

### Supplementary References

51. Sakai Y, Masamune A, Satoh A, et al. Macrophage migration inhibitory factor is a critical mediator of severe acute pancreatitis. *Gastroenterology* 2003;124:725–736.
52. Zaninovic V, Gukovskaya AS, Gukovsky I, et al. Cerulein upregulates ICAM-1 in pancreatic acinar cells, which mediates neutrophil adhesion to these cells. *Am J Physiol Gastrointest Liver Physiol* 2000;279:G666–G676.
53. Hartman H, Abdulla A, Awla D, et al. P-selectin mediates neutrophil rolling and recruitment in acute pancreatitis. *Br J Surg* 2012;99:246–255.
54. Sandoval D, Gukovskaya A, Reavey P, et al. The role of neutrophils and platelet-activating factor in mediating experimental pancreatitis. *Gastroenterology* 1996;111:1081–1091.
55. Gukovskaya AS, Vaquero E, Zaninovic V, et al. Neutrophils and NADPH oxidase mediate intrapancreatic trypsin activation in murine experimental acute pancreatitis. *Gastroenterology* 2002;122:974–984.
56. Abdulla A, Awla D, Thorlacius H, et al. Role of neutrophils in the activation of trypsinogen in severe acute pancreatitis. *J Leukoc Biol* 2011;90:975–982.
57. Awla D, Abdulla A, Zhang S, et al. Lymphocyte function antigen-1 regulates neutrophil recruitment and tissue damage in acute pancreatitis. *Br J Pharmacol* 2011;163:413–423.
58. Hartwig W, Klafs M, Kirschfink M, et al. Interaction of complement and leukocytes in severe acute pancreatitis: potential for therapeutic intervention. *Am J Physiol Gastrointest Liver Physiol* 2006;291:G844–G850.
59. Werner J, Hartwig W, Hackert T, et al. Multidrug strategies are effective in the treatment of severe experimental pancreatitis. *Surgery* 2012;151:372–381.
60. Marrache F, Tu SP, Bhagat G, et al. Overexpression of interleukin-1beta in the murine pancreas results in chronic pancreatitis. *Gastroenterology* 2008;135:1277–1287.
61. Moreno C, Nicaise C, Gustot T, et al. Chemokine receptor CCR5 deficiency exacerbates cerulein-induced acute pancreatitis in mice. *Am J Physiol Gastrointest Liver Physiol* 2006;291:G1089–G1099.
62. White GE, Iqbal AJ, Greaves DR. CC chemokine receptors and chronic inflammation—therapeutic opportunities and pharmacological challenges. *Pharmacol Rev* 2013;65:47–89.
63. Demols A, Van Laethem JL, Quertinmont E, et al. Endogenous interleukin-10 modulates fibrosis and regeneration in experimental chronic pancreatitis. *Am J Physiol Gastrointest Liver Physiol* 2002;282:G1105–G1112.
64. Feng D, Park O, Radaeva S, et al. Interleukin-22 ameliorates cerulein-induced pancreatitis in mice by inhibiting the autophagic pathway. *Int J Biol Sci* 2012;8:249–257.
65. Koike Y, Kanai T, Saeki K, et al. MyD88-dependent interleukin-10 production from regulatory CD11b(+)Gr-1(high) cells suppresses development of acute cerulein pancreatitis in mice. *Immunol Lett* 2012;148:172–177.
66. Xue J, Nguyen DT, Habtezion A. Aryl hydrocarbon receptor regulates pancreatic IL-22 production and protects mice from acute pancreatitis. *Gastroenterology* 2012;143:1670–1680.
67. Naugler WE, Karin M. The wolf in sheep's clothing: the role of interleukin-6 in immunity, inflammation and cancer. *Trends Mol Med* 2008;14:109–119.
68. Jones SA, Scheller J, Rose-John S. Therapeutic strategies for the clinical blockade of IL-6/gp130 signaling. *J Clin Invest* 2011;121:3375–3383.
69. Scheller J, Chalaris A, Schmidt-Arras D, et al. The pro- and anti-inflammatory properties of the cytokine interleukin-6. *Biochim Biophys Acta* 2011;1813:878–888.
70. Chao KC, Chao KF, Chuang CC, et al. Blockade of interleukin 6 accelerates acinar cell apoptosis and attenuates experimental acute pancreatitis in vivo. *Br J Surg* 2006;93:332–338.
71. Cuzzocrea S, Mazzon E, Dugo L, et al. Absence of endogenous interleukin-6 enhances the inflammatory response during acute pancreatitis induced by cerulein in mice. *Cytokine* 2002;18:274–285.
72. Witt H, Apte MV, Keim V, et al. Chronic pancreatitis: challenges and advances in pathogenesis, genetics, diagnosis, and therapy. *Gastroenterology* 2007;132:1557–1573.
73. Sparmann G, Behrend S, Merkord J, et al. Cytokine mRNA levels and lymphocyte infiltration in pancreatic tissue during experimental chronic pancreatitis induced by dibutyryl dichloride. *Dig Dis Sci* 2001;46:1647–1656.
74. Hense S, Sparmann G, Weber H, et al. Immunologic characterization of acute pancreatitis in rats induced by dibutyryl dichloride (DBTC). *Pancreas* 2003;27:e6–12.
75. Sakaguchi Y, Inaba M, Tsuda M, et al. The Wistar Bonn Kobori rat, a unique animal model for autoimmune pancreatitis with extrapancreatic exocrinopathy. *Clin Exp Immunol* 2008;152:1–12.
76. Schmitz-Winnenthal H, Pietsch DH, Schimmack S, et al. Chronic pancreatitis is associated with disease-specific regulatory T-cell responses. *Gastroenterology* 2010;138:1178–1188.
77. Hunger RE, Mueller C, Z'Graggen K, et al. Cytotoxic cells are activated in cellular infiltrates of alcoholic chronic pancreatitis. *Gastroenterology* 1997;112:1656–1663.
78. Kaiser AM, Saluja AK, Sengupta A, et al. Relationship between severity, necrosis, and apoptosis in five models of experimental acute pancreatitis. *Am J Physiol Cell Physiol* 1995;269:C1295–C1304.
79. Bhatia M. Apoptosis versus necrosis in acute pancreatitis. *Am J Physiol Gastrointest Liver Physiol* 2004;286:G189–G196.
80. Mareninova OA, Sung KF, Hong P, et al. Cell death in pancreatitis: caspases protect from necrotizing pancreatitis. *J Biol Chem* 2006;281:3370–3381.
81. Nakamura Y, Do JH, Yuan J, et al. Inflammatory cells regulate p53 and caspases in acute pancreatitis. *Am J Physiol Gastrointest Liver Physiol* 2010;298:G92–G100.
82. Aghdassi AA, Mayerle J, Christochowitz S, et al. Animal models for investigating chronic pancreatitis. *Fibrogenesis Tissue Repair* 2011;4:26.
83. Pezzilli R, Ceciliato R, Barakat B, et al. Immune-manipulation of the inflammatory response in acute pancreatitis. What can be expected? *JOP* 2004;5:115–121.
84. Bang UC, Semb S, Nojgaard C, et al. Pharmacological approach to acute pancreatitis. *World J Gastroenterol* 2008;14:2968–2976.
85. Kylianpa ML, Repo H, Puolakkainen PA. Inflammation and immunosuppression in severe acute pancreatitis. *World J Gastroenterol* 2010;16:2867–2872.
86. Algul H, Treiber M, Lesina M, et al. Pancreas-specific RelA/p65 truncation increases susceptibility of acini to inflammation-associated cell death following cerulein pancreatitis. *J Clin Invest* 2007;117:1490–1501.
87. Baumann B, Wagner M, Aleksic T, et al. Constitutive IKK2 activation in acinar cells is sufficient to induce pancreatitis in vivo. *J Clin Invest* 2007;117:1502–1513.
88. Zhou M, Chen B, Sun H, et al. The protective effects of Lipoxin A4 during the early phase of severe acute pancreatitis in rats. *Scand J Gastroenterol* 2011;46:211–219.
89. Serhan CN, Krishnamoorthy S, Recchiuti A, et al. Novel anti-inflammatory-pro-resolving mediators and their receptors. *Curr Top Med Chem* 2011;11:629–647.
90. Bardeesy N, DePinho RA. Pancreatic cancer biology and genetics. *Nat Rev Cancer* 2002;2:897–909.
91. Hezel AF, Kimmelman AC, Stanger BZ, et al. Genetics and biology of pancreatic ductal adenocarcinoma. *Genes Dev* 2006;20:1218–1249.

92. Maitra A, Hruban RH. Pancreatic cancer. *Annu Rev Pathol* 2008; 3:157–188.
93. Erkan M, Hausmann S, Michalski CW, et al. The role of stroma in pancreatic cancer: diagnostic and therapeutic implications. *Nat Rev Gastroenterol Hepatol* 2012;9:454–467.
94. Feig C, Gopinathan A, Neesse A, et al. The pancreas cancer microenvironment. *Clin Cancer Res* 2012;18:4266–4276.
95. Grivnikov SI, Greten FR, Karin M. Immunity, inflammation, and cancer. *Cell* 2010;140:883–899.
96. Fukuda A, Wang SC, Morris JP 4th, et al. Stat3 and MMP7 contribute to pancreatic ductal adenocarcinoma initiation and progression. *Cancer Cell* 2011;19:441–455.
97. Lesina M, Kurkowski MU, Ludes K, et al. Stat3/Socs3 activation by IL-6 transsignaling promotes progression of pancreatic intraepithelial neoplasia and development of pancreatic cancer. *Cancer Cell* 2011;19:456–469.
98. Li N, Grivnikov SI, Karin M. The unholy trinity: inflammation, cytokines, and STAT3 shape the cancer microenvironment. *Cancer Cell* 2011;19:429–431.
99. Ling J, Kang Y, Zhao R, et al. KrasG12D-induced IKK2/beta/NF-kappaB activation by IL-1alpha and p62 feedforward loops is required for development of pancreatic ductal adenocarcinoma. *Cancer Cell* 2012;21:105–120.
100. Maniati E, Bossard M, Cook N, et al. Crosstalk between the canonical NF-kappaB and Notch signaling pathways inhibits Ppargamma expression and promotes pancreatic cancer progression in mice. *J Clin Invest* 2011;121:4685–4699.
101. Clark CE, Hingorani SR, Mick R, et al. Dynamics of the immune reaction to pancreatic cancer from inception to invasion. *Cancer Res* 2007;67:9518–9527.
102. Cox AD, Olive KP. Silencing the killers: paracrine immune suppression in pancreatic cancer. *Cancer Cell* 2012;21:715–716.
103. Bayne LJ, Beatty GL, Jhala N, et al. Tumor-derived granulocyte-macrophage colony-stimulating factor regulates myeloid inflammation and T cell immunity in pancreatic cancer. *Cancer Cell* 2012;21:822–835.
104. Pylayeva-Gupta Y, Lee KE, Hajdu CH, et al. Oncogenic Kras-induced GM-CSF production promotes the development of pancreatic neoplasia. *Cancer Cell* 2012;21:836–847.
105. Guerra C, Schuhmacher AJ, Canamero M, et al. Chronic pancreatitis is essential for induction of pancreatic ductal adenocarcinoma by K-Ras oncogenes in adult mice. *Cancer Cell* 2007;11:291–302.
106. Guerra C, Collado M, Navas C, et al. Pancreatitis-induced inflammation contributes to pancreatic cancer by inhibiting oncogene-induced senescence. *Cancer Cell* 2011;19:728–739.
107. Rhim AD, Mirek ET, Aiello NM, et al. EMT and dissemination precede pancreatic tumor formation. *Cell* 2012;148:349–361.
108. Grivnikov SI, Karin M. Inflammation and oncogenesis: a vicious connection. *Curr Opin Genet Dev* 2010;20:65–71.
109. Daniluk J, Liu Y, Deng D, et al. An NF-kappaB pathway-mediated positive feedback loop amplifies Ras activity to pathological levels in mice. *J Clin Invest* 2012;122:1519–1528.
110. Levine B, Kroemer G. Autophagy in the pathogenesis of disease. *Cell* 2008;132:27–42.
111. Mizushima N. Autophagy: process and function. *Genes Dev* 2007;21:2861–2873.
112. Mizushima N, Yoshimori T, Ohsumi Y. The role of atg proteins in autophagosome formation. *Annu Rev Cell Dev Biol* 2011;27:107–132.
113. Klionsky DJ, Abdalla FC, Abieliovich H, et al. Guidelines for the use and interpretation of assays for monitoring autophagy. *Autophagy* 2012;8:445–544.
114. Ravikumar B, Sarkar S, Davies JE, et al. Regulation of mammalian autophagy in physiology and pathophysiology. *Physiol Rev* 2010;90:1383–1435.
115. Saftig P, Klumperman J. Lysosome biogenesis and lysosomal membrane proteins: trafficking meets function. *Nat Rev Mol Cell Biol* 2009;10:623–635.
116. Gukovskaya AS, Gukovsky I. Autophagy and pancreatitis. *Am J Physiol Gastrointest Liver Physiol* 2012;303:G993–G1003.
117. Adler G, Rohr G, Kern HF. Alteration of membrane fusion as a cause of acute pancreatitis in the rat. *Dig Dis Sci* 1982;27:993–1002.
118. Aho HJ, Nevalainen TJ, Havia VT, et al. Human acute pancreatitis: a light and electron microscopic study. *Acta Pathol Microbiol Immunol Scand A* 1982;90:367–373.
119. Helin H, Mero M, Markkula H, et al. Pancreatic acinar ultrastructure in human acute pancreatitis. *Virchows Arch A Pathol Anat Histol* 1980;387:259–270.
120. Koike H, Steer ML, Meldelesi J. Pancreatic effects of ethionine: blockade of exocytosis and appearance of crinophagy and autophagy precede cellular necrosis. *Am J Physiol* 1982;242:G297–G307.
121. Niederau C, Grendell JH. Intracellular vacuoles in experimental acute pancreatitis in rats and mice are an acidified compartment. *J Clin Invest* 1988;81:229–236.
122. Willemer S, Kloppel G, Kern HF, et al. Immunocytochemical and morphometric analysis of acinar zymogen granules in human acute pancreatitis. *Virchows Arch A Pathol Anat Histopathol* 1989;415:115–123.
123. Mareninova OA, Hermann K, French SW, et al. Impaired autophagic flux mediates acinar cell vacuole formation and trypsinogen activation in rodent models of acute pancreatitis. *J Clin Invest* 2009;119:3340–3355.
124. Grasso D, Ropolo A, Lo Re A, et al. Zymophagy, a novel selective autophagy pathway mediated by VMP1-USP9x-p62, prevents pancreatic cell death. *J Biol Chem* 2011;286:8308–8324.
125. Fortunato F, Burgers H, Bergmann F, et al. Impaired autolysosome formation correlates with Lamp-2 depletion: role of apoptosis, autophagy, and necrosis in pancreatitis. *Gastroenterology* 2009;137:350–360, 360.e1–5.
126. Hashimoto D, Ohmuraya M, Hirota M, et al. Involvement of autophagy in trypsinogen activation within the pancreatic acinar cells. *J Cell Biol* 2008;181:1065–1072.
127. Komatsu M, Kageyama S, Ichimura Y. p62/SQSTM1/A170: physiology and pathology. *Pharmacol Res* 2012;66:457–462.
128. Moscat J, Diaz-Meco MT. p62: a versatile multitasker takes on cancer. *Trends Biochem Sci* 2012;37:230–236.
129. Gukovsky I, Pandol SJ, Mareninova OA, et al. Impaired autophagy and organellar dysfunction in pancreatitis. *J Gastroenterol Hepatol* 2012;27(Suppl 2):27–32.
130. Gukovsky I, Pandol SJ, Gukovskaya AS. Organellar dysfunction in the pathogenesis of pancreatitis. *Antioxid Redox Signal* 2011;15:2699–2710.
131. Alirezaei M, Flynn CT, Whittom JL. Interactions between enteroviruses and autophagy in vivo. *Autophagy* 2012;8:973–975.
132. Boonen M, van Meel E, Oorschot V, et al. Vacuolization of mucolipidosis type II mouse exocrine gland cells represents accumulation of autolysosomes. *Mol Biol Cell* 2011;22:1135–1147.
133. Ohmuraya M, Hirota M, Araki M, et al. Autophagic cell death of pancreatic acinar cells in serine protease inhibitor Kazal type 3-deficient mice. *Gastroenterology* 2005;129:696–705.
134. Romac JM, Ohmuraya M, Bittner C, et al. Transgenic expression of pancreatic secretory trypsin inhibitor-1 rescues SPINK3-deficient mice and restores a normal pancreatic phenotype. *Am J Physiol Gastrointest Liver Physiol* 2010;298:G518–G524.
135. Li N, Wu X, Holzer RG, et al. Loss of acinar cell Ikka triggers spontaneous pancreatitis in mice. *J Clin Invest* 2013 April 8. Epub ahead of print.

136. Halangk W, Lerch MM, Brandt-Nedelev B, et al. Role of cathepsin B in intracellular trypsinogen activation and the onset of acute pancreatitis. *J Clin Invest* 2000;106:773–781.
137. Wartmann T, Mayerle J, Kahne T, et al. Cathepsin L inactivates human trypsinogen, whereas cathepsin L-deletion reduces the severity of pancreatitis in mice. *Gastroenterology* 2010;138:726–737.
138. Aghajan M, Li N, Karin M. Obesity, autophagy and the pathogenesis of liver and pancreatic cancers. *J Gastroenterol Hepatol* 2012;27(Suppl 2):10–14.
139. Kimmelman AC. The dynamic nature of autophagy in cancer. *Genes Dev* 2011;25:1999–2010.
140. White E. Deconvoluting the context-dependent role for autophagy in cancer. *Nature reviews Cancer* 2012;12:401–410.
141. Yang S, Wang X, Contino G, et al. Pancreatic cancers require autophagy for tumor growth. *Genes Dev* 2011;25:717–729.
142. Yang S, Kimmelman AC. A critical role for autophagy in pancreatic cancer. *Autophagy* 2011;7:912–913.
143. Guo JY, Chen HY, Mathew R, et al. Activated Ras requires autophagy to maintain oxidative metabolism and tumorigenesis. *Genes Dev* 2011;25:460–470.
144. Ying H, Kimmelman AC, Lyssiotis CA, et al. Oncogenic Kras maintains pancreatic tumors through regulation of anabolic glucose metabolism. *Cell* 2012;149:656–670.
145. Lock R, Roy S, Kenific CM, et al. Autophagy facilitates glycolysis during Ras-mediated oncogenic transformation. *Mol Biol Cell* 2011;22:165–178.
146. Kim JH, Kim HY, Lee YK, et al. Involvement of mitophagy in oncogenic K-Ras-induced transformation: overcoming a cellular energy deficit from glucose deficiency. *Autophagy* 2011;7:1187–1198.
147. Bellot G, Garcia-Medina R, Gounon P, et al. Hypoxia-induced autophagy is mediated through hypoxia-inducible factor induction of BNIP3 and BNIP3L via their BH3 domains. *Mol Cell Biol* 2009;29:2570–2581.
148. Papandreou I, Lim AL, Laderoute K, et al. Hypoxia signals autophagy in tumor cells via AMPK activity, independent of HIF-1, BNIP3, and BNIP3L. *Cell Death Differ* 2008;15:1572–1581.
149. Rausch V, Liu L, Apel A, et al. Autophagy mediates survival of pancreatic tumour-initiating cells in a hypoxic microenvironment. *J Pathol* 2012;227:325–335.
150. Degenhardt K, Mathew R, Beaudoin B, et al. Autophagy promotes tumor cell survival and restricts necrosis, inflammation, and tumorigenesis. *Cancer Cell* 2006;10:51–64.
151. Kuraishi A, Karin M, Grivennikov SI. Tumor promotion via injury- and death-induced inflammation. *Immunity* 2011;35:467–477.
152. Baumgart M, Werther M, Bockholt A, et al. Genomic instability at both the base pair level and the chromosomal level is detectable in earliest PanIN lesions in tissues of chronic pancreatitis. *Pancreas* 2010;39:1093–1103.
153. Inami Y, Waguri S, Sakamoto A, et al. Persistent activation of Nrf2 through p62 in hepatocellular carcinoma cells. *J Cell Biol* 2011;193:275–284.
154. Takamura A, Komatsu M, Hara T, et al. Autophagy-deficient mice develop multiple liver tumors. *Genes Dev* 2011;25:795–800.
155. Bhanot UK, Moller P. Mechanisms of parenchymal injury and signaling pathways in ectatic ducts of chronic pancreatitis: implications for pancreatic carcinogenesis. *Lab Invest* 2009;89:489–497.
156. Komatsu M, Waguri S, Koike M, et al. Homeostatic levels of p62 control cytoplasmic inclusion body formation in autophagy-deficient mice. *Cell* 2007;131:1149–1163.
157. Komatsu M, Kurokawa H, Waguri S, et al. The selective autophagy substrate p62 activates the stress responsive transcription factor Nrf2 through inactivation of Keap1. *Nat Cell Biol* 2010;12:213–223.
158. DeNicola GM, Karreth FA, Humpton TJ, et al. Oncogene-induced Nrf2 transcription promotes ROS detoxification and tumorigenesis. *Nature* 2011;475:106–109.
159. Deretic V. Autophagy: an emerging immunological paradigm. *J Immunol* 2012;189:15–20.
160. Green DR, Galluzzi L, Kroemer G. Mitochondria and the autophagy-inflammation-cell death axis in organismal aging. *Science* 2011;333:1109–1112.
161. Shi CS, Shenderov K, Huang NN, et al. Activation of autophagy by inflammatory signals limits IL-1beta production by targeting ubiquitinated inflammasomes for destruction. *Nat Immunol* 2012;13:255–263.
162. Hotamisligil GS, Erbay E. Nutrient sensing and inflammation in metabolic diseases. *Nat Rev Immunol* 2008;8:923–934.
163. Osborn O, Olefsky JM. The cellular and signaling networks linking the immune system and metabolism in disease. *Nat Med* 2012;18:363–374.
164. Weisberg SP, McCann D, Desai M, et al. Obesity is associated with macrophage accumulation in adipose tissue. *J Clin Invest* 2003;112:1796–1808.
165. Johnson AR, Milner JJ, Makowski L. The inflammation highway: metabolism accelerates inflammatory traffic in obesity. *Immuno Rev* 2012;249:218–238.
166. Stienstra R, van Diepen JA, Tack CJ, et al. Inflammasome is a central player in the induction of obesity and insulin resistance. *Proc Natl Acad Sci U S A* 2011;108:15324–15329.
167. Hasnain SZ, Lourie R, Das I, et al. The interplay between endoplasmic reticulum stress and inflammation. *Immunol Cell Biol* 2012;90:260–270.
168. Yang L, Li P, Fu S, et al. Defective hepatic autophagy in obesity promotes ER stress and causes insulin resistance. *Cell Metab* 2010;11:467–478.
169. Anderson EJ, Lustig ME, Boyle KE, et al. Mitochondrial H2O2 emission and cellular redox state link excess fat intake to insulin resistance in both rodents and humans. *J Clin Invest* 2009;119:573–581.
170. Frossard JL, Lescuyer P, Pastor CM. Experimental evidence of obesity as a risk factor for severe acute pancreatitis. *World J Gastroenterol* 2009;15:5260–5265.
171. Navina S, Acharya C, DeLany JP, et al. Lipotoxicity causes multisystem organ failure and exacerbates acute pancreatitis in obesity. *Sci Transl Med* 2011;3:107ra110.
172. Pini M, Sennello JA, Cabay RJ, et al. Effect of diet-induced obesity on acute pancreatitis induced by administration of interleukin-12 plus interleukin-18 in mice. *Obesity (Silver Spring)* 2010;18:476–481.
173. Sennello JA, Fayad R, Pini M, et al. Interleukin-18, together with interleukin-12, induces severe acute pancreatitis in obese but not in nonobese leptin-deficient mice. *Proc Natl Acad Sci U S A* 2008;105:8085–8090.
174. Zyromski NJ, Mathur A, Pitt HA, et al. A murine model of obesity implicates the adipokine milieu in the pathogenesis of severe acute pancreatitis. *Am J Physiol Gastrointest Liver Physiol* 2008;295:G552–G558.
175. Franco-Pons N, Gea-Sorli S, Closa D. Release of inflammatory mediators by adipose tissue during acute pancreatitis. *J Pathol* 2010;221:175–182.
176. Wiseman M. The second World Cancer Research Fund/American Institute for Cancer Research expert report. Food, nutrition, physical activity, and the prevention of cancer: a global perspective. *Proc Nutr Soc* 2008;67:253–256.
177. Chu GC, Kimmelman AC, Hezel AF, et al. Stromal biology of pancreatic cancer. *J Cell Biochem* 2007;101:887–907.
178. Neesse A, Michl P, Frese KK, et al. Stromal biology and therapy in pancreatic cancer. *Gut* 2011;60:861–868.

179. Curti ML, Jacob P, Borges MC, et al. Studies of gene variants related to inflammation, oxidative stress, dyslipidemia, and obesity: implications for a nutrigenetic approach. *J Obes* 2011; 2011:497401.
180. Miron N, Miron MM, Milea VG, et al. Proinflammatory cytokines: an insight into pancreatic oncogenesis. *Roum Arch Microbiol Immunol* 2010;69:183–189.
181. Khasawneh J, Schulz MD, Walch A, et al. Inflammation and mitochondrial fatty acid beta-oxidation link obesity to early tumor promotion. *Proc Natl Acad Sci U S A* 2009;106:3354–3359.
182. Sun B, Karin M. Obesity, inflammation, and liver cancer. *J Hepat* 2012;56:704–713.
183. Vandamagsar B, Youm YH, Ravussin A, et al. The NLRP3 inflammasome instigates obesity-induced inflammation and insulin resistance. *Nat Med* 2011;17:179–188.
184. Park EJ, Lee JH, Yu GY, et al. Dietary and genetic obesity promote liver inflammation and tumorigenesis by enhancing IL-6 and TNF expression. *Cell* 2010;140:197–208.
185. Crawford HC, Scoggins CR, Washington MK, et al. Matrix metalloproteinase-7 is expressed by pancreatic cancer precursors and regulates acinar-to-ductal metaplasia in exocrine pancreas. *J Clin Invest* 2002;109:1437–1444.
186. Yamamoto H, Itoh F, Iku S, et al. Expression of matrix metalloproteinases and tissue inhibitors of metalloproteinases in human pancreatic adenocarcinomas: clinicopathologic and prognostic significance of matrilysin expression. *J Clin Oncol* 2001; 19:1118–1127.
187. Calle EE, Kaaks R. Overweight, obesity and cancer: epidemiological evidence and proposed mechanisms. *Nat Rev Cancer* 2004;4:579–591.
188. Altomare DA, Tanno S, De Rienzo A, et al. Frequent activation of AKT2 kinase in human pancreatic carcinomas. *J Cell Biochem* 2002;87:470–476.
189. Taniguchi CM, Emanuelli B, Kahn CR. Critical nodes in signalling pathways: insights into insulin action. *Nat Rev Mol Cell Biol* 2006;7:85–96.
190. Hursting SD, Berger NA. Energy balance, host-related factors, and cancer progression. *J Clin Oncol* 2010;28:4058–4065.
191. Cirillo D, Rachiglio AM, la Montagna R, et al. Leptin signaling in breast cancer: an overview. *J Cell Biochem* 2008;105:956–964.
192. Fenton JL, Hursting SD, Perkins SN, et al. Interleukin-6 production induced by leptin treatment promotes cell proliferation in an *Apc* (Min/+) colon epithelial cell line. *Carcinogenesis* 2006;27: 1507–1515.
193. Dalamaga M, Migdalis I, Farnoli JL, et al. Pancreatic cancer expresses adiponectin receptors and is associated with hypo-leptinemia and hyperadiponectinemia: a case-control study. *Cancer Causes Control* 2009;20:625–633.
194. Chang MC, Chang YT, Su TC, et al. Adiponectin as a potential differential marker to distinguish pancreatic cancer and chronic pancreatitis. *Pancreas* 2007;35:16–21.
195. Stolzenberg-Solomon RZ, Weinstein S, Pollak M, et al. Prediagnostic adiponectin concentrations and pancreatic cancer risk in male smokers. *Am J Epidemiol* 2008;168:1047–1055.
196. McCleary-Wheeler AL, Lomberk GA, Weiss FU, et al. Insights into the epigenetic mechanisms controlling pancreatic carcinogenesis. *Cancer Lett* 2013;328:212–221.
197. Burk U, Schubert J, Wellner U, et al. A reciprocal repression between ZEB1 and members of the miR-200 family promotes EMT and invasion in cancer cells. *EMBO Rep* 2008;9:582–589.
198. Ali S, Ahmad A, Banerjee S, et al. Gemcitabine sensitivity can be induced in pancreatic cancer cells through modulation of miR-200 and miR-21 expression by curcumin or its analogue CDF. *Cancer Res* 2010;70:3606–3617.
199. Wendlandt EB, Graff JW, Gioannini TL, et al. The role of microRNAs miR-200b and miR-200c in TLR4 signaling and NF-κB activation. *Innate Immun* 2012;18:846–855.
200. Chartoumpekis DV, Zaravinos A, Ziros PG, et al. Differential expression of microRNAs in adipose tissue after long-term high-fat diet-induced obesity in mice. *PLoS One* 2012;7: e34872.