

1. Hanahan D, Weinberg R. The hallmarks of cancer. *Cell* 2000;100:57–70.
2. Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. *Cell* 2011;144:646–674.
3. Lemmon MA, Schlessinger J. Cell signaling by receptor tyrosine kinases. *Cell* 2010;141:1117–1134.
4. Witsch E, Sela M, Yarden Y. Roles for growth factors in cancer progression. *Physiology* 2010;25:85–101.
5. Hynes NE, MacDonald G. ErbB receptors and signaling pathways in cancer. *Curr Opin Cell Biol* 2009;21:177–184.
6. Perona T. Cell signalling: growth factors and tyrosine kinase receptors. *Clin Transl Oncol* 2006;8:77–82.
7. Franco OE, Shaw AK, Strand DW, et al. Cancer associated fibroblasts in cancer pathogenesis. *Semin Cell Dev Biol* 2010;21:33–39.
8. Bhowmick NA, Neilson EG, Moses HL. Stromal fibroblasts in cancer initiation and progression. *Nature* 2004;432:332–337.
9. Davies MA, Samuels Y. Analysis of the genome to personalize therapy for melanoma. *Oncogene* 2010;29:5545–5555.
10. Jiang BH, Liu LZ. PI3K/PTEEN signaling in angiogenesis and tumorigenesis. *Adv Cancer Res* 2009;102:19–65.
11. Yuan TL, Cantley LC. PI3K pathway alterations in cancer: variations on a theme. *Oncogene* 2008;27:5497–5510.
12. Wertz IE, Dixit VM. Regulation of death receptor signaling by the ubiquitin system. *Cell Death Differ* 2010;17:14–24.
13. Cabrita MA, Christofori G. Sprouty proteins, masterminds of receptor tyrosine kinase signaling. *Angiogenesis* 2008;11:53–62.
14. Amit I, Citri A, Shay T, et al. A module of negative feedback regulators defines growth factor signaling. *Nature Genet* 2007;39:503–512.
15. Mossesson Y, Mills GB, Yarden Y. Derailed endocytosis: an emerging feature of cancer. *Nat Rev Cancer* 2008;8:835–850.
16. Sudarsanam S, Johnson DE. Functional consequences of mTOR inhibition. *Curr Opin Drug Discov Devel* 2010;13:31–40.
17. O'Reilly KE, Rojo F, She QB, et al. mTOR inhibition induces upstream receptor tyrosine kinase signaling and activates Akt. *Cancer Res* 2006;66:1500–1508.
18. Dang CV. MYC on the path to cancer. *Cell* 2012;149:22–35.
19. Collado M, Serrano M. Senescence in tumours: evidence from mice and humans. *Nat Rev Cancer* 2010;10:51–57.
20. Evan GI, d'Adda di Fagnagna F. Cellular senescence: hot or what? *Curr Opin Genet Dev* 2009;19:25–31.
21. Lowe SW, Cepero E, Evan G. Intrinsic tumour suppression. *Nature* 2004;432:307–315.
22. Mooi WJ, Peeper DS. Oncogene-induced cell senescence—halting on the road to cancer. *N Engl J Med* 2006;355:1037–1046.
23. Burkhardt DL, Sage J. Cellular mechanisms of tumour suppression by the retinoblastoma gene. *Nat Rev Cancer* 2008;8:671–682.
24. Deshpande A, Sicinski P, Hinds PW. Cyclins and cdk in development and cancer: a perspective. *Oncogene* 2005;24:2909–2915.
25. Sherr CJ, McCormick F. The RB and p53 pathways in cancer. *Cancer Cell* 2002;2:103–112.
26. Lipinski MM, Jacks T. The retinoblastoma gene family in differentiation and development. *Oncogene* 1999;18:7873–7882.
27. Chebraniou N, Donehower LA. Mouse models in tumor suppression. *Oncogene* 1998;17: 3385–3400.
28. McClatchey AI, Yap AS. Contact inhibition (of proliferation) redux. *Curr Opin Cell Biol* 2012;24:685–694.
29. Curto M, Cole BK, Lallemand D, et al. Contact-dependent inhibition of EGFR signaling by Nf2/Merlin. *J Cell Biol* 2007;177:893–903.
30. Okada T, Lopez-Lago M, Giancotti FG. Merlin/NF-2 mediates contact inhibition of growth by suppressing recruitment of Rac to the plasma membrane. *J Cell Biol* 2005;171:361–371.
31. Stamenkovic I, Yu Q. Merlin, a “magic” linker between the extracellular cues and intracellular signaling pathways that regulate cell motility, proliferation, and survival. *Curr Protein Pept Sci* 2010;11:471–484.
32. Pickup M, Novitskiv S, Moses HL. The roles of TGFβ in the tumour microenvironment. *Nat Rev Cancer* 2013;13:788–799.
33. Ikushima H, Miyazono K. TGFβ signaling: a complex web in cancer progression. *Nat Rev Cancer* 2010;10:415–424.
34. Massagué J. TGF-β in cancer. *Cell* 2008;134:215–230.
35. Bierie B, Moses HL. Tumour microenvironment: TGF-β: the molecular Jekyll and Hyde of cancer. *Nat Rev Cancer* 2006;6:506–520.
36. Strasser A, Cory S, Adams JM. Deciphering the rules of programmed cell death to improve therapy of cancer and other diseases. *EMBO J* 2011;30:3667–3683.
37. Adams JM, Cory S. The Bcl-2 apoptotic switch in cancer development and therapy. *Oncogene* 2007;26:1324–1337.
38. Evan G, Littlewood T. A matter of life and cell death. *Science* 2004;281:1317–1322.
39. Willis SN, Adams JM. Life in the balance: how BH3-only proteins induce apoptosis. *Curr Opin Cell Biol* 2005;17:617–625.
40. Junttila MR, Evan GI. p53 — a jack of all trades but master of none. *Nat Rev Cancer* 2009;9:821–829.
41. White E. Deconvoluting the context-dependent role for autophagy in cancer. *Nat Rev Cancer* 2012;12:401–410.
42. Levine B, Kroemer G. Autophagy in the pathogenesis of disease. *Cell* 2008;132:27–42.
43. Mizushima N. Autophagy: process and function. *Genes Dev* 2007;21:2861–2873.
44. Sinha S, Levine B. The autophagy effector Beclin 1: a novel BH3-only protein. *Oncogene* 2008;27:S137–S148.
45. Mathew R, Karantza-Wadsworth V, White E. Role of autophagy in cancer. *Nat Rev Cancer* 2007;7:961–967.
46. White E, DiPaola RS. The double-edged sword of autophagy modulation in cancer. *Clin Cancer Res* 2009;15:5308–5316.
47. Apel A, Zentgraf H, Büchler MW, et al. Autophagy—A double-edged sword in oncology. *Int J Cancer* 2009;125:991–995.
48. Amaravadi RK, Thompson CB. The roles of therapy-induced autophagy and necrosis in cancer treatment. *Clin Cancer Res* 2007;13:7271–7279.
49. Lu Z, Luo RZ, Lu Y, et al. The tumor suppressor gene ARHI regulates autophagy and tumor dormancy in human ovarian cancer cells. *J Clin Invest* 2008;118:3917–3929.
50. Vanden Berghe T, Linkermann A, Jouan-Lanhouet S, et al. Regulated necrosis: the expanding network of non-apoptotic cell death pathways. *Nat Rev Mol Cell Biol* 2014;15:135–147.
51. Galluzzi L, Kroemer G. Necroptosis: a specialized pathway of programmed necrosis. *Cell* 2008;135:1161–1163.
52. Zong WX, Thompson CB. Necrotic death as a cell fate. *Genes Dev* 2006;20:1–15.
53. Grivennikov SI, Greten FR, Karin M. Immunity, inflammation, and cancer. *Cell* 2010;140:883–899.
54. White E, Karp C, Strohecker AM, et al. Role of autophagy in suppression of inflammation and cancer. *Curr Opin Cell Biol* 2010;22:212–217.
55. Blasco MA. Telomeres and human disease: ageing, cancer and beyond. *Nat Rev Genet* 2005;6:611–622.
56. Shay JW, Wright WE. Hayflick, his limit, and cellular ageing. *Nat Rev Mol Cell Biol* 2000;1:72–76.
57. Shay JW, Wright WE. Telomeres and telomerase in cancer. *Semin Cancer Biol* 2011;21:349–353.
58. Artandi SE, DePinho RA. Telomeres and telomerase in cancer. *Carcinogenesis* 2010;31:9–18.
59. Cesare AJ, Reddel RR. Alternative lengthening of telomeres: models, mechanisms and implications. *Nat Rev Genet* 2010;11:319–330.
60. Ince TA, Richardson AL, Bell GW, et al. Transformation of different human breast epithelial cell types leads to distinct tumor phenotypes. *Cancer Cell* 2007;12:160–170.
61. Passos JF, Saretzki G, von Zglinicki T. DNA damage in telomeres and mitochondria during cellular senescence: is there a connection? *Nucleic Acids Res* 2007;35:7505–7513.
62. Zhang H, Herbert BS, Pan KH, et al. Disparate effects of telomere attrition on gene expression during replicative senescence of human mammary epithelial cells cultured under different conditions. *Oncogene* 2004;23:6193–6198.
63. Sherr CJ, DePinho RA. Cellular senescence: mitotic clock or culture shock? *Cell* 2000;102:407–410.
64. Feldser DM, Greider CW. Short telomeres limit tumor progression in vivo by inducing senescence. *Cancer Cell* 2007;11:461–469.
65. Kawai T, Hiroi S, Nakanishi K, et al. Telomere length and telomerase expression in atypical adenomatous hyperplasia and small bronchioloalveolar carcinoma of the lung. *Am J Clin Pathol* 2007;127:254–262.
66. Hansel DE, Meeker AK, Hicks J. Telomere length variation in biliary tract metaplasia, dysplasia, and carcinoma. *Mod Pathol* 2006;19:772–779.
67. Artandi SE, DePinho RA. Mice without telomerase: what can they teach us about human cancer? *Nature Med* 2000;6:852–855.
68. Raynaud CM, Hernandez J, Llorca FP, et al. DNA damage repair and telomere length in normal breast, preneoplastic lesions, and invasive cancer. *Am J Clin Oncol* 2010;33:341–345.
69. Chin K, de Solorzano CO, Knowles D, et al. In situ analyses of genome instability in breast cancer. *Nature Genet* 2004;36:984–988.
70. Hanahan D, Folkman J. Patterns and emerging mechanisms of the angiogenic switch during tumorigenesis. *Cell* 1996;86:353–364.
71. Baeriswyl V, Christofori G. The angiogenic switch in carcinogenesis. *Semin Cancer Biol* 2009;19:329–337.
72. Bergers G, Benjamin LE. Tumorigenesis and the angiogenic switch. *Nat Rev Cancer* 2003;3:401–410.
73. Ferrara N. Vascular endothelial growth factor. *Arterioscler Thromb Vasc Biol* 2009;29:789–791.
74. Mac Gabhann F, Popel AS. Systems biology of vascular endothelial growth factors. *Microcirculation* 2008;15:715–738.
75. Carmeliet P. VEGF as a key mediator of angiogenesis in cancer. *Oncology* 2005;69:4–10.
76. Kessenbrock K, Plaks V, Werb Z. Matrix metalloproteinases: regulators of the tumor microenvironment. *Cell* 2010;141:52–67.
77. Kazerounian S, Yee KO, Lawler J. Thrombospondins in cancer. *Cell Mol Life Sci* 2008;65:700–712.

78. Nagy JA, Chang SH, Shih SC, et al. Heterogeneity of the tumor vasculature. *Semin Thromb Hemost* 2010;36:321–331.
79. Baluk P, Hashizume H, McDonald DM. Cellular abnormalities of blood vessels as targets in cancer. *Curr Opin Genet Dev* 2005;15:102–111.
80. Raica M, Cimpean AM, Ribatti D. Angiogenesis in pre-malignant conditions. *Eur J Cancer* 2009;45:1924–1934.
81. Olive KP, Jacobetz MA, Davidson CJ, et al. Inhibition of Hedgehog signaling enhances delivery of chemotherapy in a mouse model of pancreatic cancer. *Science* 2009;324:1457–1461.
82. Zee YK, O'Connor JP, Parker CJ, et al. Imaging angiogenesis of genitourinary tumors. *Nat Rev Urol* 2010;7:69–82.
83. Turner HE, Harris AL, Melmed S, et al. Angiogenesis in endocrine tumors. *Endocr Rev* 2003;24:600–632.
84. Xie L, Duncan MB, Pahler J, et al. Counterbalancing angiogenic regulatory factors control the rate of cancer progression and survival in a stage-specific manner. *Proc Natl Acad Sci U S A* 2011;108:9939–9944.
85. Ribatti D. Endogenous inhibitors of angiogenesis: a historical review. *Leuk Res* 2009;33:638–644.
86. Folkman J. Angiogenesis. *Annu Rev Med* 2006;57:1–18.
87. Folkman J. Role of angiogenesis in tumor growth and metastasis. *Semin Oncol* 2002;29:15–18.
88. Nyberg P, Xie L, Kalluri R. Endogenous inhibitors of angiogenesis. *Cancer Res* 2005;65:3967–3979.
89. Cao Y. Adipose tissue angiogenesis as a therapeutic target for obesity and metabolic diseases. *Nat Rev Drug Discov* 2010;9:107–115.
90. Seppinen L, Sormunen R, Soini Y, et al. Lack of collagen XVIII accelerates cutaneous wound healing, while overexpression of its endostatin domain leads to delayed healing. *Matrix Biol* 2008;27:535–546.
91. Raza A, Franklin MJ, Dudek AZ. Pericytes and vessel maturation during tumor angiogenesis and metastasis. *Am J Hematol* 2010;85:593–598.
92. Kovacic JC, Boehm M. Resident vascular progenitor cells: an emerging role for non-terminally differentiated vessel-resident cells in vascular biology. *Stem Cell Res* 2009;2:2–15.
93. Bergers C, Song S. The role of pericytes in blood-vessel formation and maintenance. *Neuro Oncol* 2005;7:452–464.
94. Qian BZ, Pollard JW. Macrophage diversity enhances tumor progression and metastasis. *Cell* 2010;141:39–51.
95. Zumsteg A, Christofori G. Corrupt policemen: inflammatory cells promote tumor angiogenesis. *Curr Opin Oncol* 2009;21:60–70.
96. Murdoch C, Muthana M, Coffelt SB, et al. The role of myeloid cells in the promotion of tumour angiogenesis. *Nat Rev Cancer* 2008;8:618–631.
97. De Palma M, Murdoch C, Venneri MA, et al. Tie2-expressing monocytes: regulation of tumor angiogenesis and therapeutic implications. *Trends Immunol* 2007;28:519–524.
98. Ferrara N. Pathways mediating VEGF-independent tumor angiogenesis. *Cytokine Growth Factor Rev* 2010;21:21–26.
99. Patenaude A, Parker J, Karsan A. Involvement of endothelial progenitor cells in tumor vascularization. *Microvasc Res* 2010;79:217–223.
100. Lamagna C, Bergers G. The bone marrow constitutes a reservoir of pericyte progenitors. *J Leukoc Biol* 2006;80:677–681.
101. Talmadge JE, Fidler IJ. AACR centennial series: the biology of cancer metastasis: historical perspective. *Cancer Res* 2010;70:5649–5669.
102. Fidler IJ. The pathogenesis of cancer metastasis: the “seed and soil” hypothesis revisited. *Nat Rev Cancer* 2003;3:453–458.
103. Bex G, van Roy F. Involvement of members of the cadherin superfamily in cancer. *Cold Spring Harb Perspect Biol* 2009;1:a003129.
104. Cavallaro U, Christofori G. Cell adhesion and signaling by cadherins and Ig-CAMs in cancer. *Nat Rev Cancer* 2004;4:118–132.
105. De Craene B, Bex G. Regulatory networks defining EMT during cancer initiation and progression. *Nat Rev Cancer* 2013;13:97–110.
106. Klymkowsky MW, Savagner P. Epithelial-mesenchymal transition: a cancer researcher's conceptual friend and foe. *Am J Pathol* 2009;174:1588–1592.
107. Polyak K, Weinberg RA. Transitions between epithelial and mesenchymal states: acquisition of malignant and stem cell traits. *Nat Rev Cancer* 2009;9:265–273.
108. Thiery JP, Acloque H, Huang RY, et al. Epithelial-mesenchymal transitions in development and disease. *Cell* 2009;139:871–890.
109. Yilmaz M, Christofori G. EMT, the cytoskeleton, and cancer cell invasion. *Cancer Metastasis Rev* 2009;28:15–33.
110. Barrallo-Gimeno A, Nieto MA. The Snail genes as inducers of cell movement and survival: implications in development and cancer. *Development* 2005;132:3151–3161.
111. Micalizzi DS, Farabaugh SM, Ford HL. Epithelial-mesenchymal transition in cancer: parallels between normal development and tumor progression. *J Mammary Gland Biol Neoplasia* 2010;15:117–134.
112. Taube JH, Herschkowitz JI, Komurov K, et al. Core epithelial-to-mesenchymal transition interactome gene-expression signature is associated with claudin-low and metaplastic breast cancer subtypes. *Proc Natl Acad Sci U S A* 2010;107:15449–15454.
113. Schmalhofer O, Brabletz S, Brabletz T. E-cadherin, beta-catenin, and ZEB1 in malignant progression of cancer. *Cancer Metastasis Rev* 2009;28:151–166.
114. Yang J, Weinberg RA. Epithelial-mesenchymal transition: at the crossroads of development and tumor metastasis. *Develop Cell* 2008;14:818–829.
115. Peinado H, Marin F, Cubillo E, et al. Snail and E47 repressors of E-cadherin induce distinct invasive and angiogenic properties in vivo. *J Cell Sci* 2004;117:2827–2839.
116. Karnoub AE, Weinberg RA. Chemokine networks and breast cancer metastasis. *Breast Dis* 2006;26:75–85.
117. Brabletz T, Jung A, Reu S, et al. Variable beta-catenin expression in colorectal cancers indicates tumor progression driven by the tumor environment. *Proc Natl Acad Sci U S A* 2001;98:10356–10361.
118. Hlubek F, Brabletz T, Budczies J, et al. Heterogeneous expression of Wnt/beta-catenin target genes within colorectal cancer. *Int J Cancer* 2007;121:1941–1948.
119. Egeblad M, Nakasone ES, Werb Z. Tumors as organs: complex tissues that interface with the entire organism. *Dev Cell* 2010;18:884–901.
120. Joyce JA, Pollard JW. Microenvironmental regulation of metastasis. *Nat Rev Cancer* 2009;9:239–252.
121. Kalluri R, Zeisberg M. Fibroblasts in cancer. *Nat Rev Cancer* 2006;6:392–401.
122. Karnoub AE, Dash AB, Vo AP, et al. Mesenchymal stem cells within tumour stroma promote breast cancer metastasis. *Nature* 2007;449:557–563.
123. Li HJ, Reinhart F, Herschman HR, et al. Cancer-stimulated mesenchymal stem cells create a carcinoma stem cell niche via prostaglandin E2 signaling. *Cancer Discov* 2012;2:840–855.
124. Palermo C, Joyce JA. Cysteine cathepsin proteases as pharmacological targets in cancer. *Trends Pharmacol Sci* 2008;29:22–28.
125. Mohamed MM, Sloane BF. Cysteine cathepsins: multifunctional enzymes in cancer. *Nat Rev Cancer* 2006;6:764–775.
126. Gocheva V, Wang HW, Gadea BB, et al. IL-4 induces cathepsin protease activity in tumor-associated macrophages to promote cancer growth and invasion. *Genes Dev* 2010;24:241–255.
127. Wyckoff JB, Wang Y, Lin EY, et al. Direct visualization of macrophage-assisted tumor cell intravasation in mammary tumors. *Cancer Res* 2007;67:2649–2656.
128. Hugo H, Ackland ML, Blick T, et al. Epithelial-mesenchymal and mesenchymal-epithelial transitions in carcinoma progression. *J Cell Physiol* 2007;213:374–383.
129. Friedl P, Wolf K. Plasticity of cell migration: a multiscale tuning model. *J Cell Biol* 2009;188:11–19.
130. Friedl P, Wolf K. Tube travel: the role of proteases in individual and collective cancer cell invasion. *Cancer Res* 2008;68:7247–7249.
131. Madsen CD, Sahai E. Cancer dissemination—lessons from leukocytes. *Dev Cell* 2010;19:13–26.
132. Sabeh F, Shimizu-Hirota R, Weiss SJ. Protease-dependent versus-independent cancer cell invasion programs: three-dimensional amoeboid movement revisited. *J Cell Biol* 2009;185:11–19.
133. Quail DF, Joyce JA. Microenvironmental regulation of tumor progression and metastasis. *Nat Med* 2013;19:1423–1437.
134. McGowan PM, Kirstein JM, Chambers AF. Micrometastatic disease and metastatic outgrowth: clinical issues and experimental approaches. *Future Oncol* 2009;5:1083–1098.
135. Aguirre-Ghiso JA. Models, mechanisms and clinical evidence for cancer dormancy. *Nat Rev Cancer* 2007;7:834–846.
136. Townson JL, Chambers AF. Dormancy of solitary metastatic cells. *Cell Cycle* 2006;5:1744–1750.
137. Demicheli R, Retsky MW, Hrushesky WJ, et al. The effects of surgery on tumor growth: a century of investigations. *Ann Oncol* 2008;19:1821–1828.
138. Barkan D, Green JE, Chambers AF. Extracellular matrix: a gatekeeper in the transition from dormancy to metastatic growth. *Eur J Cancer* 2010;46:1181–1188.
139. Gupta GP, Minn AJ, Kang Y, et al. Identifying site-specific metastasis genes and functions. *Cold Spring Harb Symp Quant Biol* 2005;70:149–158.
140. Naumov GN, Folkman J, Straume O, et al. Tumor-vascular interactions and tumor dormancy. *APMIS* 2008;116:569–585.
141. Kenific CM, Thorburn A, Debnath J. Autophagy and metastasis: another double-edged sword. *Curr Opin Cell Biol* 2010;22:241–245.
142. Teng MW, Swann JB, Koebel CM, et al. Immune-mediated dormancy: an equilibrium with cancer. *J Leukoc Biol* 2008;84:988–993.
143. Campbell PJ, Yachida S, Mudie LJ, et al. The patterns and dynamics of genomic instability in metastatic pancreatic cancer. *Nature* 2010;467:1109–1113.
144. Luebeck EG. Cancer: genomic evolution of metastasis. *Nature* 2010;467:1053–1055.
145. Yachida S, Jones S, Bozic I, et al. Distant metastasis occurs late during the genetic evolution of pancreatic cancer. *Nature* 2010;467:1114–1117.
146. Coghlin C, Murray GI. Current and emerging concepts in tumour metastasis. *J Pathol* 2010;222:1–15.
147. Klein CA. Parallel progression of primary tumours and metastases. *Nat Rev Cancer* 2009;9:302–312.
148. Gerhardt H, Semb H. Pericytes: gatekeepers in tumour cell metastasis? *J Mol Med* 2008;86:135–144.
149. Kim MY, Oskarsson T, Acharya S, et al. Tumor self-seeding by circulating cancer cells. *Cell* 2009;139:1315–1326.
150. Bos PD, Zhang XH, Nadal C, et al. Genes that mediate breast cancer metastasis to the brain. *Nature* 2009;459:1005–1009.

151. Olson P, Lu J, Zhang H, et al. MicroRNA dynamics in the stages of tumorigenesis correlate with hallmark capabilities of cancer. *Genes Dev* 2009;23:2152–2165.
152. Nguyen DX, Bos PD, Massagué J. Metastasis: from dissemination to organ-specific colonization. *Nat Rev Cancer* 2009;9:274–284.
153. Warburg OH. *The Metabolism of Tumours: Investigations from the Kaiser Wilhelm Institute for Biology, Berlin-Dahlem*. London, UK: Arnold Constable; 1930.
154. Warburg O. On the origin of cancer cells. *Science* 1956;123:309–314.
155. Warburg O. On respiratory impairment in cancer cells. *Science* 1956;124:269–270.
156. Jones RG, Thompson CB. Tumor suppressors and cell metabolism: a recipe for cancer growth. *Genes Dev* 2009;23:537–548.
157. DeBerardinis RJ, Lum JJ, Hatzivassiliou G, et al. The biology of cancer: metabolic reprogramming fuels cell growth and proliferation. *Cell Metab* 2008;7:11–20.
158. Hsu PP, Sabatini DM. Cancer cell metabolism: Warburg and beyond. *Cell* 2008;134:703–707.
159. Ward PS, Thompson CB. Metabolic reprogramming: a cancer hallmark even warburg did not anticipate. *Cancer Cell* 2012;21:297–308.
160. Semenza GL. HIF-1: upstream and downstream of cancer metabolism. *Curr Opin Genet Dev* 2010;20:51–56.
161. Semenza GL. Defining the role of hypoxia-inducible factor 1 in cancer biology and therapeutics. *Oncogene* 2010;29:625–634.
162. Kroemer G, Pouyssegur J. Tumor cell metabolism: cancer's Achilles' heel. *Cancer Cell* 2008;13:472–482.
163. Potter V. The biochemical approach to the cancer problem. *Fed Proc* 1958;17:691–697.
164. Vander Heiden MG, Cantley LC, Thompson CB. Understanding the Warburg effect: the metabolic requirements of cell proliferation. *Science* 2009;324:1029–1033.
165. Semenza GL. Tumor metabolism: cancer cells give and take lactate. *J Clin Invest* 2008;118:3835–3837.
166. Nakajima EC, Van Houten B. Metabolic symbiosis in cancer: refocusing the Warburg lens. *Mol Carcinog* 2013;52:329–337.
167. Kennedy KM, Dewhirst MW. Tumor metabolism of lactate: the influence and therapeutic potential for MCT and CD147 regulation. *Future Oncol* 2010;6:127–148.
168. Feron O. Pyruvate into lactate and back: from the Warburg effect to symbiotic energy fuel exchange in cancer cells. *Radiother Oncol* 2009;92:329–333.
169. Magistretti PJ. Neuron-glia metabolic coupling and plasticity. *J Exp Biol* 2006;209:2304–2311.
170. Hardee ME, Dewhirst MW, Agarwal N, et al. Novel imaging provides new insights into mechanisms of oxygen transport in tumors. *Curr Mol Med* 2009;9:435–441.
171. Burnet FM. The concept of immunological surveillance. *Prog Exp Tumor Res* 1970;13:1–27.
172. Thomas L. On immunosurveillance in human cancer. *Yale J Biol Med* 1982;55:329–333.
173. Vajdic CM, van Leeuwen MT. Cancer incidence and risk factors after solid organ transplantation. *Int J Cancer* 2009;125:1747–1754.
174. Elinav E, Nowarski R, Thaiss CA, et al. Inflammation-induced cancer: cross-talk between tumours, immune cells and microorganisms. *Nat Rev Cancer* 2013;13:759–771.
175. Swann JB, Smyth MJ. Immune surveillance of tumors. *J Clin Invest* 2007;117:1137–1146.
176. Fridman WH, Mlecnik B, Bindea G, et al. Immunosurveillance in human non-viral cancers. *Curr Opin Immunol* 2011;23:272–278.
177. Galon J, Angell HK, Bedognetti D, et al. The continuum of cancer immunosurveillance: prognostic, predictive, and mechanistic signatures. *Immunity* 2013;39:11–26.
178. Kim R, Emi M, Tanabe K. Cancer immunoediting from immune surveillance to immune escape. *Immunology* 2007;121:1–14.
179. Smyth MJ, Dunn GP, Schreiber RD. Cancer immunosurveillance and immune-editing: the roles of immunity in suppressing tumor development and shaping tumor immunogenicity. *Adv Immunol* 2006;90:1–50.
180. Bindea G, Mlecnik B, Fridman WH, et al. Natural immunity to cancer in humans. *Curr Opin Immunol* 2010;22:215–222.
181. Ferrone C, Dranoff G. Dual roles for immunity in gastrointestinal cancers. *J Clin Oncol* 2010;28:4045–4051.
182. Nelson BH. The impact of T-cell immunity on ovarian cancer outcomes. *Immunol Rev* 2008;222:101–116.
183. Pagès F, Galon J, Dieu-Nosjean MC, et al. Immune infiltration in human tumors: a prognostic factor that should not be ignored. *Oncogene* 2010;29:1093–1102.
184. Strauss DC, Thomas JM. Transmission of donor melanoma by organ transplantation. *Lancet Oncol* 2010;11:790–796.
185. Yang L, Pang Y, Moses HL. TGF-beta and immune cells: an important regulatory axis in the tumor microenvironment and progression. *Trends Immunol* 2010;31:220–227.
186. Shields JD, Kourtis IC, Tomei AA, et al. Induction of lymphoidlike stroma and immune escape by tumors that express the chemokine CCL21. *Science* 2010;328:749–752.
187. Korman AJ, Peggs KS, Allison J. Checkpoint blockade in cancer immunotherapy. *Adv Immunol* 2006;90:297–339.
188. Fife BT, Pauken KE, Eagar TN, et al. Interactions between programmed death-1 and programmed death ligand-1 promote tolerance by blocking the T cell receptor-induced stop signal. *Nat Immunol* 2009;10:1185–1192.
189. Pardoll DM. The blockade of immune checkpoints in cancer immunotherapy. *Nat Rev Cancer* 2012;12:252–264.
190. Motz GT, Coukos G. Deciphering and reversing tumor immune suppression. *Immunity* 2013;39:61–73.
191. Gabrilovich DI, Nagaraj S. Myeloid-derived suppressor cells as regulators of the immune system. *Nat Rev Immunol* 2009;9:162–174.
192. Mougikakos D, Choudhury A, Lladser A, et al. Regulatory T cells in cancer. *Adv Cancer Res* 2010;107:57–117.
193. Ostrand-Rosenberg S, Sinha P. Myeloid-derived suppressor cells: linking inflammation and cancer. *J Immunol* 2009;182:4499–4506.
194. Garraway LA, Lander ES. Lessons from the cancer genome. *Cell* 2013;153:17–37.
195. You JS, Jones PA. Cancer genetics and epigenetics: two sides of the same coin? *Cancer Cell* 2012;22:9–20.
196. Berdasco M, Esteller M. Aberrant epigenetic landscape in cancer: how cellular identity goes awry. *Dev Cell* 2010;19:698–711.
197. Esteller M. Cancer epigenomics: DNA methylomes and histone-modification maps. *Nat Rev Genet* 2007;8:286–298.
198. Jones PA, Baylin SB. The epigenomics of cancer. *Cell* 2007;128:683–692.
199. Negrini S, Gorgoulis VG, Halazonetis TD. Genomic instability—an evolving hallmark of cancer. *Nat Rev Mol Cell Bio* 2010;11:220–228.
200. Loeb LA. A mutator phenotype in cancer. *Cancer Res* 2001;61:3230–3239.
201. Jackson SP, Bartek J. The DNA-damage response in human biology and disease. *Nature* 2009;461:1071–1078.
202. Kastan MB. DNA damage responses: mechanisms and roles in human disease. *Mol Cancer Res* 2008;6:517–524.
203. Sigal A, Rotter V. Oncogenic mutations of the p53 tumor suppressor: the demons of the guardian of the genome. *Cancer Res* 2000;60:6788–6793.
204. Lane DP. Cancer. p53, guardian of the genome. *Nature* 1992;358:15–16.
205. Kinzler KW, Vogelstein B. Cancer-susceptibility genes. Gatekeepers and caretakers. *Nature* 1997;386:761–763.
206. Ciccio A, Elledge SJ. The DNA damage response: making it safe to play with knives. *Mol Cell* 2010;40:179–204.
207. Harper JW, Elledge SJ. The DNA damage response: ten years after. *Mol Cell* 2007;28:739–745.
208. Friedberg EC, Aguilera A, Gellert M, et al. DNA repair: from molecular mechanism to human disease. *DNA Repair (Amst)* 2006;5:986–996.
209. Barnes DE, Lindahl T. Repair and genetic consequences of endogenous DNA base damage in mammalian cells. *Annu Rev Genet* 2004;38:445–476.
210. Korkola J, Gray JW. Breast cancer genomes—form and function. *Curr Opin Genet Dev* 2010;20:4–14.
211. Dvorak HF. Tumors: wounds that do not heal. Similarities between tumor stroma generation and wound healing. *N Engl J Med* 1986;315:1650–1659.
212. De Nardo DG, Andreu P, Coussens LM. Interactions between lymphocytes and myeloid cells regulate pro- versus anti-tumor immunity. *Cancer Metastasis Rev* 2010;29:309–316.
213. Hanahan D, Coussens LM. Accessories to the crime: functions of cells recruited to the tumor microenvironment. *Cancer Cell* 2012;21:309–322.
214. de Visser KE, Eichten A, Coussens LM. Paradoxical roles of the immune system during cancer development. *Nat Rev Cancer* 2006;6:24–37.
215. Servais C, Erez N. From sentinel cells to inflammatory culprits: cancer-associated fibroblasts in tumour-related inflammation. *J Pathol* 2013;229:198–207.
216. Dirat B, Bochet L, Escourrou G, et al. Unraveling the obesity and breast cancer links: a role for cancer-associated adipocytes? *Endocr Dev* 2010;19:45–52.
217. Pietras K, Ostman A. Hallmarks of cancer: interactions with the tumor stroma. *Exp Cell Res* 2010;316:1324–1331.
218. Räsänen K, Vaheri A. Activation of fibroblasts in cancer stroma. *Exp Cell Res* 2010;316:2713–2722.
219. Shimoda M, Mellody KT, Orimo A. Carcinoma-associated fibroblasts are a rate-limiting determinant for tumour progression. *Sem Cell Dev Biol* 2010;21:19–25.
220. Welti J, Loges S, Dimmeler S, et al. Recent molecular discoveries in angiogenesis and antiangiogenic therapies in cancer. *J Clin Invest* 2013;123:3190–3200.
221. Pasquale EB. Eph receptors and ephrins in cancer: bidirectional signalling and beyond. *Nat Rev Cancer* 2010;10:165–180.
222. Ahmed Z, Bicknell R. Angiogenic signalling pathways. *Methods Mol Biol* 2009;467:3–24.
223. Dejana E, Orsenigo F, Molendini C, et al. Organization and signaling of endothelial cell-to-cell junctions in various regions of the blood and lymphatic vascular trees. *Cell Tissue Res* 2009;335:17–25.
224. Carmeliet P, Jain RK. Angiogenesis in cancer and other diseases. *Nature* 2000;407:249–257.
225. Ruoslahti E, Bhatia SN, Sailor MJ. Targeting of drugs and nanoparticles to tumors. *J Cell Biol* 2010;188:759–768.
226. Ruoslahti E. Specialization of tumour vasculature. *Nat Rev Cancer* 2002;2:83–90.

227. Motz GT, Coukos G. The parallel lives of angiogenesis and immunosuppression: cancer and other tales. *Nat Rev Immunol* 2011;11:702–711.
228. Carmeliet P, Jain RK. Principles and mechanisms of vessel normalization for cancer and other angiogenic diseases. *Nat Rev Drug Discov* 2011;10:417–427.
229. Tammela T, Alitalo K. Lymphangiogenesis: Molecular mechanisms and future promise. *Cell* 2010;140:460–476.
230. Card CM, Yu SS, Swartz MA. Emerging roles of lymphatic endothelium in regulating adaptive immunity. *J Clin Invest* 2014;124:943–952.
231. Gaengel K, Genové G, Armulik A, et al. Endothelial-mural cell signaling in vascular development and angiogenesis. *Arterioscler Thromb Vasc Biol* 2009;29:630–638.
232. Schäfer M, Werner S. Cancer as an overhealing wound: an old hypothesis revisited. *Nat Rev Mol Cell Biol* 2008;9:628–638.
233. Karin M, Lawrence T, Nizet V. Innate immunity gone awry: linking microbial infections to chronic inflammation and cancer. *Cell* 2006;124:823–835.
234. Coffeldt SB, Lewis CE, Naldini L, et al. Elusive identities and overlapping phenotypes of proangiogenic myeloid cells in tumors. *Am J Pathol* 2010;176:1564–1576.
235. Johansson M, Denardo DG, Coussens LM. Polarized immune responses differentially regulate cancer development. *Immunol Rev* 2008;222:145–154.
236. Mantovani A. Molecular pathways linking inflammation and cancer. *Curr Mol Med* 2010;10:369–373.
237. Mantovani A, Allavena P, Sica A, et al. Cancer-related inflammation. *Nature* 2008;454:436–444.
238. DeNardo DG, Brennan DJ, Rexhepaj E, et al. Leukocyte complexity predicts breast cancer survival and functionally regulates response to chemotherapy. *Cancer Discov* 2011;1:54–67.
239. De Palma M, Coukos G, Hanahan D. A new twist on radiation oncology: low-dose irradiation elicits immunostimulatory macrophages that unlock barriers to tumor immunotherapy. *Cancer Cell* 2013;24:559–561.
240. Koh BI, Kang Y. The pro-metastatic role of bone marrow-derived cells: a focus on MSCs and regulatory T cells. *EMBO Rep* 2012;13:412–422.
241. Bergfeld SA, DeClerck YA. Bone marrow-derived mesenchymal stem cells and the tumor microenvironment. *Cancer Metastasis Rev* 2010;29:249–261.
242. Fang S, Salven P. Stem cells in tumor angiogenesis. *J Mol Cell Cardiol* 2011;50:290–295.
243. Giaccia AJ, Schipani E. Role of carcinoma-associated fibroblasts and hypoxia in tumor progression. *Curr Top Microbiol Immunol* 2010;345:31–45.
244. Labelle M, Hynes RO. The initial hours of metastasis: the importance of cooperative host-tumor cell interactions during hematogenous dissemination. *Cancer Discov* 2012;2:1091–1099.
245. Peinado H, Lavotzkin S, Lyden D. The secreted factors responsible for pre-metastatic niche formation: old sayings and new thoughts. *Semin Cancer Biol* 2011;21:139–146.
246. Reya T, Morrison SJ, Clarke MF, et al. Stem cells, cancer, and cancer stem cells. *Nature* 2001;414:105–111.
247. Bonnet D, Dick JE. Human acute myeloid leukemia is organized as a hierarchy that originates from a primitive hematopoietic cell. *Nature Med* 1997;3:730–737.
248. Gilbertson RJ, Rich JN. Making a tumour's bed: glioblastoma stem cells and the vascular niche. *Nat Rev Cancer* 2007;7:733–736.
249. al-Hajj M, Wicha M, Benito-Hernandez A, et al. Prospective identification of tumorigenic breast cancer cells. *Proc Natl Acad Sci U S A* 2003;100:3983–3988.
250. Beck B, Blanpain C. Unravelling cancer stem cell potential. *Nat Rev Cancer* 2013;13:727–738.
251. Magee JA, Piskounova E, Morrison SJ. Cancer stem cells: impact, heterogeneity, and uncertainty. *Cancer Cell* 2012;21:283–296.
252. Cho RW, Clarke MF. Recent advances in cancer stem cells. *Curr Opin Genet Devel* 2008;18:1–6.
253. Lobo NA, Shimono Y, Qian D, et al. The biology of cancer stem cells. *Annu Rev Cell Dev Biol* 2007;23:675–699.
254. Meacham CE, Morrison SJ. Tumour heterogeneity and cancer cell plasticity. *Nature* 2013;501:328–337.
255. Singh A, Settleman J. EMT, cancer stem cells and drug resistance: an emerging axis of evil in the war on cancer. *Oncogene* 2010;29:4741–4751.
256. Brabletz T, Jung A, Spaderna S, et al. Opinion: migrating cancer stem cells – an integrated concept of malignant tumor progression. *Nat Rev Cancer* 2005;5:744–749.
257. Boiko AD, Razorenova OV, van de Rijn M, et al. Human melanoma-initiating cells express neural crest nerve growth factor receptor CD271. *Nature* 2010;466:133–137.
258. Gupta P, Chaffer CL, Weinberg RA. Cancer stem cells: mirage or reality? *Nature Med* 2009;15:1010–1012.
259. Quintana E, Shackleton M, Sabel MS, et al. Efficient tumour formation by single human melanoma cells. *Nature* 2008;456:593–598.
260. Chaffer CL, Brueckmann I, Scheel C, et al. Normal and neoplastic nonstem cells can spontaneously convert to stem-like state. *Proc Natl Acad Sci U S A* 2011;108:7950–7955.
261. Thiery JP, Sleeman JR. Complex networks orchestrate epithelial-mesenchymal transitions. *Nat Rev Mol Cell Biol* 2006;7:131–142.
262. Creighton CJ, Li X, Landis M, et al. Residual breast cancers after conventional therapy display mesenchymal as well as tumor-initiating features. *Proc Natl Acad Sci U S A* 2009;106:13820–13825.
263. Buck E, Eyzaguirre A, Barr S, et al. Loss of homotypic cell adhesion by epithelial-mesenchymal transition or mutation limits sensitivity to epidermal growth factor receptor inhibition. *Mol Cancer Therap* 2007;6:532–541.
264. Rhim AD, Mirek ET, Aiello NM, et al. EMT and dissemination precede pancreatic tumor formation. *Cell* 2012;148:349–361.
265. Soda Y, Marumoto T, Friedmann-Morvinski D, et al. Transdifferentiation of glioblastoma cells into vascular endothelial cells. *Proc Natl Acad Sci U S A* 2011;108:4274–4280.
266. El Hallani S, Boisselier B, Peglion F, et al. A new alternative mechanism in glioblastoma vascularization: tubular vasculogenic mimicry. *Brain* 2010;133:973–982.
267. Wang R, Chadalavada K, Wilshire J, et al. Glioblastoma stem-like cells give rise to tumour endothelium. *Nature* 2010;468:829–833.
268. Folkman J, Kalluri R. Cancer without disease. *Nature* 2004;427:787.
269. Azam F, Mehta S, Harris AL. Mechanisms of resistance to antiangiogenesis therapy. *Eur J Cancer* 2010;46:1323–1332.
270. Ebos JM, Lee CR, Kerbel RS. Tumor and host-mediated pathways of resistance and disease progression in response to antiangiogenic therapy. *Clin Cancer Res* 2009;15:5020–5025.
271. Bergers G, Hanahan D. Modes of resistance to anti-angiogenic therapy. *Nat Rev Cancer* 2008;8:592–603.
272. Ellis LM, Reardon DA. Cancer: the nuances of therapy. *Nature* 2009;458:290–292.
273. Norden AD, Drappatz J, Wen PY. Antiangiogenic therapies for high-grade glioma. *Nat Rev Neurol* 2009;5:610–620.
274. Verhoef JJ, van Tellingen O, Claes A, et al. Concerns about anti-angiogenic treatment in patients with glioblastoma multiforme. *BMC Cancer* 2009;9:444.
275. Hanahan D. Rethinking the war on cancer. *Lancet* 2014;383:558–563.
276. Pencheva N, Tavazoie SF. Control of metastatic progression by microRNA regulatory networks. *Nat Cell Biol* 2013;15:546–554.
277. Garzon R, Marcucci G, Croce CM. Targeting microRNAs in cancer: rationale, strategies and challenges. *Nat Rev Drug Discov* 2010;9:775–789.