

References

- Abigerges, D., J.P. Armand, G.G. Chabot, L. Da Costa, E. Fadel, C. Cote, P. Herait, and D. Gandia. 1994. Irinotecan (CPT-11) high-dose escalation using intensive high-dose loperamide to control diarrhea. *J Natl Cancer Inst.* 86:446-9.
- Adams, J.M. 2003. Ways of dying: multiple pathways to apoptosis. *Genes Dev.* 17:2481-95.
- Adams, J.M., and Cory, S. 1998. The Bcl-2 protein family: arbiters of cell survival. *Science.* 281:1322-6.
- Akgul, C., D.A. Moulding, and S.W. Edwards. 2004. Alternative splicing of Bcl-2-related genes: functional consequences and potential therapeutic applications. *Cell Mol Life Sci.* 61:2189-99.
- Alimonti, A., A. Gelibter, I. Pavese, F. Satta, F. Cognetti, G. Ferretti, D. Rasio, A. Vecchione, and M. Di Palma. 2004. New approaches to prevent intestinal toxicity of irinotecan-based regimens. *Cancer Treat Rev.* 30:555-62.
- Altmann, S.W., H.R. Davis, Jr., L.J. Zhu, X. Yao, L.M. Hoos, G. Tetzloff, S.P. Iyer, M. Maguire, A. Golovko, M. Zeng, L. Wang, N. Murgolo, and M.P. Graziano. 2004. Niemann-Pick C1 Like 1 protein is critical for intestinal cholesterol absorption. *Science.* 303:1201-4.
- Ando, Y., and Y. Hasegawa. 2005. Clinical pharmacogenetics of irinotecan (CPT-11). *Drug Metab Rev.* 37:565-74.
- Anilkumar, T.V., C.E. Sarraf, T. Hunt, and M.R. Alison. 1992. The nature of cytotoxic drug-induced cell death in murine intestinal crypts. *British Journal of Cancer.* 65:552-8.
- Antonsson, B., F. Conti, A. Ciavatta, S. Montessuit, S. Lewis, I. Martinou, L. Bernasconi, A. Bernard, J.J. Mermod, G. Mazzei, K. Maundrell, F. Gambale, R. Sadoul, and J.C. Martinou. 1997. Inhibition of Bax channel-forming activity by Bcl-2. *Science.* 277:370-2.
- Arai, T., Y. Kida, B.V. Harmon, and G.C. Gobe. 1996. Comparative alterations in p53 expression and apoptosis in the irradiated rat small and large intestine. *British Journal of Cancer.* 74:406-12.
- Araki, E., M. Ishikawa, M. Iigo, T. Koide, M. Itabashi, and A. Hoshi. 1993. Relationship between development of diarrhea and the concentration of SN-38, an active metabolite of CPT-11, in the intestine and the blood plasma of athymic mice following intraperitoneal administration of CPT-11. *Jpn J Cancer Res.* 84:697-702.
- Arcellana-Panlilio, M., and S.M. Robbins. 2002. Cutting-edge technology. I. Global gene expression profiling using DNA microarrays. *American Journal of Physiology - Gastrointestinal & Liver Physiology.* 282:G397-402.

- Ashkenazi, A., and V.M. Dixit. 1998. Death receptors: signaling and modulation. *Science*. 281:1305-8.
- Baker, S.J., S. Markowitz, E.R. Fearon, J.K. Willson, and B. Vogelstein. 1990. Suppression of human colorectal carcinoma cell growth by wild-type p53. *Science*. 249:912-5.
- Barisani, D., A. Parafioriti, M.T. Bardella, H. Zoller, D. Conte, E. Armiraglio, C. Trovato, R.O. Koch, and G. Weiss. 2004. Adaptive changes of duodenal iron transport proteins in celiac disease. *Physiol Genomics*. 17:316-25.
- Bartek, J., and J. Lukas. 2003. DNA repair: Damage alert. *Nature*. 421:486-8.
- Beck, P.L., J.F. Wong, Y. Li, S. Swaminathan, R.J. Xavier, K.L. Devaney, and D.K. Podolsky. 2004. Chemotherapy- and radiotherapy-induced intestinal damage is regulated by intestinal trefoil factor. *In Gastroenterology*. Vol. 126. 796-808.
- Benchimol, S. 2001. p53-dependent pathways of apoptosis. *Cell Death & Differentiation*. 8:1049-51.
- Booth, D., and C.S. Potten. 2001. Protection against mucosal injury by growth factors and cytokines. *Journal of the National Cancer Institute. Monographs*:16-20.
- Borner, C. 2003. The Bcl-2 protein family: sensors and checkpoints for life-or-death decisions. *Mol Immunol*. 39:615-47.
- Boushey, R.P., B. Yusta, and D.J. Drucker. 2001. Glucagon-like peptide (GLP)-2 reduces chemotherapy-associated mortality and enhances cell survival in cells expressing a transfected GLP-2 receptor. *Cancer Research*. 61:687-93.
- Bouvard, V., T. Zaitchouk, M. Vacher, A. Duthu, M. Canivet, C. Choisy-Rossi, M. Nieruchalski, and E. May. 2000. Tissue and cell specific expression of the p53-target genes: bax, fas, mdm2 and waf1/p21, before and following ionising irradiation in mice. *Oncogene*. 19:649-60.
- Bradham, C.A., T. Qian, K. Streetz, C. Trautwein, D.A. Brenner, and J.J. Lemasters. 1998. The mitochondrial permeability transition is required for tumor necrosis factor alpha-mediated apoptosis and cytochrome c release. *Molecular & Cellular Biology*. 18:6353-64.
- Brittan, M., and N.A. Wright. 2002. Gastrointestinal stem cells. *J Pathol*. 197:492-509.
- Bruno, M.E., and C.S. Kaetzel. 2005. Long-term exposure of the HT-29 human intestinal epithelial cell line to TNF causes sustained up-regulation of the polymeric Ig receptor and proinflammatory genes through transcriptional and posttranscriptional mechanisms. *J Immunol*. 174:7278-84.
- Cai, W.B., S.A. Roberts, E. Bowley, J.H. Hendry, and C.S. Potten. 1997. Differential survival of murine small and large intestinal crypts following ionizing radiation. *International Journal of Radiation Biology*. 71:145-55.

- Cao, S., J.D. Black, A.B. Troutt, and Y.M. Rustum. 1998a. Interleukin 15 offers selective protection from irinotecan-induced intestinal toxicity in a preclinical animal model. *Cancer Res.* 58:3270-4.
- Cao, S., A.B. Troutt, and Y.M. Rustum. 1998b. Interleukin 15 protects against toxicity and potentiates antitumor activity of 5-fluorouracil alone and in combination with leucovorin in rats bearing colorectal cancer. *Cancer Res.* 58:1695-9.
- Cairo, G., and A. Pietrangelo. 1995. Nitric-oxide-mediated activation of iron-regulatory protein controls hepatic iron metabolism during acute inflammation. *Eur J Biochem.* 232:358-63.
- Carneiro-Filho, B.A., I.P. Lima, D.H. Araujo, M.C. Cavalcante, G.H. Carvalho, G.A. Brito, V. Lima, S.M. Monteiro, F.N. Santos, R.A. Ribeiro, and A.A. Lima. 2004. Intestinal barrier function and secretion in methotrexate-induced rat intestinal mucositis. *Dig Dis Sci.* 49:65-72.
- Catz, S.D., and J.L. Johnson. 2001. Transcriptional regulation of bcl-2 by nuclear factor kappa B and its significance in prostate cancer. *Oncogene.* 20:7342-51.
- Chang, Q., and B.L. Tepperman. 2003. Effect of selective PKC isoform activation and inhibition on TNF-alpha-induced injury and apoptosis in human intestinal epithelial cells. *Br J Pharmacol.* 140:41-52.
- Chao, D.T., and S.J. Korsmeyer. 1998. BCL-2 family: regulators of cell death. *Annual Review of Immunology.* 16:395-419.
- Chen, C., L.C. Edelstein, and C. Gelinas. 2000. The Rel/NF-kappaB family directly activates expression of the apoptosis inhibitor Bcl-x(L). *Molecular & Cellular Biology.* 20:2687-95.
- Chernavsky, A.C., A.E. Rubio, S. Vanzulli, N. Rubinstein, S. de Rosa, and L. Fainboim. 2002. Evidences of the involvement of Bak, a member of the Bcl-2 family of proteins, in active coeliac disease. *Autoimmunity.* 35:29-37.
- Chipuk, J.E., T. Kuwana, L. Bouchier-Hayes, N.M. Droin, D.D. Newmeyer, M. Schuler, and D.R. Green. 2004. Direct activation of Bax by p53 mediates mitochondrial membrane permeabilization and apoptosis. *Science.* 303:1010-4.
- Chu, Q.S., L.A. Hammond, G. Schwartz, L. Ochoa, S.Y. Rha, L. Denis, K. Molpus, B. Roedig, S.P. Letrent, B. Damle, A.P. DeCillis, and E.K. Rowinsky. 2004. Phase I and pharmacokinetic study of the oral fluoropyrimidine S-1 on a once-daily-for-28-day schedule in patients with advanced malignancies. *Clin Cancer Res.* 10:4913-21.
- Chu, K.U., S. Higashide, B.M. Evers, S. Rajaraman, J. Ishizuka, C.M. Townsend, Jr., and J.C. Thompson. 1994. Bombesin improves survival from methotrexate-induced enterocolitis. *Ann Surg.* 220:570-6; discussion 576-7.
- Clavijo, J., I.A. Gomez-de-Segura, L. Gomez-Garcia, M.T. Vallejo-Cremades, M.

- Sanchez, and E. de Miguel. 2004. Growth hormone protects the intestines but not the tumour from 5-fluorouracil toxicity in the short term in the rat. *Eur J Gastroenterol Hepatol.* 16:75-82.
- Cohen, G.M. 1997. Caspases: the executioners of apoptosis. *Biochemical Journal.* 326:1-16.
- Cory, S., D.C. Huang, and J.M. Adams. 2003. The Bcl-2 family: roles in cell survival and oncogenesis. *Oncogene.* 22:8590-607.
- Cowen, D., C. Tardieu, M. Schubert, D. Peterson, M. Resbeut, C. Faucher, and J.C. Franquin. 1997. Low energy Helium-Neon laser in the prevention of oral mucositis in patients undergoing bone marrow transplant: results of a double blind randomized trial. *Int J Radiat Oncol Biol Phys.* 38:697-703.
- Creagh, E.M., H. Conroy, and S.J. Martin. 2003. Caspase-activation pathways in apoptosis and immunity. *Immunol Rev.* 193:10-21.
- Crompton, M. 1999. The mitochondrial permeability transition pore and its role in cell death. *Biochemical Journal.* 341:233-49.
- Culmsee, C., X. Zhu, Q.S. Yu, S.L. Chan, S. Camandola, Z. Guo, N.H. Greig, and M.P. Mattson. 2001. A synthetic inhibitor of p53 protects neurons against death induced by ischemic and excitotoxic insults, and amyloid beta-peptide. *Journal of Neurochemistry.* 77:220-8.
- Cummins, A.G., J.T. LaBrooy, D.P. Stanley, R. Rowland, and D.J. Shearman. 1990. Quantitative histological study of enteropathy associated with HIV infection. *Gut.* 31:317-21.
- Decary, S., J.T. Decesse, V. Ogryzko, J.C. Reed, I. Naguibneva, A. Harel-Bellan, and C.E. Cremisi. 2002. The retinoblastoma protein binds the promoter of the survival gene bcl-2 and regulates its transcription in epithelial cells through transcription factor AP-2. *Molecular & Cellular Biology.* 22:7877-88.
- Decker-Baumann, C., K. Buhl, S. Frohmuller, A. von Herbay, M. Dueck, and P.M. Schlag. 1999. Reduction of chemotherapy-induced side-effects by parenteral glutamine supplementation in patients with metastatic colorectal cancer. *European Journal of Cancer.* 35:202-7.
- DeLeo, A.B., G. Jay, E. Appella, G.C. Dubois, L.W. Law, and L.J. Old. 1979. Detection of a transformation-related antigen in chemically induced sarcomas and other transformed cells of the mouse. *Proc Natl Acad Sci U S A.* 76:2420-4.
- Desagher, S., A. Osen-Sand, A. Nichols, R. Eskes, S. Montessuit, S. Lauper, K. Maundrell, B. Antonsson, and J.C. Martinou. 1999. Bid-induced conformational change of Bax is responsible for mitochondrial cytochrome c release during apoptosis. *Journal of Cell Biology.* 144:891-901.

- Dippold, W.G., G. Jay, A.B. DeLeo, G. Khoury, and L.J. Old. 1981. p53 transformation-related protein: detection by monoclonal antibody in mouse and human cells. *Proc Natl Acad Sci U S A.* 78:1695-9.
- Duncan, M., and G. Grant. 2003. Oral and intestinal mucositis - causes and possible treatments. *Aliment Pharmacol Ther.* 18:853-74.
- el-Deiry, W.S. 1998. Regulation of p53 downstream genes. *Semin Cancer Biol.* 8:345-57.
- Eells, J.T., M.T. Wong-Riley, J. VerHoeve, M. Henry, E.V. Buchman, M.P. Kane, L.J. Gould, R. Das, M. Jett, B.D. Hodgson, D. Margolis, and H.T. Whelan. 2004. Mitochondrial signal transduction in accelerated wound and retinal healing by near-infrared light therapy. *Mitochondrion.* 4:559-67.
- Erster, S., M. Mihara, R.H. Kim, O. Petrenko, and U.M. Moll. 2004. In vivo mitochondrial p53 translocation triggers a rapid first wave of cell death in response to DNA damage that can precede p53 target gene activation. *Mol Cell Biol.* 24:6728-41.
- Eskes, R., S. Desagher, B. Antonsson, and J.C. Martinou. 2000. Bid induces the oligomerization and insertion of Bax into the outer mitochondrial membrane. *Molecular & Cellular Biology.* 20:929-35.
- Fadeel, B., B. Zhivotovsky, and S. Orrenius. 1999. All along the watchtower: on the regulation of apoptosis regulators. *FASEB Journal.* 13:1647-57.
- Fei, P., E.J. Bernhard, and W.S. El-Deiry. 2002. Tissue-specific induction of p53 targets in vivo. *Cancer Res.* 62:7316-27.
- Finlay, C.A., P.W. Hinds, and A.J. Levine. 1989. The p53 proto-oncogene can act as a suppressor of transformation. *Cell.* 57:1083-93.
- Fleischer, A., A. Rebollo, and V. Ayllon. 2003. BH3-only proteins: the lords of death. *Archivum Immunologiae et Therapiae Experimentalis.* 51:9-17.
- Foyouzi-Youssefi, R., S. Arnaudeau, C. Borner, W.L. Kelley, J. Tschopp, D.P. Lew, N. Demaurex, and K.H. Krause. 2000. Bcl-2 decreases the free Ca²⁺ concentration within the endoplasmic reticulum. *Proceedings of the National Academy of Sciences of the United States of America.* 97:5723-8.
- Funk, M.A., and D.H. Baker. 1991. Effect of soy products on methotrexate toxicity in rats. *Journal of Nutrition.* 121:1684-92.
- Gauthier, R., C. Harnois, J.F. Drolet, J.C. Reed, A. Vezina, and P.H. Vachon. 2001a. Human intestinal epithelial cell survival: differentiation state-specific control mechanisms. *American Journal of Physiology - Cell Physiology.* 280:C1540-54.
- Gauthier, R., P. Laprise, E. Cardin, C. Harnois, A. Plourde, J.C. Reed, A. Vezina, and P.H. Vachon. 2001b. Differential sensitivity to apoptosis between the human small and large

- intestinal mucosae: linkage with segment-specific regulation of BCL-2 homologs and involvement of signaling pathways. *Journal of Cellular Biochemistry*. 82:339-55.
- Gavrieli, Y., Y. Sherman, and S.A. Ben-Sasson. 1992. Identification of programmed cell death in situ via specific labeling of nuclear DNA fragmentation. *Journal of Cell Biology*. 119:493-501.
- Ghribi, O., D.A. DeWitt, M.S. Forbes, M.M. Herman, and J. Savory. 2001. Co-involvement of mitochondria and endoplasmic reticulum in regulation of apoptosis: changes in cytochrome c, Bcl-2 and Bax in the hippocampus of aluminum-treated rabbits. *Brain Research*. 903:66-73.
- Gibson, R.J., J.M. Bowen, A.G. Cummins, and D.M. Keefe. 2005. Relationship between dose of methotrexate, apoptosis, p53/p21 expression and intestinal crypt proliferation in the rat. *Clin Exp Med*. 4:188-95.
- Gibson, R.J., J.M. Bowen, and D.M. Keefe. 2005. Palifermin reduces diarrhea and increases survival following irinotecan treatment in tumor-bearing DA rats. *Int J Cancer*.
- Gibson, R.J. 2004. Chemotherapy-induced mucositis: Mechanisms of damage, time course of events and possible preventative strategies. In Medicine. The University of Adelaide, Adelaide.
- Gibson, R.J., J.M. Bowen, M.R. Inglis, A.G. Cummins, and D.M. Keefe. 2003. Irinotecan causes severe small intestinal damage, as well as colonic damage, in the rat with implanted breast cancer. *J Gastroenterol Hepatol*. 18:1095-100.
- Gibson, R.J., D.M. Keefe, J.M. Clarke, G.O. Regester, F.M. Thompson, G.J. Goland, B.G. Edwards, and A.G. Cummins. 2002a. The effect of keratinocyte growth factor on tumour growth and small intestinal mucositis after chemotherapy in the rat with breast cancer. *Cancer Chemotherapy & Pharmacology*. 50:53-8.
- Gibson, R.J., D.M. Keefe, F.M. Thompson, J.M. Clarke, G.J. Goland, and A.G. Cummins. 2002b. Effect of interleukin-11 on ameliorating intestinal damage after methotrexate treatment of breast cancer in rats. *Digestive Diseases & Sciences*. 47:2751-7.
- Gibson, L.F., J. Fortney, G. Magro, S.G. Ericson, J.P. Lynch, and K.S. Landreth. 1999. Regulation of BAX and BCL-2 expression in breast cancer cells by chemotherapy. *Breast Cancer Research & Treatment*. 55:107-17.
- Gottlieb, T.M., and M. Oren. 1998. p53 and apoptosis. *Seminars in Cancer Biology*. 8:359-68.
- Govindarajan, R. 2002. Irinotecan/thalidomide in metastatic colorectal cancer. *Oncology (Huntington)*. 16:23-6.
- Govindarajan, R., K.M. Heaton, R. Broadwater, A. Zeitlin, N.P. Lang, and M. Hauer-Jensen. 2000. Effect of thalidomide on gastrointestinal toxic effects of irinotecan. *Lancet*. 356:566-7.

- Green, D., and J.C. Reed. 1998. Mitochondria and apoptosis. *Science*. 281:1309-12.
- Greider, C., A. Chattopadhyay, C. Parkhurst, and E. Yang. 2002. BCL-x(L) and BCL2 delay Myc-induced cell cycle entry through elevation of p27 and inhibition of G1 cyclin-dependent kinases. *Oncogene*. 21:7765-75.
- Gross, A., J.M. McDonnell, and S.J. Korsmeyer. 1999. BCL-2 family members and the mitochondria in apoptosis. *Genes & Development*. 13:1899-911.
- Grossmann, J., M. Artinger, A.W. Grasso, H.J. Kung, J. Scholmerich, C. Fiocchi, and A.D. Levine. 2001. Hierarchical cleavage of focal adhesion kinase by caspases alters signal transduction during apoptosis of intestinal epithelial cells. *Gastroenterology*. 120:79-88.
- Grutter, M.G. 2000. Caspases: key players in programmed cell death. *Curr Opin Struct Biol*. 10:649-55.
- Gudkov, A.V., and E.A. Komarova. 2005. Prospective therapeutic applications of p53 inhibitors. *Biochem Biophys Res Commun*. 331:726-36.
- Gudkov, A., and E. Komarova. 2003. Isolation of p53 inhibitors by screening chemical libraries in cell-based readout system. *Methods Mol Biol*. 223:635-48.
- Haldar, S., N. Jena, and C.M. Croce. 1995. Inactivation of Bcl-2 by phosphorylation. *Proceedings of the National Academy of Sciences of the United States of America*. 92:4507-11.
- Hall, P.A., P.J. Coates, B. Ansari, and D. Hopwood. 1994. Regulation of cell number in the mammalian gastrointestinal tract: the importance of apoptosis. *Journal of Cell Science*. 107:3569-77.
- Hallahan, D.E., S. Virudachalam, D.W. Kufe, and R.R. Weichselbaum. 1994. Ketoconazole attenuates radiation-induction of tumor necrosis factor. *Int J Radiat Oncol Biol Phys*. 29:777-80.
- Hanada, M., C. Aime-Sempe, T. Sato, and J.C. Reed. 1995. Structure-function analysis of Bcl-2 protein. Identification of conserved domains important for homodimerization with Bcl-2 and heterodimerization with Bax. *Journal of Biological Chemistry*. 270:11962-9.
- Hannun, Y.A. 1997. Apoptosis and the dilemma of cancer chemotherapy. *Blood*. 89:1845-53.
- Harris, S.L., and A.J. Levine. 2005. The p53 pathway: positive and negative feedback loops. *Oncogene*. 24:2899-908.
- Hengartner, M.O. 1999. Programmed cell death in the nematode *C. elegans*. *Annals of the New York Academy of Sciences*. 887:92-104.

- Hengartner, M.O., and H.R. Horvitz. 1994. The ins and outs of programmed cell death during *C. elegans* development. *Philosophical Transactions of the Royal Society of London - Series B: Biological Sciences*. 345:243-6.
- Henry-Mowatt, J., C. Dive, J.C. Martinou, and D. James. 2004. Role of mitochondrial membrane permeabilization in apoptosis and cancer. *Oncogene*. 23:2850-60.
- Herr, I., and K.M. Debatin. 2001. Cellular stress response and apoptosis in cancer therapy. *Blood*. 98:2603-14.
- Herr, I., D. Wilhelm, T. Bohler, P. Angel, and K.M. Debatin. 1997. Activation of CD95 (APO-1/Fas) signaling by ceramide mediates cancer therapy-induced apoptosis. *EMBO Journal*. 16:6200-8.
- Hershko, T., and D. Ginsberg. 2004. Up-regulation of Bcl-2 homology 3 (BH3)-only proteins by E2F1 mediates apoptosis. *J Biol Chem*. 279:8627-34.
- Hecht, J.R. 1998. Gastrointestinal toxicity of irinotecan. *Oncology (Williston Park)*. 12:72-8.
- Hickman, J.A., C.S. Potten, A.J. Merritt, and T.C. Fisher. 1994. Apoptosis and cancer chemotherapy. *Philosophical Transactions of the Royal Society of London - Series B: Biological Sciences*. 345:319-25.
- Hinds, P., C. Finlay, and A.J. Levine. 1989. Mutation is required to activate the p53 gene for cooperation with the ras oncogene and transformation. *J Virol*. 63:739-46.
- Ho, J., and S. Benchimol. 2003. Transcriptional repression mediated by the p53 tumour suppressor. *Cell Death Differ*. 10:404-8.
- Hockenberry, D.M., Z.N. Oltvai, X.M. Yin, C.L. Milliman, and S.J. Korsmeyer. 1993. Bcl-2 functions in an antioxidant pathway to prevent apoptosis. *Cell*. 75:241-51.
- Horie, T., H. Matsumoto, M. Kasagi, A. Sugiyama, M. Kikuchi, C. Karasawa, S. Awazu, Y. Itakura, and T. Fuwa. 1999. Protective effect of aged garlic extract on the small intestinal damage of rats induced by methotrexate treatment. *Planta Medica*. 65:545-8.
- Howarth, G.S., and C.A. Shoubridge. 2001. Enhancement of intestinal growth and repair by growth factors. *Current Opinion in Pharmacology*. 1:568-74.
- Howarth, G., G.L. Francis, J.C. Cool, X. Xu, R.W. Byard, and L.C. Read. 1996. Milk growth factors enriched from cheese whey ameliorate intestinal damage by methotrexate when administered orally to rats. *Journal of Nutrition*. 126:2519-30.
- Hsu, Y.T., K.G. Wolter, and R.J. Youle. 1997. Cytosol-to-membrane redistribution of Bax and Bcl-X(L) during apoptosis. *Proceedings of the National Academy of Sciences of the United States of America*. 94:3668-72.

- Hu, Z.B., M.D. Minden, and E.A. McCulloch. 1996. Regulation of the synthesis of bcl-2 protein by growth factors. *Leukemia*. 10:1925-9.
- Hudmon, A., and H. Schulman. 2002. Structure-function of the multifunctional Ca²⁺/calmodulin-dependent protein kinase II. *Biochem J*. 364:593-611.
- Huennekens, F.M. 1994. The methotrexate story: a paradigm for development of cancer chemotherapeutic agents. *Advances in Enzyme Regulation*. 34:397-419.
- Iglesias-Serret, D., M. Pique, J. Gil, G. Pons, and J.M. Lopez. 2003. Transcriptional and translational control of Mcl-1 during apoptosis. *Arch Biochem Biophys*. 417:141-52.
- Ijiri, K., and C.S. Potten. 1983. Response of intestinal cells of differing topographical and hierarchical status to ten cytotoxic drugs and five sources of radiation. *Br J Cancer*. 47:175-85.
- Ijiri, K., and C.S. Potten. 1987. Further studies on the response of intestinal crypt cells of different hierarchical status to eighteen different cytotoxic agents. *British Journal of Cancer*. 55:113-23.
- Ikuno, N., H. Soda, M. Watanabe, and M. Oka. 1995. Irinotecan (CPT-11) and characteristic mucosal changes in the mouse ileum and cecum. *J Natl Cancer Inst*. 87:1876-83.
- Inomata, A., I. Horii, and K. Suzuki. 2002. 5-Fluorouracil-induced intestinal toxicity: what determines the severity of damage to murine intestinal crypt epithelia? *Toxicol Lett*. 133:231-40.
- Jones, B.A., and G.J. Gores. 1997. Physiology and pathophysiology of apoptosis in epithelial cells of the liver, pancreas, and intestine. *American Journal of Physiology*. 273:G1174-88.
- Jarry, A., G. Vallette, E. Cassagnau, A. Moreau, C. Bou-Hanna, P. Lemarre, E. Letessier, J.C. Le Neel, J.P. Galmiche, and C.L. Laboisson. 1999. Interleukin 1 and interleukin 1beta converting enzyme (caspase 1) expression in the human colonic epithelial barrier. Caspase 1 downregulation in colon cancer. *Gut*. 45:246-51.
- Johnson, M.R., A. Hageboutros, K. Wang, L. High, J.B. Smith, and R.B. Diasio. 1999. Life-threatening toxicity in a dihydropyrimidine dehydrogenase-deficient patient after treatment with topical 5-fluorouracil. *Clin Cancer Res*. 5:2006-11.
- Junqueira, L., J. Carnerio, and J. Long. 1986. Basic Histology. Lange Medical Publications. 327-53 pp.
- Kannan, K., N. Amariglio, G. Rechavi, J. Jakob-Hirsch, I. Kela, N. Kaminski, G. Getz, E. Domany, and D. Givol. 2001. DNA microarrays identification of primary and secondary target genes regulated by p53. *Oncogene*. 20:2225-34.

- Kantrow, S.P., J.L. Gierman, V.R. Jaligam, P. Zhang, C.A. Piantadosi, W.R. Summer, and J.R. Lancaster, Jr. 2000. Regulation of tumor necrosis factor cytotoxicity by calcineurin. *FEBS Letters.* 483:119-24.
- Katona, C., J. Kralovanszky, A. Rosta, E. Pandi, G. Fonyad, K. Toth, and A. Jeney. 1998. Putative role of dihydropyrimidine dehydrogenase in the toxic side effect of 5-fluorouracil in colorectal cancer patients. *Oncology.* 55:468-74.
- Kondo, S., B.P. Barna, T. Morimura, J. Takeuchi, J. Yuan, A. Akbasak, and G.H. Barnett. 1995. Interleukin-1 beta-converting enzyme mediates cisplatin-induced apoptosis in malignant glioma cells. *Cancer Res.* 55:6166-71.
- Keefe, D.M., R.J. Gibson, and M. Hauer-Jensen. 2004. Gastrointestinal mucositis. *Semin Oncol Nurs.* 20:38-47.
- Keefe, D.M. 2004. Gastrointestinal mucositis: a new biological model. *Support Care Cancer.* 12:6-9.
- Keefe, D.M., J. Brealey, G.J. Goland, and A.G. Cummins. 2000. Chemotherapy for cancer causes apoptosis that precedes hypoplasia in crypts of the small intestine in humans. *Gut.* 47:632-7.
- Keefe, D.M. 1998. The effect of cytotoxic chemotherapy on the mucosa of the small intestine. In Department of Medicine. University of Adelaide, Adelaide.
- Keefe, D.M., A.G. Cummins, B.M. Dale, D. Kotasek, T.A. Robb, and R.E. Sage. 1997. Effect of high-dose chemotherapy on intestinal permeability in humans. *Clinical Science.* 92:385-9.
- Kelekar, A., and C.B. Thompson. 1998. Bcl-2-family proteins: the role of the BH3 domain in apoptosis. *Trends in Cell Biology.* 8:324-30.
- Kelekar, A., B.S. Chang, J.E. Harlan, S.W. Fesik, and C.B. Thompson. 1997. Bad is a BH3 domain-containing protein that forms an inactivating dimer with Bcl-XL. *Molecular & Cellular Biology.* 17:7040-6.
- Kerr, J.F., C.M. Winterford, and B.V. Harmon. 1994. Apoptosis. Its significance in cancer and cancer therapy.[erratum appears in Cancer 1994 Jun 15;73(12):3108]. *Cancer.* 73:2013-26.
- Kerr, J.F., A.H. Wyllie, and A.R. Currie. 1972. Apoptosis: a basic biological phenomenon with wide-ranging implications in tissue kinetics. *British Journal of Cancer.* 26:239-57.
- Kerr, J.F. 1971. Shrinkage necrosis: a distinct mode of cellular death. *Journal of Pathology.* 105:13-20.
- Khaled, A.R., K. Kim, R. Hofmeister, K. Muegge, and S.K. Durum. 1999. Withdrawal of IL-7 induces Bax translocation from cytosol to mitochondria through a rise in intracellular

- pH. *Proceedings of the National Academy of Sciences of the United States of America.* 96:14476-81.
- Kitada, S., M. Krajewska, X. Zhang, D. Scudiero, J.M. Zapata, H.G. Wang, A. Shabaik, G. Tudor, S. Krajewski, T.G. Myers, G.S. Johnson, E.A. Sausville, and J.C. Reed. 1998. Expression and localization of pro-apoptotic Bcl-2 family protein Bad in normal human tissue and tumor cell lines. *American Journal of Pathology.* 152:51-61.
- Kitada, S., S. Krajewski, T. Miyashita, M. Krajewska, and J.C. Reed. 1996. Gamma-radiation induces upregulation of Bax protein and apoptosis in radiosensitive cells in vivo. *Oncogene.* 12:187-92.
- Kluck, R.M., E. Bossy-Wetzel, D.R. Green, and D.D. Newmeyer. 1997. The release of cytochrome c from mitochondria: a primary site for Bcl-2 regulation of apoptosis. *Science.* 275:1132-6.
- Ko, L.J., and C. Prives. 1996. p53: puzzle and paradigm. *Genes Dev.* 10:1054-72.
- Komarov, P.G. 1999. A chemical inhibitor of p53 that protects mice from the side effects of cancer therapy. *Science.* 285:1733-7.
- Komarova, E.A., R.V. Kondratov, K. Wang, K. Christov, T.V. Golovkina, J.R. Goldblum, and A.V. Gudkov. 2004. Dual effect of p53 on radiation sensitivity in vivo: p53 promotes hematopoietic injury, but protects from gastro-intestinal syndrome in mice. *Oncogene.* 23:3265-71.
- Komarova, E.A., N. Neznanov, P.G. Komarov, M.V. Chernov, K. Wang, and A.V. Gudkov. 2003. p53 inhibitor pifithrin alpha can suppress heat shock and glucocorticoid signaling pathways. *Journal of Biological Chemistry.* 278:15465-8.
- Komarova, E.A., and A.V. Gudkov. 2001. Chemoprotection from p53-dependent apoptosis: potential clinical applications of the p53 inhibitors. *Biochemical Pharmacology.* 62:657-67.
- Komarova, E.A., and A.V. Gudkov. 2000. Suppression of p53: a new approach to overcome side effects of antitumor therapy. *Biochemistry (Moscow).* 65:41-8.
- Komarova, E.A., and A.V. Gudkov. 1998. Could p53 be a target for therapeutic suppression? *Seminars in Cancer Biology.* 8:389-400.
- Konopleva, M., S. Zhao, Z. Xie, H. Segall, A. Younes, D.F. Claxton, Z. Estrov, S.M. Kornblau, and M. Andreeff. 1999. Apoptosis. Molecules and mechanisms. *Advances in Experimental Medical Biology.* 457:217-36.
- Krajewska, M., J.M. Zapata, I. Meinholt-Heerlein, H. Hedayat, A. Monks, H. Handorf, A. Shabaik, L. Bebendorf, O. Lallioniemi, H. Kim, L. Heifnerberger, J.C. Reed, and S. Krajewski. 2002. Expression of Bcl-2 family member Bid in normal and malignant tissues. *Neoplasia.* 4:129-40.

- Krajewski, S., M. Krajewska, and J.C. Reed. 1996. Immunohistochemical analysis of in vivo patterns of Bak expression, a proapoptotic member of the Bcl-2 protein family. *Cancer Research*. 56:2849-55.
- Krajewski, S., S. Bodrug, M. Krajewska, A. Shabaik, R. Gascoyne, K. Berean, and J.C. Reed. 1995. Immunohistochemical analysis of Mcl-1 protein in human tissues. Differential regulation of Mcl-1 and Bcl-2 protein production suggests a unique role for Mcl-1 in control of programmed cell death in vivo. *American Journal of Pathology*. 146:1309-19.
- Krajewski, S., M. Krajewska, A. Shabaik, T. Miyashita, H.G. Wang, and J.C. Reed. 1994a. Immunohistochemical determination of in vivo distribution of Bax, a dominant inhibitor of Bcl-2. *American Journal of Pathology*. 145:1323-36.
- Krajewski, S., M. Krajewska, A. Shabaik, H.G. Wang, S. Irie, L. Fong, and J.C. Reed. 1994b. Immunohistochemical analysis of in vivo patterns of Bcl-X expression. *Cancer Research*. 54:5501-7.
- Lamkanfi, M., M. Kalai, X. Saelens, W. Declercq, and P. Vandenabeele. 2004. Caspase-1 activates nuclear factor of the kappa-enhancer in B cells independently of its enzymatic activity. *J Biol Chem*. 279:24785-93.
- Lane, D.P., X. Lu, T. Hupp, and P.A. Hall. 1994. The role of the p53 protein in the apoptotic response. *Philosophical Transactions of the Royal Society of London - Series B: Biological Sciences*. 345:277-80.
- Lane, D.P., and L.V. Crawford. 1979. T antigen is bound to a host protein in SV40-transformed cells. *Nature*. 278:261-3.
- Launay, S., O. Hermine, M. Fontenay, G. Kroemer, E. Solary, and C. Garrido. 2005. Vital functions for lethal caspases. *Oncogene*. 24:5137-48.
- Lavrik, I.N., A. Golks, and P.H. Krammer. 2005. Caspases: pharmacological manipulation of cell death. *J Clin Invest*. 115:2665-72.
- Leu, J.I., P. Dumont, M. Hafey, M.E. Murphy, and D.L. George. 2004. Mitochondrial p53 activates Bak and causes disruption of a Bak-Mcl1 complex. *Nat Cell Biol*. 6:443-50.
- Leung, L.K., and T.T. Wang. 1999. Differential effects of chemotherapeutic agents on the Bcl-2/Bax apoptosis pathway in human breast cancer cell line MCF-7. *Breast Cancer Research & Treatment*. 55:73-83.
- Linette, G.P., Y. Li, K. Roth, and S.J. Korsmeyer. 1996. Cross talk between cell death and cell cycle progression: BCL-2 regulates NFAT-mediated activation. *Proceedings of the National Academy of Sciences of the United States of America*. 93:9545-52.
- Linseman, D.A., R.A. Phelps, R.J. Bouchard, S.S. Le, T.A. Laessig, M.L. McClure, and K.A. Heidenreich. 2002. Insulin-like growth factor-I blocks Bcl-2 interacting mediator of cell death (Bim) induction and intrinsic death signaling in cerebellar granule neurons. *J Neurosci*. 22:9287-97.

- Linzer, D.I., and A.J. Levine. 1979. Characterization of a 54K dalton cellular SV40 tumor antigen present in SV40-transformed cells and uninfected embryonal carcinoma cells. *Cell.* 17:43-52.
- Liu, Q.A., and M.O. Hengartner. 1999. The molecular mechanism of programmed cell death in *C. elegans*. *Annals of the New York Academy of Science.* 887:92-104.
- Luo, X., I. Budihardjo, H. Zou, C. Slaughter, and X. Wang. 1998. Bid, a Bcl2 interacting protein, mediates cytochrome c release from mitochondria in response to activation of cell surface death receptors. *Cell.* 94:481-90.
- Lönnstedt, I., and T. Britton. 2005. Hierarchical Bayes models for cDNA microarray gene expression. *Biostatistics.* 6:279-91.
- Lönnstedt, I., and T.P. Speed. 2002. Replicated microarray data. *Statistica Sinica.* 12:31-46.
- Lorenzo, E., C. Ruiz-Ruiz, A.J. Quesada, G. Hernandez, A. Rodriguez, A. Lopez-Rivas, and J.M. Redondo. 2002. Doxorubicin induces apoptosis and CD95 gene expression in human primary endothelial cells through a p53-dependent mechanism. *J Biol Chem.* 277:10883-92.
- Lowe, S.W., H.E. Ruley, T. Jacks, and D.E. Housman. 1993. p53-dependent apoptosis modulates the cytotoxicity of anticancer agents. *Cell.* 74:957-67.
- Lu, J., M.S. Caplan, A.P. Saraf, D. Li, L. Adler, X. Liu, and T. Jilling. 2004. Platelet-activating factor-induced apoptosis is blocked by Bcl-2 in rat intestinal epithelial cells. *Am J Physiol Gastrointest Liver Physiol.* 286:G340-50.
- Ludwigczek, O., E. Vannier, I. Borggraefe, A. Kaser, B. Siegmund, C.A. Dinarello, and H. Tilg. 2004. Imbalance between interleukin-1 agonists and antagonists: relationship to severity of inflammatory bowel disease. *Clin Exp Immunol.* 138:323-9.
- Markova, V. 1998. Quantitative analysis of the expression of apoptosis-related genes. *Folia Medica (Plovdiv).* 40:51-7.
- Marshman, E., P.D. Ottewell, C.S. Potten, and A.J. Watson. 2001. Caspase activation during spontaneous and radiation-induced apoptosis in the murine intestine. *J Pathol.* 195:285-92.
- Martinon, F., and J. Tschopp. 2004. Inflammatory caspases: linking an intracellular innate immune system to autoinflammatory diseases. *Cell.* 117:561-74.
- Marzo, I., C. Brenner, N. Zamzami, S.A. Susin, G. Beutner, D. Brdiczka, R. Remy, Z.H. Xie, J.C. Reed, and G. Kroemer. 1998. The permeability transition pore complex: a target for apoptosis regulation by caspases and bcl-2-related proteins. *Journal of Experimental Medicine.* 187:1261-71.

- Matkowskyj, K.A., D. Schonfeld, and R.V. Benya. 2000. Quantitative immunohistochemistry by measuring cumulative signal strength using commercially available software photoshop and matlab. *Journal of Histochemistry & Cytochemistry*. 48:303-12.
- McDonnell, T.J., A. Beham, M. Sarkiss, M.M. Andersen, and P. Lo. 1996. Importance of the Bcl-2 family in cell death regulation. *Experientia*. 52:1008-17.
- McGee, D.W., S.J. Vitkus, and P. Lee. 1996. The effect of cytokine stimulation on IL-1 receptor mRNA expression by intestinal epithelial cells. *Cell Immunol*. 168:276-80.
- Merritt, A.J., T.D. Allen, C.S. Potten, and J.A. Hickman. 1997. Apoptosis in small intestinal epithelial from p53-null mice: evidence for a delayed, p53-independent G2/M-associated cell death after gamma-irradiation. *Oncogene*. 14:2759-66.
- Merritt, A.J., C.S. Potten, A.J. Watson, D.Y. Loh, K. Nakayama, and J.A. Hickman. 1995. Differential expression of bcl-2 in intestinal epithelia. Correlation with attenuation of apoptosis in colonic crypts and the incidence of colonic neoplasia. *Journal of Cell Science*. 108:2261-71.
- Merritt, A.J., C.S. Potten, C.J. Kemp, J.A. Hickman, A. Balmain, D.P. Lane, and P.A. Hall. 1994. The role of p53 in spontaneous and radiation-induced apoptosis in the gastrointestinal tract of normal and p53-deficient mice. *Cancer Research*. 54:614-7.
- Mihara, M., S. Erster, A. Zaika, O. Petrenko, T. Chittenden, P. Pancoska, and U.M. Moll. 2003. p53 has a direct apoptogenic role at the mitochondria. *Mol Cell*. 11:577-90.
- Mitchell, E.P., and P.S. Schein. 1984. Gastrointestinal toxicity of chemotherapeutic agents. In *Toxicity of chemotherapy*. Grune & Stratton. 269-89.
- Miyashita, T., and J.C. Reed. 1995. Tumor suppressor p53 is a direct transcriptional activator of the human bax gene. *Cell*. 80:293-9.
- Miyashita, T., M. Harigai, M. Hanada, and J.C. Reed. 1994. Identification of a p53-dependent negative response element in the bcl-2 gene. *Cancer Research*. 54:3131-5.
- Miyashita, T., S. Krajewski, M. Krajewska, H.G. Wang, H.K. Lin, D.A. Liebermann, B. Hoffman, and J.C. Reed. 1994b. Tumor suppressor p53 is a regulator of bcl-2 and bax gene expression in vitro and in vivo. *Oncogene*. 9:1799-805.
- Miyashita, T., and J.C. Reed. 1993. Bcl-2 oncprotein blocks chemotherapy-induced apoptosis in a human leukemia cell line. *Blood*. 81:151-7.
- Moll, U.M., and A. Zaika. 2001. Nuclear and mitochondrial apoptotic pathways of p53. *FEBS Lett*. 493:65-9.
- Morelli, D., S. Menard, M.I. Colnaghi, and A. Balsari. 1996. Oral administration of anti-doxorubicin monoclonal antibody prevents chemotherapy-induced gastrointestinal toxicity in mice. *Cancer Research*. 56:2082-5.

- Morvan, F.O., B. Baroukh, D. Ledoux, J.P. Caruelle, D. Barritault, G. Godeau, and J.L. Saffar. 2004. An engineered biopolymer prevents mucositis induced by 5-fluorouracil in hamsters. *Am J Pathol.* 164:739-46.
- Moss, S.F., B. Agarwal, N. Arber, R.J. Guan, M. Krajewska, S. Krajewski, J.C. Reed, and P.R. Holt. 1996. Increased intestinal Bak expression results in apoptosis. *Biochemical & Biophysical Research Communications.* 223:199-203.
- Moucadel, V., M.S. Totaro, C.D. Dell, P. Soubeyran, J.C. Dagorn, J.N. Freund, and J.L. Iovanna. 2002. The homeobox gene Cdx1 belongs to the p53-p21(WAF)-Bcl-2 network in intestinal epithelial cells. *Biochemical & Biophysical Research Communications.* 297:607-15.
- Mulder, T.P., A. van der Sluys Veer, H.W. Verspaget, G. Griffioen, A.S. Pena, A.R. Janssens, and C.B. Lamers. 1994. Effect of oral zinc supplementation on metallothionein and superoxide dismutase concentrations in patients with inflammatory bowel disease. *J Gastroenterol Hepatol.* 9:472-7.
- Muller, M., C.A. Scaffidi, P.R. Galle, W. Stremmel, and P.H. Krammer. 1998a. The role of p53 and the CD95 (APO-1/Fas) death system in chemotherapy-induced apoptosis. *European Cytokine Network.* 9:685-6.
- Muller, M., S. Wilder, D. Bannasch, D. Israeli, K. Lehlbach, M. Li-Weber, S.L. Friedman, P.R. Galle, W. Stremmel, M. Oren, and P.H. Krammer. 1998b. p53 activates the CD95 (APO-1/Fas) gene in response to DNA damage by anticancer drugs. *Journal of Experimental Medicine.* 188:2033-45.
- Nagai, Y., T. Horie, and S. Awazu. 1993. Vitamin A, a useful biochemical modulator capable of preventing intestinal damage during methotrexate treatment. *Pharmacol Toxicol.* 73:69-74.
- Nagata, S. 1994. Apoptosis regulated by a death factor and its receptor: Fas ligand and Fas. *Philosophical Transactions of the Royal Society of London - Series B: Biological Sciences.* 345:281-7.
- Nakano, K., and K.H. Vousden. 2001. PUMA, a novel proapoptotic gene, is induced by p53. *Molecular Cell.* 7:683-94.
- Narita, M., S. Shimizu, T. Ito, T. Chittenden, R.J. Lutz, H. Matsuda, and Y. Tsujimoto. 1998. Bax interacts with the permeability transition pore to induce permeability transition and cytochrome c release in isolated mitochondria. *Proceedings of the National Academy of Sciences of the United States of America.* 95:14681-6.
- Nicholson, D.W., and N.A. Thornberry. 1997. Caspases: killer proteases. *Trends in Biochemical Sciences.* 22:299-306.
- Nita, M.E., H. Nagawa, O. Tominaga, N. Tsuno, S. Fujii, S. Sasaki, C.G. Fu, T. Takenoue, T. Tsuruo, and T. Muto. 1998. 5-Fluorouracil induces apoptosis in human colon cancer cell lines with modulation of Bcl-2 family proteins. *British Journal of Cancer.* 78:986-92.

- Norbury, C.J., and B. Zhivotovsky. 2004. DNA damage-induced apoptosis. *Oncogene*. 23:2797-808.
- Oda, E., R. Ohki, H. Murasawa, J. Nemoto, T. Shibue, T. Yamashita, T. Tokino, T. Taniguchi, and N. Tanaka. 2000. Noxa, a BH3-only member of the Bcl-2 family and candidate mediator of p53-induced apoptosis. *Science*. 288:1053-8.
- Okuno, S., S. Shimizu, T. Ito, M. Nomura, E. Hamada, Y. Tsujimoto, and H. Matsuda. 1998. Bcl-2 prevents caspase-independent cell death. *Journal of Biological Chemistry*. 273:34272-7.
- Oltvai, Z.N., C.L. Milliman, and S.J. Korsmeyer. 1993. Bcl-2 heterodimerizes in vivo with a conserved homolog, Bax, that accelerates programmed cell death. *Cell*. 74:609-19.
- O'Reilly, L.A., C. Print, G. Hausmann, K. Moriishi, S. Cory, D.C. Huang, and A. Strasser. 2001. Tissue expression and subcellular localization of the pro-survival molecule Bcl-w. *Cell Death & Differentiation*. 8:486-94.
- O'Reilly, L.A., L. Cullen, J. Visvader, G.J. Lindeman, C. Print, M.L. Bath, D.C. Huang, and A. Strasser. 2000. The proapoptotic BH3-only protein bim is expressed in hematopoietic, epithelial, neuronal, and germ cells. *American Journal of Pathology*. 157:449-61.
- Oren, M. 1992. The involvement of oncogenes and tumor suppressor genes in the control of apoptosis. *Cancer & Metastasis Reviews*. 11:141-8.
- Palacios, C., A. Gutierrez del Arroyo, A. Silva, and M.K. Collins. 2000. The role of p53 in death of IL-3-dependent cells in response to cytotoxic drugs. *Oncogene*. 19:3556-9.
- Papaconstantinou, H.T., C. Xie, W. Zhang, N.H. Ansari, M.R. Hellmich, C.M. Townsend, Jr., and T.C. Ko. 2001. The role of caspases in methotrexate-induced gastrointestinal toxicity. *Surgery*. 130:859-65.
- Papaconstantinou, H.T., D.H. Chung, W. Zhang, N.H. Ansari, M.R. Hellmich, C.M. Townsend, Jr., and T.C. Ko. 2000. Prevention of mucosal atrophy: role of glutamine and caspases in apoptosis in intestinal epithelial cells. *Journal of Gastrointestinal Surgery*. 4:416-23.
- Park, J., and D.M. Hockenberry. 1996. BCL-2, a novel regulator of apoptosis. *Journal of Cellular Biochemistry*. 60:12-7.
- Pattini, K., and G. Banting. 2004. Ins(1,4,5)P₃ metabolism and the family of IP₃-3Kinases. *Cell Signal*. 16:643-54.
- Philchenkov, A. 2004. Caspases: potential targets for regulating cell death. *J Cell Mol Med*. 8:432-44.
- Pico, J., A. Avila-Garavito, and P. Naccache. 1998. Mucositis: Its occurrence, consequences and treatment in the oncology setting. *The Oncologist*. 3:446-451.

- Pinkoski, M.J., T. Brunner, D.R. Green, and T. Lin. 2000. Fas and Fas ligand in gut and liver. *American Journal of Physiology - Gastrointestinal & Liver Physiology*. 278:G354-66.
- Plevova, P. 2002. Radiotherapy- and chemotherapy-induced normal tissue damage: the role of cytokines and adhesion molecules. *Radiol Oncol*. 36:109-119.
- Potten, C.S. 2004. Radiation, the ideal cytotoxic agent for studying the cell biology of tissues such as the small intestine. *Radiat Res*. 161:123-36.
- Potten, C.S., C. Booth, G.L. Tudor, D. Booth, G. Brady, P. Hurley, G. Ashton, R. Clarke, S. Sakakibara, and H. Okano. 2003. Identification of a putative intestinal stem cell and early lineage marker; musashi-1. *Differentiation*. 71:28-41.
- Potten, C.S. 1998. Stem cells in gastrointestinal epithelium: numbers, characteristics and death. *Philosophical Transactions of the Royal Society of London - Series B: Biological Sciences*. 353:821-30.
- Potten, C.S., and H.K. Grant. 1998. The relationship between ionizing radiation-induced apoptosis and stem cells in the small and large intestine. *British Journal of Cancer*. 78:993-1003.
- Potten, C.S. 1997. Epithelial cell growth and differentiation. II. Intestinal apoptosis. *Am J Physiol*. 273:G253-7.
- Potten, C.S., C. Booth, and D.M. Pritchard. 1997a. The intestinal epithelial stem cell: the mucosal governor. *Int J Exp Pathol*. 78:219-43.
- Potten, C.S., J.W. Wilson, and C. Booth. 1997b. Regulation and significance of apoptosis in the stem cells of the gastrointestinal epithelium. *Stem Cells*. 15:82-93.
- Potten, C.S., G. Owen, D. Hewitt, C.A. Chadwick, H. Hendry, B.I. Lord, and L.B. Woolford. 1995. Stimulation and inhibition of proliferation in the small intestinal crypts of the mouse after in vivo administration of growth factors. *Gut*. 36:864-73.
- Potten, C.S. 1992. The significance of spontaneous and induced apoptosis in the gastrointestinal tract of mice. *Cancer & Metastasis Reviews*. 11:179-95.
- Potten, C.S., Y.Q. Li, P.J. O'Connor, and D.J. Winton. 1992. A possible explanation for the differential cancer incidence in the intestine, based on distribution of the cytotoxic effects of carcinogens in the murine large bowel. *Carcinogenesis*. 13:2305-12.
- Potten, C.S. 1990. A comprehensive study of the radiobiological response of the murine (BDF1) small intestine. *Int J Radiat Biol*. 58:925-73.
- Potten, C.S., and M. Loeffler. 1990. Stem cells: attributes, cycles, spirals, pitfalls and uncertainties. Lessons for and from the crypt. *Development*. 110:1001-20.

- Pratesi, G., P. Perego, and F. Zunino. 2001. Role of Bcl-2 and its post-transcriptional modification in response to antitumor therapy. *Biochemical Pharmacology*. 61:381-6.
- Pritchard, D.M., C. Print, L. O'Reilly, J.M. Adams, C.S. Potten, and J.A. Hickman. 2000. Bcl-w is an important determinant of damage-induced apoptosis in epithelia of small and large intestine. *Oncogene*. 19:3955-9.
- Pritchard, D.M., C.S. Potten, S.J. Korsmeyer, S. Roberts, and J.A. Hickman. 1999. Damage-induced apoptosis in intestinal epithelia from bcl-2-null and bax-null mice: investigations of the mechanistic determinants of epithelial apoptosis in vivo. *Oncogene*. 18:7287-93.
- Pritchard, D.M., J.A. Hickman, C.S. Potten, and A.M. Wardley. 1998. A quantitative histometric murine in vivo model of radiation-induced oral mucositis. *American Journal of Pathology*. 153:899-909.
- Pritchard, D.M., C.S. Potten, and J.A. Hickman. 1998. The relationships between p53-dependent apoptosis, inhibition of proliferation, and 5-fluorouracil-induced histopathology in murine small intestinal epithelia. *Cancer Research*. 58:5453-65.
- Puthalakath, H., and A. Strasser. 2002. Keeping killers on a tight leash: transcriptional and post-translational control of the pro-apoptotic activity of BH3-only proteins. *Cell Death & Differentiation*. 9:505-12.
- Puthalakath, D.C. Huang, L.A. O'Reilly, S.M. King, and A. Strasser. 1999. The proapoptotic activity of the Bcl-2 family member Bim is regulated by interaction with the dynein motor complex. *Molecular Cell*. 3:287-96.
- Raisova, M., A.M. Hossini, J. Eberle, C. Riebeling, T. Wieder, I. Sturm, P.T. Daniel, C.E. Orfanos, and C.C. Geilen. 2001. The Bax/Bcl-2 ratio determines the susceptibility of human melanoma cells to CD95/Fas-mediated apoptosis. *Journal of Investigative Dermatology*. 117:333-40.
- Ray, R.M., S.A. McCormack, and L.R. Johnson. 2001. Polyamine depletion arrests growth of IEC-6 and Caco-2 cells by different mechanisms. *Am J Physiol Gastrointest Liver Physiol*. 281:G37-43.
- Ray, R.M., B.J. Zimmerman, S.A. McCormack, T.B. Patel, and L.R. Johnson. 1999. Polyamine depletion arrests cell cycle and induces inhibitors p21(Waf1/Cip1), p27(Kip1), and p53 in IEC-6 cells. *Am J Physiol*. 276:C684-91.
- Reed, J.C. 2000. Mechanisms of apoptosis. *American Journal of Pathology*. 157:1415-30
- Reed, J.C., and J. Zhang. 1997. Bcl-2 interrupts the ceramide-mediated pathway of cell death. *Journal of Biological Chemistry*. 272:31482-8.
- Reinke, V., and G. Lozano. 1997. Differential activation of p53 targets in cells treated with ultraviolet radiation that undergo both apoptosis and growth arrest. *Radiat Res*. 148:115-22.

- Renehan, A., R. Gossiel, S.E. Davidson, S.A. Roberts, C. Chadwick, D.P. Wilks, C.S. Potten. 1995. What is apoptosis, and why is it important? *Radiotherapy & Oncology*. 37:1-9.
- Renehan, A.G., S.P. Bach, and C.S. Potten. 2001. The relevance of apoptosis for cellular homeostasis and tumorigenesis in the intestine. *Canadian Journal of Gastroenterology*. 15:166-76.
- Rosse, T. 1998. Bcl-2 prolongs cell survival after Bax-induced release of cytochrome c. *Nature*. 391:486-99.
- Russo, A., S. Corsale, P. Cammareri, V. Agnese, S. Cascio, G. Di Fede, M. Macaluso, and V. Bazan. 2005. Pharmacogenomics in colorectal carcinomas: future perspectives in personalized therapy. *J Cell Physiol*. 204:742-9.
- R. Giegerich, F. Meyer, and C. Schleiermacher. 1996. GeneFisher - Software support for the detection of postulated genes. In Proceedings of the Fourth International Conference on Intelligent Systems for Molecular Biology.
- Sabbatini, M., C. Bozzo, M. Castellucci, and M. Cannas. 2004. Morphometric quantification of apoptotic stages in cell culture. *Cells Tissues Organs*. 178:139-45.
- Saini, K.S., and N.I. Walker. 1998. Biochemical and molecular mechanisms regulating apoptosis. *Molecular & Cellular Biochemistry*. 178:9-25.
- Sax, J.K., P. Fei, M.E. Murphy, E. Bernhard, S.J. Korsmeyer, and W.S. El-Deiry. 2002. BID regulation by p53 contributes to chemosensitivity. *Nat Cell Biol*. 4:842-9.
- Scaffidi, C., S. Fulda, A. Srinivasan, C. Friesen, F. Li, K.J. Tomaselli, K.M. Debatin, P.H. Krammer, and M.E. Peter. 1998. Two CD95 (APO-1/Fas) signaling pathways. *EMBO Journal*. 17:1675-87.
- Schafer, T., C. Scheuer, K. Roemer, M.D. Menger, and B. Vollmar. 2003. Inhibition of p53 protects liver tissue against endotoxin-induced apoptotic and necrotic cell death. *FASEB Journal*. 17:660-7.
- Scheinin, T., T. Bohling, L. Halme, S. Kontiainen, L. Bjorge, and S. Meri. 1999. Decreased expression of protectin (CD59) in gut epithelium in ulcerative colitis and Crohn's disease. *Hum Pathol*. 30:1427-30.
- Schinzel, A., T. Kaufmann, and C. Borner. 2004. Bcl-2 family members: intracellular targeting, membrane-insertion, and changes in subcellular localization. *Biochim Biophys Acta*. 1644:95-105.
- Schreiber, S., R.P. MacDermott, A. Raedler, R. Pinna, M.J. Bertovich, and G.S. Nash. 1991. Increased activation of isolated intestinal lamina propria mononuclear cells in inflammatory bowel disease. *Gastroenterology*. 101:1020-30.

- Shibata, Y., H. Takiguchi, K. Tamura, K. Yamanaka, M. Tezuka, and Y. Abiko. 1996. Stimulation of interleukin-1beta-converting enzyme activity during growth inhibition by CPT-11 in the human myeloid leukemia cell line K562. *Biochem Mol Med.* 57:25-30.
- Sedlak, T.W., Z.N. Oltvai, E. Yang, K. Wang, L.H. Boise, C.B. Thompson, and S.J. Korsmeyer. 1995. Multiple Bcl-2 family members demonstrate selective dimerizations with Bax. *Proceedings of the National Academy of Sciences of the United States of America.* 92:7834-8.
- Sherwood, L. 1997. Human Physiology - from cells to systems. Wadsworth Publishing Company. 446-600 pp.
- Shibue, T., K. Takeda, E. Oda, H. Tanaka, H. Murasawa, A. Takaoka, Y. Morishita, S. Akira, T. Taniguchi, and N. Tanaka. 2003. Integral role of Noxa in p53-mediated apoptotic response. *Genes Dev.* 17:2233-8.
- Shimizu, S., A. Konishi, T. Kodama, and Y. Tsujimoto. 2000. BH4 domain of antiapoptotic Bcl-2 family members closes voltage-dependent anion channel and inhibits apoptotic mitochondrial changes and cell death.[erratum appears in Proc Natl Acad Sci U S A 2000 Aug 1;97(16):9347]. *Proceedings of the National Academy of Sciences of the United States of America.* 97:3100-5.
- Shinoura, N., R. Satou, Y. Yoshida, A. Asai, T. Kirino, and H. Hamada. 2000. Adenovirus-mediated transfer of Bcl-X(L) protects neuronal cells from Bax-induced apoptosis. *Experimental Cell Research.* 254:221-31.
- Shinohara, H., J.J. Killion, C.D. Bucana, S. Yano, and I.J. Fidler. 1999. Oral administration of the immunomodulator JBT-3002 induces endogenous interleukin 15 in intestinal macrophages for protection against irinotecan-mediated destruction of intestinal epithelium. *Clin Cancer Res.* 5:2148-56.
- Shinohara, H., J.J. Killion, H. Kuniyasu, R. Kumar, and I.J. Fidler. 1998. Prevention of intestinal toxic effects and intensification of irinotecan's therapeutic efficacy against murine colon cancer liver metastases by oral administration of the lipopeptide JBT 3002. *Clin Cancer Res.* 4:2053-63.
- Slee, E.A., D.J. O'Connor, and X. Lu. 2004. To die or not to die: how does p53 decide? *Oncogene.* 23:2809-18.
- Slee, E.A., C. Adrain, and S.J. Martin. 1999. Serial killers: ordering caspase activation events in apoptosis. *Cell Death & Differentiation.* 6:1067-74.
- Smith, N.D., J.N. Rubenstein, S.E. Eggner, and J.M. Kozlowski. 2003. The p53 tumor suppressor gene and nuclear protein: basic science review and relevance in the management of bladder cancer. *J Urol.* 169:1219-28.
- Smith, F.P., D.L. Kisner, L. Widerlite, and P.S. Schein. 1979. Chemotherapeutic alteration of small intestinal morphology and function: a progress report. *J Clin Gastroenterol.* 1:203-7.

- Solary, E., B. Favre, D. Caillot, I. Sidaner, and H. Guy. 2000. Positive and negative regulation of apoptotic pathways by cytotoxic agents in hematological malignancies. *Leukemia*. 14:1833-49.
- Sonis, S.T. 2004. A biological approach to mucositis. *J Support Oncol.* 2:21-32; discussion 35-6.
- Sonis, S.T. 2004a. The pathobiology of mucositis. *Nat Rev Cancer.* 4:277-84.
- Sonis, S.T. 2004b. Pathobiology of mucositis. *Semin Oncol Nurs.* 20:11-5.
- Sonis, S.T., L.S. Elting, D. Keefe, D.E. Peterson, M. Schubert, M. Hauer-Jensen, B.N. Bekele, J. Raber-Durlacher, J.P. Donnelly, and E.B. Rubenstein. 2004. Perspectives on cancer therapy-induced mucosal injury: pathogenesis, measurement, epidemiology, and consequences for patients. *Cancer.* 100:1995-2025.
- Sonis, S.T., J. Scherer, S. Phelan, C.A. Lucey, J.E. Barron, K.E. O'Donnell, R.J. Brennan, H. Pan, P. Busse, and J.D. Haley. 2002. The gene expression sequence of radiated mucosa in an animal mucositis model. *Cell Prolif.* 35 Suppl 1:93-102.
- Sonis, S.T. 2002. The biologic role for nuclear factor-kappaB in disease and its potential involvement in mucosal injury associated with anti-neoplastic therapy. *Crit Rev Oral Biol Med.* 13:380-9.
- Sonis, S.T., J. Scherer, S. Phelan, C.A. Lucey, J.E. Barron, K.E. O'Donnell, R.J. Brennan, H. Pan, P. Busse, and J.D. Haley. 2002. The gene expression sequence of radiated mucosa in an animal mucositis model. *Cell Prolif.* 35 Suppl 1:93-102.
- Sonis, S.T., D.E. Peterson, D.B. McGuire, and D.A. Williams. 2001. Prevention of mucositis in cancer patients. *J Natl Cancer Inst Monogr:*1-2.
- Srivastava, R.K., A.R. Srivastava, S.J. Korsmeyer, M. Nesterova, Y.S. Cho-Chung, and D.L. Longo. 1998. Involvement of microtubules in the regulation of Bcl2 phosphorylation and apoptosis through cyclic AMP-dependent protein kinase. *Molecular & Cellular Biology.* 18:3509-17.
- Strasser, A., L. O'Connor, and V.M. Dixit. 2000a. Apoptosis signaling. *Annual Review of Biochemistry.* 69:217-45.
- Strasser, A., H. Puthalakath, P. Bouillet, D.C. Huang, L. O'Connor, L.A. O'Reilly, L. Cullen, S. Cory, and J.M. Adams. 2000b. The role of bim, a proapoptotic BH3-only member of the Bcl-2 family in cell-death control. *Annals of the New York Academy of Sciences.* 917:541-8.
- Susin, S.A., N. Zamzami, and G. Kroemer. 1998. Mitochondria as regulators of apoptosis: doubt no more. *Biochim Biophys Acta.* 1366:151-65.
- Suzuki, T., S. Sadahiro, M. Fukasawa, K. Ishikawa, A. Kamijo, S. Yasuda, H. Makuchi, Y. Ohizumi, and C. Murayama. 2004. Predictive factors of tumor shrinkage and

- histological regression in patients who received preoperative radiotherapy for rectal cancer. *Jpn J Clin Oncol.* 34:740-6.
- Takahashi, M., H. Saito, T. Okuyama, T. Miyashita, M. Kosuga, F. Sumisa, M. Yamada, H. Ebinuma, and H. Ishii. 1999. Overexpression of Bcl-2 protects human hepatoma cells from Fas-antibody-mediated apoptosis. *Journal of Hepatology.* 31:315-22.
- Takasuna, K., T. Hagiwara, M. Hirohashi, M. Kato, M. Nomura, E. Nagai, T. Yokoi, and T. Kamataki. 1998. Inhibition of intestinal microflora beta-glucuronidase modifies the distribution of the active metabolite of the antitumor agent, irinotecan hydrochloride (CPT-11) in rats. *Cancer Chemother Pharmacol.* 42:280-6.
- Takasuna, K., T. Hagiwara, M. Hirohashi, M. Kato, M. Nomura, E. Nagai, T. Yokoi, and T. Kamataki. 1996. Involvement of beta-glucuronidase in intestinal microflora in the intestinal toxicity of the antitumor camptothecin derivative irinotecan hydrochloride (CPT-11) in rats. *Cancer Res.* 56:3752-7.
- Tamatani, M., S. Ogawa, G. Nunez, and M. Tohyama. 1998. Growth factors prevent changes in Bcl-2 and Bax expression and neuronal apoptosis induced by nitric oxide. *Cell Death & Differentiation.* 5:911-9.
- Taminiau, J.A., D.G. Gall, and J.R. Hamilton. 1980. Response of the rat small-intestine epithelium to methotrexate. *Gut.* 21:486-92.
- Tarnawski, A.S., and I. Szabo. 2001. Apoptosis - programmed cell death and its relevance to gastrointestinal epithelium: survival signal from the matrix. *Gastroenterology.* 120:294-9.
- Tenenbaum, L. 1994. Cancer chemotherapy and biotherapy. W.B. Saunders Company. 7-8 pp.
- Tepperman, B.L., B.D. Soper, and Q. Chang. 2005. Effect of protein kinase C activation on intracellular Ca²⁺ signaling and integrity of intestinal epithelial cells. *Eur J Pharmacol.* 518:1-9.
- Thornberry, N.A. 1998. Caspases: key mediators of apoptosis. *Chemistry & Biology.* 5:R97-103.
- Thornberry, N.A., and Y. Lazebnik. 1998. Caspases: enemies within. *Science.* 281:1312-6.
- Tran, C.D., G.S. Howarth, P. Coyle, J.C. Philcox, A.M. Rofe, and R.N. Butler. 2003. Dietary supplementation with zinc and a growth factor extract derived from bovine cheese whey improves methotrexate-damaged rat intestine. *Am J Clin Nutr.* 77:1296-303.
- Trier, J.S. 1962. Morphologic alterations induced by methotrexate in the mucosa of human proximal intestine. I. Serial observations by light microscopy. *Gastroenterology.* 42:295-305.

- Trier, J.S. 1962b. Morphologic alterations induced by methotrexate in the mucosa of human proximal intestine. II. Electron microscopic observations. *Gastroenterology*. 43:407-24.
- Trifan, O.C., W.F. Durham, V.S. Salazar, J. Horton, B.D. Levine, B.S. Zweifel, T.W. Davis, and J.L. Masferrer. 2002. Cyclooxygenase-2 inhibition with celecoxib enhances antitumor efficacy and reduces diarrhea side effect of CPT-11. *Cancer Res.* 62:5778-84.
- Troester, M.A., K.A. Hoadley, T. Sorlie, B.S. Herbert, A.L. Borresen-Dale, P.E. Lonning, J.W. Shay, W.K. Kaufmann, and C.M. Perou. 2004. Cell-type-specific responses to chemotherapeutics in breast cancer. *Cancer Res.* 64:4218-26.
- Upadhyay, S., G. Li, H. Liu, Y.Q. Chen, F.H. Sarkar, and H.R. Kim. 1995. bcl-2 suppresses expression of p21WAF1/CIP1 in breast epithelial cells. *Cancer Research*. 55:4520-4.
- Vakeva, A., P. Laurila, and S. Meri. 1992. Loss of expression of protectin (CD59) is associated with complement membrane attack complex deposition in myocardial infarction. *Lab Invest.* 67:608-16.
- van Loo, G., X. Saelens, M. van Gurp, M. MacFarlane, S.J. Martin, and P. Vandenabeele. 2002. The role of mitochondrial factors in apoptosis: a Russian roulette with more than one bullet. *Cell Death Differ.* 9:1031-42.
- van't Land, B., N.M. van Beek, J.J. van den Berg, and L. M'Rabet. 2004. Lactoferrin reduces methotrexate-induced small intestinal damage, possibly through inhibition of GLP-2-mediated epithelial cell proliferation. *Dig Dis Sci.* 49:425-33.
- van't Land, B., N.M. Blijlevens, J. Marteijn, S. Timal, J.P. Donnelly, T.J. de Witte, and L. M'Rabet. 2004. Role of curcumin and the inhibition of NF-kappaB in the onset of chemotherapy-induced mucosal barrier injury. *Leukemia*. 18:276-84.
- van't Land, B., H.P. Meijer, J. Frerichs, M. Koetsier, D. Jager, R.L. Smeets, L. M'Rabet, and M. Hoijer. 2002. Transforming Growth Factor-beta2 protects the small intestine during methotrexate treatment in rats possibly by reducing stem cell cycling. *British Journal of Cancer*. 87:113-8.
- Verburg, M., I.B. Renes, H.P. Meijer, J.A. Taminiau, H.A. Buller, A.W. Einerhand, and J. Dekker. 2000. Selective sparing of goblet cells and paneth cells in the intestine of methotrexate-treated rats. *American Journal of Physiology - Gastrointestinal & Liver Physiology*. 279:G1037-47.
- Vogelstein, B., D. Lane, and A.J. Levine. 2000. Surfing the p53 network. *Nature*. 408:307-10.
- Vollmar, B., A.M. El-Gibaly, C. Scheuer, M.W. Strik, H.P. Bruch, and M.D. Menger. 2002. Acceleration of cutaneous wound healing by transient p53 inhibition. *Laboratory Investigation*. 82:1063-71.

- Vousden, K.H., and X. Lu. 2002. Live or let die: the cell's response to p53. *Nat Rev Cancer.* 2:594-604.
- Wang, S., E.A. Konorev, S. Kotamraju, J. Joseph, S. Kalivendi, and B. Kalyanaraman. 2004. Doxorubicin induces apoptosis in normal and tumor cells via distinctly different mechanisms. intermediacy of H(2)O(2)- and p53-dependent pathways. *J Biol Chem.* 279:25535-43.
- Wang, J.Y., S. Naderi, and T.T. Chen. 2001. Role of retinoblastoma tumor suppressor protein in DNA damage response. *Acta Oncologica.* 40:689-95.
- Watson, A.J. 1995. Necrosis and apoptosis in the gastrointestinal tract. *Alimentary Pharmacology & Therapeutics.* 9:215-26.
- Wei, M.C. 2001. Proapoptotic BAX and BAK: a requisite gateway to mitochondrial dysfunction and death. *Science.* 292:727-30.
- Weller, M. 1998. Predicting response to cancer chemotherapy: the role of p53. *Cell & Tissue Research.* 292:435-45.
- Westcarr, S., P. Farshori, J. Wyche, and W.A. Anderson. 1999. Apoptosis and differentiation in the crypt-villus unit of the rat small intestine. *Journal of Submicroscopic Cytology & Pathology.* 31:15-30.
- Wilson, J.W., D.M. Pritchard, J.A. Hickman, and C.S. Potten. 1998. Radiation-induced p53 and p21WAF-1/CIP1 expression in the murine intestinal epithelium: apoptosis and cell cycle arrest. *American Journal of Pathology.* 153:899-909.
- Yang, X., Z. Hu, S.Y. Chan, E. Chan, B.C. Goh, W. Duan, and S. Zhou. 2005. Novel agents that potentially inhibit irinotecan-induced diarrhea. *Curr Med Chem.* 12:1343-58.
- Yang, Y.H., M.J. Buckley, and T.P. Speed. 2001. Analysis of cDNA microarray images. *Brief Bioinform.* 2:341-9.
- Yang, E., and S.J. Korsmeyer. 1996. Molecular thanatopsis: a discourse on the BCL2 family and cell death. *Blood.* 88:386-401.
- Yang, E., J. Zha, J. Jockel, L.H. Boise, C.B. Thompson, and S.J. Korsmeyer. 1995. Bad, a heterodimeric partner for Bcl-XL and Bcl-2, displaces Bax and promotes cell death. *Cell.* 80:285-91.
- Yeoh, A.S., J.M. Bowen, R.J. Gibson, and D.M. Keefe. 2005. Nuclear factor kappaB (NFkappaB) and cyclooxygenase-2 (Cox-2) expression in the irradiated colorectum is associated with subsequent histopathological changes. *Int J Radiat Oncol Biol Phys.*
- Yin, X.M., Z.N. Oltvai, D.J. Veis-Novack, and G.P. Linette. 1995. Bcl-2 gene family and the regulation of programmed cell death. *Biochimica et Biophysica Acta.* 1271:63-6.

- Yuan, Q., R.M. Ray, and L.R. Johnson. 2002. Polyamine depletion prevents camptothecin-induced apoptosis by inhibiting the release of cytochrome c. *Am J Physiol Cell Physiol.* 282:C1290-7.
- Yu, J., W.D. Shannon, M.A. Watson, and H.L. McLeod. 2005. Gene expression profiling of the irinotecan pathway in colorectal cancer. *Clin Cancer Res.* 11:2053-62.
- Yu, J., and L. Zhang. 2005. The transcriptional targets of p53 in apoptosis control. *Biochem Biophys Res Commun.* 331:851-8.
- Zhang, M., W. Liu, D. Ding, and R. Salvi. 2003. Pifithrin-a supresses p53 and protects cochlear and vestibular hair cells from cisplatin-induced apoptosis. *Neuroscience.* 120:191-205.
- Zhao, J., L. Huang, N. Belmar, R. Buelow, and T. Fong. 2004. Oral RDP58 allows CPT-11 dose intensification for enhanced tumor response by decreasing gastrointestinal toxicity. *Clin Cancer Res.* 10:2851-9.
- Zhu, M., Q.S. Yu, R.G. Cutler, C.W. Culmsee, H.W. Holloway, D.K. Lahiri, M.P. Mattson, and N.H. Greig. 2002. Novel p53 inactivators with neuroprotective action: syntheses and pharmacological evaluation of 2-imino-2,3,4,5,6,7-hexahydrobenzothiazole and 2-imino-2,3,4,5,6,7-hexahydrobenzoxazole derivatives. *Journal of Medicinal Chemistry.* 45:5090-7.
- Zhu, J., S. Nozell, J. Wang, J. Jiang, W. Zhou, and X. Chen. 2001. p73 cooperates with DNA damage agents to induce apoptosis in MCF7 cells in a p53-dependent manner. *Oncogene.* 20:4050-7.
- Zong, W.X., T. Lindsten, A.J. Ross, G.R. MacGregor, and C.B. Thompson. 2001. BH3-only proteins that bind pro-survival Bcl-2 family members fail to induce apoptosis in the absence of Bax and Bak. *Genes & Development.* 15:1481-6.

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