lymphoblastic leukemia. *Leukemia* 2004, 18:934–8.
125. Cavé H, Van Der Werff Ten Bosch J, Suciú S, Guidal C, Waterkeyn C, Otten J, Bakkus M, Thielemans K, Grandchamp B, Vilmer E: Clinical significance of minimal residual disease in childhood acute lymphoblastic leukemia. European Organization for Research and Treatment of Cancer--Childhood Leukemia Cooperative Group. *N Engl J Med* 1998, 339:591–598.
126. Van Dongen JJ, Seriu T, Panzer-Grümayer ER, Biondi A, Pongers-Willems MJ, Corral L, Stolz F, Schrappe M, Masera G, Kamps WA, Gadner H, Van Wering ER, Ludwig WD, Basso G, De Bruijn MA, Cazzaniga G, Hettlinger K, Van Der Does-van Den Berg A, Hop WC, Riehm H, Bartram CR: Prognostic value of minimal residual disease in acute lymphoblastic leukaemia in childhood. *Lancet* 2001, 353:1239–1241.

127. Coustan-Smith E, Ribeiro RC, Stow P, Zhou Y, Pui CH, Rivera GK, Pedrosa F, Campana D: A simplified flow cytometric assay identifies children with acute lymphoblastic leukemia who have a superior clinical outcome. *Blood* 2006, 108:97–102.
128. Krejci O, Van Der Velden VHJ, Bader P, Kreyenberg H, Goulden N, Hancock J, Schilham MW, Lankester A, Révész T, Klingebiel T, Van Dongen JJM: Level of minimal residual disease prior to haematopoietic stem cell transplantation predicts prognosis in paediatric patients with acute lymphoblastic leukaemia: a report of the Pre-BMT MRD Study Group. *Bone Marrow Transplant* 2003:849–851.
129. Flotho C, Coustan-Smith E, Pei D, Iwamoto S, Song G, Cheng C, Pui CH, Downing JR, Campana D: Genes contributing to minimal residual disease in childhood acute lymphoblastic leukemia: prognostic significance of CASP8AP2. *Blood* 2006, 108:1050–1057.
130. Locatelli F, Schrappe M, Bernardo ME, Rutella S: How I treat relapsed childhood acute lymphoblastic leukemia. *Blood* 2012, 120:2807–16.
131. Pui CH: Central Nervous System Disease in Acute Lymphoblastic Leukemia: Prophylaxis and Treatment. *Hematology* 2006, 2006:142–146.
132. Onciu M: Acute Lymphoblastic Leukemia. *Hematol Oncol Clin N Am* 2009, 23:655–674.
133. Cancela CSP, Murao M, Viana MB, de Oliveira BM: Incidence and risk factors for central nervous system relapse in children and adolescents with acute lymphoblastic leukemia. *Rev Bras Hematol Hemoter* 2012, 34:436–41.
134. Lazarus HM, Richards SM, Chopra R, Litzow MR, Burnett AK, Wiernik PH, Franklin IM, Tallman MS, Cook L, Buck G, Durrant IJ, Rowe JM, Goldstone AH: Central nervous system involvement in adult acute lymphoblastic leukemia at diagnosis: results from the international ALL trial MRC UKALL XII/ECOG E2993. *Blood* 2006, 108:465–72.
135. WA B: Biology and pathogenesis of CNS leukemia. *Am J Pediatr Hematol Oncol* 1989, 11:57–63.
136. Del Principe MI, Maurillo L, Buccisano F, Sconocchia G, Cefalo M, De Santis G, Di Veroli A, Ditto C, Nasso D, Postorino M, Refrigeri M, Attrotto C, Del Poeta G, Amadori S, Venditti A: Central Nervous System Involvement in Adult Acute Lymphoblastic Leukemia: Diagnostic Tools, Prophylaxis and Therapy. *Mediterr J Hematol Infect Dis* 2014, 6:2014075.
137. Fukuda S: Fighting against the CNS Invasion of Pediatric Leukemia. *Pediatr Ther* 2012, 02:4172.
138. Steinherz PG: CNS Leukemia : Problem of Diagnosis , Treatment , and Outcome. *J Clin Oncol* 1995, 13:310–313.
139. Pavlovsky S, Eppinger-Helft M, Sackmann Muriel F: Factors that influence the appearance of central nervous system leukemia. *Blood* 1973, 42:935–8.

140. Pui CH, Dahl G V, Kalwinsky DK, Look AT, Mirro J, Dodge RK, Simone J V, Thomas A, Dahi G V, Kalwinsky K, Dodge RK, Simone J V: Central nervous system leukemia in children with acute nonlymphoblastic leukemia. *Blood* 1985, 66:1062–1067.
141. Abbott BL, Rubnitz JE, Tong X, Srivastava DK, Pui CH, Ribeiro RC, Razzouk BI: Clinical significance of central nervous system involvement at diagnosis of pediatric acute myeloid leukemia: a single institution's experience. *Leukemia* 2003, 17:2090–6.
142. Rocha JCC, Cheng C, Liu W, Kishi S, Das S, Cook EH, Sandlund JT, Rubnitz J, Ribeiro R, Campana D, Pui C, Evans WE, Relling M V: Pharmacogenetics of outcome in children with acute lymphoblastic leukemia. *Blood* 2005, 105:4752–4758.
143. Mahmoud HH, Rivera GK, Hancock ML, Krance RA, Kun LE, Behm FG, Ribeiro RC, Sandlund JT, Crist WM, Pui CH: Low leukocyte counts with blast cells in cerebrospinal fluid of children with newly diagnosed acute lymphoblastic leukemia. *N Engl J Med* 1993, 329:314–319.
144. Te Loo DM, Kamps WA, Van Der Does-van Den Berg A, Van Wering ER, De Graaf SS: Prognostic significance of blasts in the cerebrospinal fluid without pleiocytosis or a traumatic lumbar puncture in children with acute lymphoblastic leukemia: experience of the Dutch Childhood Oncology Group. *J Clin Oncol* 2006, 24:2332–2336.
145. Rizzari C, Valsecchi MG, Aricò M, Miniero R, Messina C, De Rossi G, Testi AM, Mura R, Galimberti S, Biondi A, Locatelli F, Conter V: Outcome of very late relapse in children with acute lymphoblastic leukemia. *Haematologica* 2004, 89:427–434.
146. Krishnan S, Wade R, Moorman a V, Mitchell C, Kinsey SE, Eden TOB, Parker C, Vora A, Richards S, Saha V: Temporal changes in the incidence and pattern of central nervous system relapses in children with acute lymphoblastic leukaemia treated on four consecutive Medical Research Council trials, 1985-2001. *Leukemia* 2010, 24:450–459.
147. Lo Nigro L, Cazzaniga G, Di Cataldo A, Pannunzio A, D'Aniello E, Masera G, Schilirò G BA: Clonal stability in children with acute lymphoblastic leukemia (ALL) who relapsed five or more years after diagnosis. *Leukemia* 1999, 13:190–5.
148. Crespo-Solis E, López-Karpovitch X, Higuera J VRB: Diagnosis of acute leukemia in cerebrospinal fluid (CSF-acute leukemia). *Curr Oncol Rep* 2012, 14:369–78.
149. Homans AC, Barker BE, Forman EN, Cornell CJ, Dickerman JD, Truman JT: Immunophenotypic characteristics of cerebrospinal fluid cells in children with acute lymphoblastic leukemia at diagnosis. *Blood* 1990, 76:1807–11.
150. Ahluwalia MS, Wallace PK, Peereboom DM: Flow cytometry as a diagnostic tool in lymphomatous or leukemic meningitis: ready for prime time? *Cancer* 2012, 118:1747–53.
151. Pine SR, Yin C, Matloub YH, Sabaawy HE, Sandoval C, Levendoglu-Tugal O, Ozkaynak MF, Jayabose S: Detection of central nervous system leukemia in children with acute lymphoblastic leukemia by real-time polymerase chain reaction. *J Mol Diagn* 2005, 7:127–32.

152. Lange BJ, Bostrom BC, Cherlow JM, Sensel MG, La MKL, Rackoff W, Heerema NA, Wimmer RS, Trigg ME, Sather HN: Double-delayed intensification improves event-free survival for children with intermediate-risk acute lymphoblastic leukemia: a report from the Children's Cancer Group. *Blood* 2002, 99:825–833.
153. Hutchinson RJ, Gaynon PS, Sather H, Bertolone SJ, Cooper HA, Tannous R, Wells LM, Heerema NA, Sailer S, Trigg ME: Intensification of therapy for children with lower-risk acute lymphoblastic leukemia: long-term follow-up of patients treated on Children's Cancer Group Trial 1881. *J Clin Oncol* 2003, 21:1790–1797.
154. Cortes JE, Thomas D, Brien SO, Giles FJ, Koller C, Faderl S, Kantarjian H: Central Nervous System Relapse in Adults with Acute Lymphoblastic Leukemia. *Cancer* 2002, 94:773–9.
155. Reman O, Pigneux A, Huguet F, Vey N, Delannoy A, Fegueux N, de Botton S, Stamatoullas A, Tournilhac O, Buzyn A, Charrin C, Boucheix C, Gabert J, Lhéritier V, Vernant JP, Fièrè D, Dombret H, Thomas X: Central nervous system involvement in adult acute lymphoblastic leukemia at diagnosis and/or at first relapse: results from the GET-LALA group. *Leuk Res* 2008, 32:1741–50.
156. Surapaneni UR, Cortes JE, Thomas D, O'Brien S, Giles FJ, Koller C, Faderl SKH: Central nervous system relapse in adults with acute lymphoblastic leukemia. *Cancer* 2002, 94:773–779.
157. Carlos Alberto Scrideli: Involvement of the cerebrospinal fluid cells in children with acute lymphoblastic leukemia: prognostic implications. *Rev Bras Hematol Hemoter* 2012, 34:408–409.
158. Jorge Cortes, Susan M. O'Brien, Sherry Pierce, Michael J. Keating, Emil J Freireich and HMK: The value of high-dose systemic chemotherapy and intrathecal therapy for central nervous system prophylaxis in different risk groups of adult acute lymphoblastic leukemia. *Blood* 1995, 86:2091–2097.
159. Moleski M: Neurophysiological Consequences of CNS Chemotherapy for Acute Lymphoblastic Leukemia. *Arch Clin Neuropsychol* 2000, 15:603–630.
160. Pui CH, Cheng C, Leung W, Rai SN, Rivera GK, Sandlund JT, Ribeiro RC, Relling M V, Kun LE, Evans WE, Hudson MM: Extended follow-up of long-term survivors of childhood acute lymphoblastic leukemia. *N Engl J Med* 2003, 349:640–649.
161. Hudson MM, Lensing S, Zacher M, Ribeiro RC, Rivera GK, Evans WE, Relling MV: Cumulative Incidence of Secondary Neoplasms as a First Event After Childhood Acute Lymphoblastic Leukemia. *JAMA* 2007, 297:1207–1215.
162. Pui CH, Howard SC: Current management and challenges of malignant disease in the CNS in paediatric leukaemia. *Lancet Oncol* 2008, 9:257–68.
163. Mayeux R: Biomarkers: potential uses and limitations. *NeuroRx* 2004, 1:182–8.

164. Karley D, Gupta D, Tiwari A: Review Biomarker for Cancer : A great Promise for Future. *World J Oncol* 2011, 2:151–157.
165. Madu CO, Lu Y: Novel diagnostic biomarkers for prostate cancer. *J Cancer* 2010:150–177.
166. Kantarjian HM, Smith T, Estey E, Polyzos A, O'Brien S, Pierce S, Beran M, Feldman E, Keating MJ: Prognostic significance of elevated serum beta 2-microglobulin levels in adult acute lymphocytic leukemia. *Am J Med* 1992, 93:599–604.
167. Musto P, Tomasi P, Cascavilla N, Ladogana S, La Sala A, Melillo L, Nobile M, Castoldi G, Carotenuto M: Significance and limits of cerebrospinal fluid beta-2-microglobulin measurement in course of acute lymphoblastic leukemia. *Am J Hematol* 1988, 28:213–218.
168. Hansen PB, Kjeldsen L, Dalhoff K, Olesen B: Cerebrospinal fluid beta-2-microglobulin in adult patients with acute leukemia or lymphoma: a useful marker in early diagnosis and monitoring of CNS-involvement. *Acta Neurol Scand* 1992, 85:224–227.
169. Caudie C, Bancel J, Dupont M, Matanza D, Poitevin F HJ: CSF levels and diagnostic utility of cerebrospinal fluid beta2-microglobulin. *Ann Biol Clin (Paris)* 2005, 63:631–7.
170. Adachi N.: Beta-2-microglobulin levels in the cerebrospinal fluid: their value as a disease marker. A review of the recent literature. *Eur Neurol* 1991, 31:181–5.
171. Lee W, Kim SJ, Lee S, Kim J, Kim M, Lim J, Kim Y, Cho B, Lee EJ, Han K: Significance of cerebrospinal fluid sIL-2R level as a marker of CNS involvement in acute lymphoblastic leukemia. *Ann Clin Lab Sci* 2005, 35:407–12.
172. El-mahallawy HA, Akl SY, Rizk SH, Attia IA, Thabet G, El-din NHALY: Assesment of Soluble Interleukin-2 Receptor in CSF for the Diagnosis of CNS Disease in Acute Lymphoblastic Leukemia. *J Egypt Natl Canc Inst* 2003, 15:43–48.
173. Petereit HF, Reske D, Tumani H, Jarius S, Markus Leweke F, Woitalla D, Pfister HW, Rubbert A: Soluble CSF interleukin 2 receptor as indicator of neurosarcoidosis. *J Neurol* 2010, 257:1855–1863.
174. Watanabe K, Kawamura N, Tokuda M, Oguni T, Konishi K, Mino M: Soluble interleukin-2 receptor level in serum of children with insulin-dependent diabetes mellitus compared with that in diseases with activated immune system. *Pathophysiology* 1996, 3:37–40.
175. Gilad R, Lampl Y, Eshel Y, Barak V, Sarova-Pinhas I: Cerebrospinal fluid soluble interleukin-2 receptor in cerebral lupus. *Br J Rheumatol* 1997, 36:190–193.
176. Gaughran F, O'Neill E, Cole M, Collins K, Daly RJ, Shanahan F: Increased soluble interleukin 2 receptor levels in schizophrenia. *Schizophr Res* 1998, 29:263–267.
177. Marie Jose Kersten, Ludo M. Eers, Paul L.I. Dellelmiijn, Peter Portegies, Rogier Q. Hintzen, R.A.W. van Lier, Albert E.G.Kr. von dem Borne and RHJ van O: Elevation of

Cerebrospinal Fluid Soluble CD27 Levels in Patients With Meningeal Localization of Lymphoid Malignancies 1996 87: 1985-1989. *Blood* 1996, 87:1985–1989.

178. Cario G, Izraeli S, Teichert A, Rhein P, Skokowa J, Möricke A, Zimmermann M, Schrauder A, Karawajew L, Ludwig W-D, Welte K, Schünemann HJ, Schlegelberger B, Schrappe M, Stanulla M: High interleukin-15 expression characterizes childhood acute lymphoblastic leukemia with involvement of the CNS. *J Clin Oncol* 2007, 25:4813–20.

179. Blanco-Jerez C, Plaza JF, Masjuan J, Orensanz LM ACJ: Increased levels of IL-15 mRNA in relapsing--remitting multiple sclerosis attacks. *J Neuroimmunol* 2002, 128:90–4.

180. Ashkar S: Osteopontin CD44 Interaction: A Novel Mechanism for the Selective Homing of Breast Tumor Cells Into Bone. *Child Hosp Corp, Bost MA* 2001.

181. Incesoy-Özdemir S, Sahin G, Bozkurt C, Oren AC, Balkaya E, Ertem U: The relationship between cerebrospinal fluid osteopontin level and central nervous system involvement in childhood acute leukemia. *Turk J Pediatr* 2013, 55:42–9.

182. Carecchio M, Comi C: The role of osteopontin in neurodegenerative diseases. *J Alzheimers Dis* 2011, 25:179–85.

183. Ousman SS, Kubes P: Immune surveillance in the central nervous system. *Nat Neurosci* 2012, 15:1096–1101.

184. Muldoon LL, Alvarez JI, Begley DJ, Boado RJ, Del Zoppo GJ, Doolittle ND, Engelhardt B, Hallenbeck JM, Lonser RR, Ohlfest JR, Prat A, Scarpa M, Smeyne RJ, Drewes LR, Neuwelt EA: Immunologic privilege in the central nervous system and the blood-brain barrier. *J Cereb Blood Flow Metab* 2013, 33:13–21.

185. Streit WJ, Mrak RE, Griffin WST: Microglia and neuroinflammation: a pathological perspective. *J Neuroinflammation* 2004, 1:14.

186. Rezai-Zadeh K, Gate D, Town T: CNS infiltration of peripheral immune cells: D-Day for neurodegenerative disease? *J Neuroimmune Pharmacol* 2009, 4:462–75.

187. Bechmann I, Galea IPV: What is the blood-brain barrier (not)? *Trends Immunol* 2007, 28:5–11.

188. Engelhardt B, Coisne C: Fluids and barriers of the CNS establish immune privilege by confining immune surveillance to a two-walled castle moat surrounding the CNS castle. *Fluids Barriers CNS* 2011, 8:4.

189. Kivisäkk P, Mahad DJ, Callahan MK, Trebst C, Tucky B, Wei T, Wu L, Baekkevold ES, Lassmann H, Staugaitis SM, Campbell JJ, Ransohoff RM: Human cerebrospinal fluid central memory CD4+ T cells: evidence for trafficking through choroid plexus and meninges via P-selectin. *Proc Natl Acad Sci U S A* 2003, 100:8389–94.

190. Carrithers MD, Visintin I, Kang SJ, Janeway CA: Differential adhesion molecule requirements for immune surveillance and inflammatory recruitment. *Brain* 2000, 123 (Pt 6):1092–101.

191. Anthony IC, Crawford DH, Bell JE: B lymphocytes in the normal brain: contrasts with HIV-associated lymphoid infiltrates and lymphomas. *Brain* 2003, 126:1058–1067.
192. Wilson EH, Weninger W, Hunter CA: Trafficking of immune cells in the central nervous system. *J Clin Invest* 2010, 120.
193. Piccio L, Rossi B, Scarpini E, Laudanna C, Giagulli C, Issekutz AC, Vestweber D, Butcher EC, Constantin G: Molecular Mechanisms Involved in Lymphocyte Recruitment in Inflamed Brain Microvessels. *J Immunol* 2002, 168:1940–1949.
194. Knut Biber, Mike W Zuurman, Inneke M Dijkstra HWB: Chemokines in the brain : neuroimmunology and beyond. *Curr Opin Pharmacol* 2002, 2:63–68.
195. Cardona AE, Li M, Liu L, Savarin C, Ransohoff RM: Chemokines in and out of the central nervous system: much more than chemotaxis and inflammation. *J Leukoc Biol* 2008, 84:587–94.
196. Babcock AA, Kuziel WA, Rivest S, Owens T: Chemokine expression by glial cells directs leukocytes to sites of axonal injury in the CNS. *J Neurosci* 2003, 23:7922–30.
197. Semple BD, Kossmann T, Morganti-Kossmann MC: Role of chemokines in CNS health and pathology: a focus on the CCL2/CCR2 and CXCL8/CXCR2 networks. *J Cereb Blood Flow Metab* 2010, 30:459–73.
198. Glass WG, Hickey MJ, Hardison JL, Liu MT, Manning JE, Lane TE: Antibody Targeting of the CC Chemokine Ligand 5 Results in Diminished Leukocyte Infiltration into the Central Nervous System and Reduced Neurologic Disease in a Viral Model of Multiple Sclerosis. *J Immunol* 2004, 172:4018–4025.
199. Takeshita, Yukio RRM: Inflammatory cell trafficking across the blood-brain barrier (BBB): Chemokine regulation and in vitromodels. *Immunol Rev* 2012, 248:228–239.
200. Ransohoff RM, Kivisäkk PKG: Three or more routes for leukocyte migration into the central nervous system. *Nat Rev Immunol* 2003, 3:569–581.
201. B E, RM. R: The ins and outs of T-lymphocyte trafficking to the CNS: anatomical sites and molecular mechanisms. *Trends Immunol* 2005, 26:485–95.
202. Akers SM, Leary HAO, Minnear FL, Craig MD, Jeffrey A, Coad JE, Gibson LF, Randolph B, Byrd RC, Sciences H, Virginia W: VE-cadherin and PECAM-1 enhance ALL migration across brain microvascular endothelial cell monolayers. *Exp Hematol* 2011, 38:733–743.
203. Förster R, Davalos-Misslitz AC, Rot A: CCR7 and its ligands: balancing immunity and tolerance. *Nat Rev Immunol* 2008, 8:362–371.
204. Holland M, Castro F V, Alexander S, Smith D, Liu J, Walker M, Bitton D, Mulryan K, Ashton G, Blaylock M, Bagley S, Connolly Y, Bridgeman J, Miller C, Krishnan S, Dempsey C, Masurekar A, Stern P, Whetton A, Saha V: RAC2, AEP, and ICAM1 expression are

associated with CNS disease in a mouse model of pre-B childhood acute lymphoblastic leukemia. *Blood* 2011, 118:638–49.

205. Arana E, Vehlow A, Harwood NE, Vigorito E, Henderson R, Turner M, Tybulewicz VLJ, Batista FD: Activation of the small GTPase Rac2 via the B cell receptor regulates B cell adhesion and immunological-synapse formation. *Immunity* 2008, 28:88–99.

206. Jones S, Thornton JM: Principles of protein-protein interactions. *Proc Natl Acad Sci USA* 1996, 93(January):13–20.

207. Berggård T, Linse S, James P: Methods for the detection and analysis of protein-protein interactions. *Proteomics* 2007, 7:2833–42.

208. Fields S: Two-hybrid and Related Systems. *Encycl LIFE Sci* 2001:1–7.

209. Charlotte M. Deane, Łukasz Salwinski, Ioannis Xenarios DE: Protein Interactions: Two Methods for Assessment of the Reliability of High Throughput Observations. *Mol Cell Proteomics* 2002, 1:349–356.

210. He R, Li X: Mammalian two-hybrid assay for detecting protein-protein interactions in vivo. *Methods Mol Biol* 2008, 439:327–337.

211. Walsh BW, Lenhart JS, Schroeder JW, Simmons LA: Far Western blotting as a rapid and efficient method for detecting interactions between DNA replication and DNA repair proteins. *Methods Mol Biol (Clifton, NJ)* 2012, 922:161–168.

212. Einarson MB, Pugacheva EN, Orlinick JR: Far Western: probing membranes. *CSH Protoc* 2007, 2007:pdb.prot4759.

213. Hall RA: Studying protein-protein interactions via blot overlay or Far Western blot. *Methods Mol Biol* 2004, 261:167–174.

214. Machida K, Mayer BJ: Detection of protein-protein interactions by far-western blotting. *Methods Mol Biol* 2009, 536:313–329.

215. Wu Y, Li Q, Chen XZ: Detecting protein-protein interactions by Far western blotting. *Nat Protoc* 2007, 2:3278–3284.

216. Edmondson DG, Dent SY: Identification of protein interactions by far western analysis. *Curr Protoc Protein Sci* 2001, Chapter 19:Unit 19.7.

217. Menon KN, Steer DL, Short M, Petratos S, Smith I, Bernard CCA: A novel unbiased proteomic approach to detect the reactivity of cerebrospinal fluid in neurological diseases. *Mol Cell Proteomics* 2011, 10:M110.000042.

218. Cho WCS: Contribution of oncoproteomics to cancer biomarker discovery. *Mol Cancer* 2007, 6:25.

219. Seibert V, Ebert MPA, Buschmann T: Advances in clinical cancer proteomics: SELDI-ToF-mass spectrometry and biomarker discovery. *Brief Funct Genomic Proteomic* 2005, 4:16–26.
220. Xiao GG, Recker RR, Deng HW: Recent advances in proteomics and cancer biomarker discovery. *Clin Med Oncol* 2008, 2:63–72.
221. Savino R, Paduano S, Preianò M, Terracciano R: The proteomics big challenge for biomarkers and new drug-targets discovery. *Int J Mol Sci* 2012, 13:13926–48.
222. Drucker E, Krapfenbauer K: Pitfalls and limitations in translation from biomarker discovery to clinical utility in predictive and personalised medicine. *EPMA J* 2013, 4:7.
223. Shi M, Caudle WM, Zhang J: Biomarker Discovery in Neurodegenerative Diseases: A Proteomic Approach. *Neurobiol Dis* 2010, 35:157–164.
224. Thongboonkerd V: Practical points in urinary proteomics. *J Proteome Res* 2007, 6:3881–90.
225. De Bock M, de Seny D, Meuwis MA, Chapelle JP, Louis E, Malaise M, Merville MP, Fillet M: Challenges for biomarker discovery in body fluids using SELDI-TOF-MS. *J Biomed Biotechnol* 2010, 2010:906082.
226. Aebersold R, Anderson L, Caprioli R, Druker B, Hartwell L: Perspective : A Program to Improve Protein Biomarker Discovery for Noninvasive Monitoring of Biomarkers. *J Proteome Res* 2005, 4:1104–1109.
227. Kroksveen AC, Opsahl JA, Aye TT, Ulvik RJ, Berven FS: Proteomics of human cerebrospinal fluid: discovery and verification of biomarker candidates in neurodegenerative diseases using quantitative proteomics. *J Proteomics* 2011, 74:371–88.
228. Good DM, Thongboonkerd V, Novak J, Bascands JL, Schanstra JP, Coon JJ, Dominiczak A, Mischak H: Body fluid proteomics for biomarker discovery: lessons from the past hold the key to success in the future. *J Proteome Res* 2007, 6:4549–55.
229. Schiess R, Wollscheid B, Aebersold R: Targeted proteomic strategy for clinical biomarker discovery. *Mol Oncol* 2009, 3:33–44.
230. Pierre Lescuyer , Denis Hochstrasser TR: How shall we use the pproteomics toolbox for biomarker discovery? *J Proteome Res* 2007, 6:3371–6.
231. Roy S, Josephson SA, Fridlyand J, Karch J, Kadoch C, Karrim J, Damon L, Treseler P, Kunwar S, Shuman MA, Jones T, Becker CH, Schulman H, Rubenstein JL: Protein biomarker identification in the CSF of patients with CNS lymphoma. *J Clin Oncol* 2008, 26:96–105.
232. Ching-Hon Pui: *Childhood Leukemias*. 2nd edition. Cambridge University Press; 2006:473–486.

233. Hijiya N, Hudson MM, Lensing S, Zacher M, Onciu M, Behm FG, Razzouk BI, Ribeiro RC, Rubnitz JE, Sandlund JT, Rivera GK, Evans WE, Relling M V, Pui CH: Cumulative incidence of secondary neoplasms as a first event after childhood acute lymphoblastic leukemia. *Jama J Am Med Assoc* 2007, 297:1207–1215.
234. Jukka Rajantie, Marja-Leena Koskiniemia, MAS: CSF fibronectin in Burkitt's lymphoma: an early marker for CNS involvement. *Eur J Haematol* 1989, 42:313–4.
235. Smithies O, Poulik MD: Two-Dimensional Electrophoresis of Serum Proteins. *Nature* 1956, 177:1033.
236. O'Farrell PH: High Resolution two dimensional Electrophoresis of Proteins. *J Biol Chem* 1975, 250:4007–4021.
237. Klose J: Protein mapping by combined isoelectric focusing and electrophoresis of mouse tissues. *Humangenetik* 1975, 26:231–243.
238. Gorg A, Obermaier C, Boguth G, Harder A, Scheibe B, Wildgruber R, Weiss W: The current state of two-dimensional electrophoresis with immobilized pH gradients. *Electrophoresis* 2000, 21:1037–1053.
239. Klose J, Kobalz U: Two-dimensional electrophoresis of proteins: An updated protocol and implications for a functional analysis of the genome. *Electrophoresis* 1995, 16:1034–1059.
240. Righetti PG, Gianazza E, Bjellqvist B: Modern aspects of isoelectric focusing: two-dimensional maps and immobilized pH gradients. *J Biochem Biophys Methods* 1983, 8:89–108.
241. Ornstein DK: Proteomics for the identification of new prostate cancer biomarkers. *Urol Oncol* 2006, 24:231–6.
242. Matt P: Biomarker discovery: proteome fractionation and separation in biological samples. *Physiol Genomics* 2008, 14:33:12–7.
243. Gallego-Delgado J: Proteomic approach in the search of new cardiovascular biomarkers. *Kidney Int Suppl* 2005, 99:S103–7.
244. Hu S: Large-scale identification of proteins in human salivary proteome by liquid chromatography/mass spectrometry and two-dimensional gel electrophoresis-mass spectrometry. *Proteomics* 2005, 5:1714–28.
245. Wang H, Hanash S: Intact-protein based sample preparation strategies for proteome analysis in combination with mass spectrometry. *Mass Spectrom Rev* 2005, 24:413–26.
246. Kirkland PA: Trizol-based method for sample preparation and isoelectric focusing of halophilic proteins. *Anal Biochem* 2006, 351:254–9.
247. Shaw MM: Sample preparation for two-dimensional gel electrophoresis. *Proteomics* 2003, 3:1408–17.

248. Wu Y: Optimized sample preparation for two-dimensional gel electrophoresis of soluble proteins from chicken bursa of Fabricius. *Proteome Sci* 2009, 8:38.
249. Thierry Rabilloud: Solubilization of proteins for electrophoretic analyses. *Electrophoresis* 1996, 17:813–829.
250. Stagsted J: Identification of specific oxidatively modified proteins in chicken muscles using a combined immunologic and proteomic approach. *J Agric Food Chem* 2004, 16;52:3967–74.
251. Herbert BR: Improved protein solubility in two-dimensional electrophoresis using tributyl phosphine as reducing agent. *Electrophoresis* 1998, 19:845–51.
252. Thierry Rabilloud: Detergents and Chaotropes for Protein Solubilization Before Two-Dimensional Electrophoresis. *Methods Mol Biol* 2009, 528:259–267.
253. Thierry Rabilloud: Improvement of the solubilization of proteins in two-dimensional electrophoresis with immobilized pH gradients. *Electrophoresis* 1997, 18:307–16.
254. Ben Herbert: Advances in protein solubilisation for two-dimensional electrophoresis. *Electrophoresis* 1999, 20:660–663.
255. Molloy MP: Two-dimensional electrophoresis of membrane proteins using immobilized pH gradients. *Anal Biochem* 2000, 10;280:1–10.
256. Antonioli P: Efficient removal of DNA from proteomic samples prior to two-dimensional map analysis. *J Chromatogr A* 2009, 1216:3606–12.
257. Berkelman T: Removal of interfering substances in samples prepared for two-dimensional (2-D) electrophoresis. *Methods Mol Biol* 2008, 424:51–62.
258. Mastro R: Protein delipidation and precipitation by tri-n-butylphosphate, acetone, and methanol treatment for isoelectric focusing and two-dimensional gel electrophoresis. *Anal Biochem* 1999, 273:313–315.
259. Centlow M: Differential proteome analysis of the preeclamptic placenta using optimized protein extraction. *J Biomed Biotechnol* 2010, 2010.
260. Askonas BA: The use of organic solvents at low temperature for the separation of enzymes; application to aqueous rabbit muscle extract. *Biochem J* 1951, 48:42–8.
261. Vogelstein B, Gillespie D: Preparative and analytical purification of DNA from agarose. *Proc Natl Acad Sci U S A* 1979, 76:615–9.
262. Osborne MR: Preparation of a methylated DNA standard, and its stability on storage. *Chem Res Toxicol* 2000, 13:257–61.
263. Jaffe N, Takaue Y, Anzai T, Robertson R: Transient neurologic disturbances induced by high-dose methotrexate treatment. *Cancer* 1985, 56:1356–60.

264. Osterlundh G: Studies of cerebral blood flow in children with acute lymphoblastic leukemia: case reports of six children treated with methotrexate examined by single photon emission computed tomography. *J Pediatr Hematol Oncol* 1997, 19:28–34.
265. Jabbour E, Thomas D, Cortes J, Kantarjian HM, O'Brien S: Central nervous system prophylaxis in adults with acute lymphoblastic leukemia. *Cancer* 2010, 116:2290–300.
266. Schrappe M, Reiter A, Ludwig W, Harbott J, Zimmermann M, Hiddemann W, Niemeier C, Feldges A, Zintl F, Kornhuber B, Welte K, Gadner H: Improved outcome in childhood acute lymphoblastic leukemia despite reduced use of anthracyclines and cranial radiotherapy : results of trial ALL-BFM 90. *Blood* 2000, 95:3310–3322.
267. Silverman LB, Declerck L, Gelber RD, Dalton VK, Asselin BL, Barr RD, Clavell LA, Hurwitz CA, Moghrabi A, Samson Y, Schorin MA, Lipton JM, Cohen HJ, Sallan SE: Results of Dana-Farber Cancer Institute Consortium protocols for children with newly diagnosed acute lymphoblastic leukemia (1981-1995). *Leukemia* 2000, 14:2247–56.
268. Burger B: Diagnostic Cerebrospinal Fluid Examination in Children With Acute Lymphoblastic Leukemia: Significance of Low Leukocyte Counts With Blasts or Traumatic Lumbar Puncture. *J Clin Oncol* 2003, 21:184–188.
269. Laningham FH, Kun LE, Reddick WE, Ogg RJ, Morris EB: Childhood central nervous system leukemia: historical perspectives, current therapy, and acute neurological sequelae. *Neuroradiology* 2008, 49:873–888.
270. de Haas V, Vet RJ, Verhagen OJ, Kroes W, van den Berg H, van der Schoot CE: Early detection of central nervous system relapse by polymerase chain reaction in children with B-precursor acute lymphoblastic leukemia. *Ann Hematol* 2002, 81:59–61.
271. Bromberg JE, Breems DA, Kraan J, Bikker G, van der Holt B, Smitt PS, van den Bent MJ, van't Veer M, Gratama JW: CSF flow cytometry greatly improves diagnostic accuracy in CNS hematologic malignancies. *Neurology* 2007, 15:1674–9.
272. Fiona E. Craig FE, Ohori NP, Gorrill TS, Swerdlow SH: Flow cytometric immunophenotyping of cerebrospinal fluid specimens. *Am J Clin Pathol* 2011, 135:22–34.
273. Chamberlain MC: Neoplastic meningitis. *Neurologist* 2006, 12:179–87.
274. Ernerudh J, Olsson T, Berlin G, Gustafsson B, Karlsson H: Cell surface markers for diagnosis of central nervous system involvement in lymphoproliferative diseases. *Ann Neurol* 1986, 20:610–5.
275. Giora M. Mavligit, Sarah E. Stuckey, Fernando F. Cabanillas, Michael J. Keating, Wallace W. Tourtellotte, S. Clifford Schold, Emil J Freireich: Diagnosis of Leukemia or Lymphoma in the Central Nervous System by Beta2-Microglobulin Determination. *N Engl J Med* 1980, 303:718–722.
276. Weller M, Stevens A, Sommer N, Melms A, Dichgans J, Wiethölter H: Comparative analysis of cytokine patterns in immunological, infectious, and oncological neurological disorders. *J Neurol Sci* 1991, 104:215–21.

277. Ernerudh J, Olsson T, Berlin G, von Schenck H: Cerebrospinal fluid immunoglobulins and beta 2-microglobulin in lymphoproliferative and other neoplastic diseases of the central nervous system. *Arch Neurol* 1987, 44:915–20.
278. Weller M, Stevens A, Sommer N, Schabet M, Wiethölter H: Humoral CSF parameters in the differential diagnosis of hematologic CNS neoplasia. *Acta Neurol Scand* 1992, 86:129–33.
279. Cui J, Li W, Wang J, Li A, Li H, Wang H, He K, Li W, Kang L, Yu M, Shen B, Wang G, Zhang X: Proteomics-based identification of human acute leukemia antigens that induce humoral immune response. *Mol Cell Proteomics* 2005, 4:1718–24.
280. Xavier T, Ganesan TS, Menon KN: A simple and efficient method for processing of cell lysates for two-dimensional gel electrophoresis. *Electrophoresis* 2010, 31:2429–35.
281. Vainberg IE, Lewis SA, Rommelaere H, Ampe C, Vandekerckhove J, Klein HL, Cowan NJ: Prefoldin, a chaperone that delivers unfolded proteins to cytosolic chaperonin. *Cell* 1998, 93:863–73.
282. Hansen WJ, Cowan NJ, Welch WJ: Cytoskeletal Proteins. *J Cell Biol* 1999, 145:265–277.
283. Rommelaere H, De Neve M, Neiryneck K, Peelaers D, Waterschoot D, Goethals M, Fraeyman N, Vandekerckhove J, Ampe C: Prefoldin recognition motifs in the nonhomologous proteins of the actin and tubulin families. *J Biol Chem* 2001, 276:41023–8.
284. Mori K, Maeda Y, Kitaura H, Taira T, Iguchi-Arigo SM, Ariga H: MM-1, a novel c-Myc-associating protein that represses transcriptional activity of c-Myc. *J Biol Chem* 1998, 273:29794–800.
285. Yoshida T, Kitaura H, Hagio Y, Sato T, Iguchi-Arigo SMM, Ariga H: Negative regulation of the Wnt signal by MM-1 through inhibiting expression of the wnt4 gene. *Exp Cell Res* 2008, 314:1217–28.
286. Delgado MD, León J: Myc roles in hematopoiesis and leukemia. *Genes Cancer* 2010, 1:605–16.
287. Fujioka Y, Taira T, Maeda Y, Tanaka S, Nishihara H, Iguchi-Arigo SM, Nagashima K, Ariga H: MM-1, a c-Myc-binding protein, is a candidate for a tumor suppressor in leukemia/lymphoma and tongue cancer. *J Biol Chem* 2001, 276:45137–44.
288. Fukuda S, Wu DW, Stark K, Pelus LM: Cloning and characterization of a proliferation-associated cytokine-inducible protein, CIP29. *Biochem Biophys Res Commun* 2002, 292:593–600.
289. Hashii Y, Kim JY, Sawada a, Tokimasa S, Hiroyuki F, Ohta H, Makiko K, Takihara Y, Ozono K, Hara J: A novel partner gene CIP29 containing a SAP domain with MLL identified in infantile myelomonocytic leukemia. *Leukemia* 2004, 18:1546–8.

290. Ballabio E, Milne T a: Molecular and Epigenetic Mechanisms of MLL in Human Leukemogenesis. *Cancers (Basel)* 2012, 4:904–44.
291. Samudio I, Harmancey R, Fiegl M, Kantarjian H, Konopleva M, Korchin B, Kaluarachchi K, Bornmann W, Duvvuri S, Taegtmeier H, Andreeff M: Pharmacologic inhibition of fatty acid oxidation sensitizes human leukemia cells to apoptosis induction. *J Clin Invest* 2010, 120:142–56.
292. Zhang J, Song M, Wang J, Sun M, Wang B, Li R, Huang Y, Hou L, Jin Y, Wang M, Tang J: Enoyl coenzyme A hydratase 1 is an important factor in the lymphatic metastasis of tumors. *Biomed Pharmacother* 2011, 65:157–62.
293. Pak JH, Choi WH, Lee HM, Joo WD, Kim JH, Kim Y-T, Kim YM, Nam JH: Peroxiredoxin 6 overexpression attenuates cisplatin-induced apoptosis in human ovarian cancer cells. *Cancer Invest* 2011, 29:21–8.
294. Fujita Y, Nakanishi T, Hiramatsu M, Mabuchi H, Miyamoto Y, Miyamoto A, Shimizu A, Tanigawa N: Proteomics-based approach identifying autoantibody against peroxiredoxin VI as a novel serum marker in esophageal squamous cell carcinoma. *Clin Cancer Res* 2006, 12:6415–20.
295. Walsh B, Pearl A, Suchy S, Tartaglio J, Visco K, Phelan SA: Overexpression of Prdx6 and resistance to peroxide-induced death in Hepal-6 cells: Prdx suppression increases apoptosis. *Redox Rep* 2009, 14:275–84.
296. Zhang X, Xiao Z, Li C, Xiao Z, Yang F, Li D, Li M, Li F, Chen Z: Triosephosphate isomerase and peroxiredoxin 6, two novel serum markers for human lung squamous cell carcinoma. *Cancer Sci* 2009, 100:2396–401.
297. Chang XZ, Li DQ, Hou YF, Wu J, Lu J-S, Di GH, Jin W, Ou ZL, Shen ZZ, Shao ZM: Identification of the functional role of peroxiredoxin 6 in the progression of breast cancer. *Breast Cancer Res* 2007, 9:R76.
298. Feng S, Cen J, Huang Y, Shen H, Yao L, Wang Y, Chen Z: Matrix metalloproteinase-2 and -9 secreted by leukemic cells increase the permeability of blood-brain barrier by disrupting tight junction proteins. *PLoS One* 2011, 6:e20599.
299. Petra Hudler, Kocevar N, Komel R: Proteomic Approaches in Biomarker Discovery: New Perspectives in Cancer Diagnostics. *Sci World J* 2014, 2014:18 pages.
300. Rodland KD: Proteomics and cancer diagnosis: the potential of mass spectrometry. *Clin Biochem* 2004, 37:579–583.
301. Abhilash Venugopal, Raghothama Chaerkady AP: Application of mass spectrometry-based proteomics for biomarker discovery in neurological disorders. *Ann Indian Acad Neurol* 2009, 12:3–11.
302. Adam B, Vlahou A, Semmes OJ, Wright GJ: Proteomic approaches to biomarker discovery in prostate and bladder cancers. *Proteomics* 2001, 1:1264–70.

303. Ye X, Blonder J, Veenstra TD: Targeted proteomics for validation of biomarkers in clinical samples. *Brief Funct Genomic Proteomic* 2009, 8:126–35.
304. Thiede B, Koehler CJ, Strozynski M, Treumann A, Stein R, Zimny-Arndt U, Schmid M, Jungblut PR: High resolution quantitative proteomics of HeLa cells protein species using stable isotope labeling with amino acids in cell culture(SILAC), two-dimensional gel electrophoresis(2DE) and nano-liquid chromatography coupled to an LTQ-OrbitrapMass spectrometer. *Mol Cell Proteomics* 2013, 12:529–38.
305. Köhler K, Seitz H: Validation processes of protein biomarkers in serum--a cross platform comparison. *Sensors (Basel)* 2012, 12:12710–28.
306. Penque D: Two-dimensional gel electrophoresis and mass spectrometry for biomarker discovery. *Proteomics - Clin Appl* 2009, 3:155–172.