

8 REFERENCES

Adli, M. & Baldwin, A.S. 2006, "IKK-i/IKK ϵ controls constitutive, cancer cell-associated NF- κ B activity via regulation of Ser-536 p65/RelA phosphorylation", *Journal of Biological Chemistry*, vol. 281, no. 37, pp. 26976-26984.

Aktas, O., Smorodchenko, A., Brocke, S., Infante-Duarte, C., Topphoff, U.S., Vogt, J., Prozorovski, T., Meier, S., Osmanova, V., Pohl, E., Bechmann, I., Nitsch, R. & Zipp, F. 2005, "Neuronal Damage in Autoimmune Neuroinflammation Mediated by the Death Ligand TRAIL", *Neuron*, vol. 46, no. 3, pp. 421-432.

- Alemán, L.M., Doench, J. & Sharp, P.A. 2007, "Comparison of siRNA-induced off-target RNA and protein effects", *RNA*, vol. 13, no. 3, pp. 385-395.
- Ali, S. & Coombes, R.C. 2000, "Estrogen receptor alpha in human breast cancer: occurrence and significance", *Journal of mammary gland biology and neoplasia*, vol. 5, no. 3, pp. 271-281.
- Amano, T., Tanabe, K., Eto, T., Narumiya, S. & Mizuno, K. 2001, "LIM-kinase 2 induces formation of stress fibres, focal adhesions and membrane blebs, dependent on its activation by Rho-associated kinase-catalysed phosphorylation at threonine-505", *The Biochemical journal*, vol. 354, no. Pt 1, pp. 149-159.
- Anan, A., Baskin-Bey, E.S., Bronk, S.F., Werneburg, N.W., Shah, V.H. & Gores, G.J. 2006, "Proteasome inhibition induces hepatic stellate cell apoptosis", *Hepatology*, vol. 43, no. 2, pp. 335-344.
- Ashkenazi, A. & Dixit, V.M. 1999, "Apoptosis control by death and decoy receptors", *Current opinion in cell biology*, vol. 11, no. 2, pp. 255-260.
- Ashkenazi, A., Pai, R.C., Fong, S., Leung, S., Lawrence, D.A., Marsters, S.A., Blackie, C., Chang, L., McMurtrey, A.E., Hebert, A., DeForge, L., Koumenis, I.L., Lewis, D., Harris, L., Bussiere, J., Koeppen, H., Shahrokh, Z. & Schwall, R.H. 1999, "Safety and antitumor activity of recombinant soluble Apo2 ligand", *Journal of Clinical Investigation*, vol. 104, no. 2, pp. 155-162.
- Ashrafi, K., Chang, F.Y., Watts, J.L., Fraser, A.G., Kamath, R.S., Ahringer, J. & Ruvkun, G. 2003, "Genome-wide RNAi analysis of *Caenorhabditis elegans* fat regulatory genes", *Nature*, vol. 421, no. 6920, pp. 268-272.
- Assuncao Guimaraes, C. & Linden, R. 2004, "Programmed cell deaths. Apoptosis and alternative deathstyles", *Eur J Biochem*, vol. 271, no. 9, pp. 1638-1650.
- Aza-Blanc, P., Cooper, C.L., Wagner, K., Batalov, S., Deveraux, Q.L. & Cooke, M.P. 2003, "Identification of modulators of TRAIL-induced apoptosis via RNAi-based phenotypic screening", *Molecular Cell*, vol. 12, no. 3, pp. 627-637.
- Bae, S.I., Cheriyath, V., Jacobs, B.S., Reu, F.J. & Borden, E.C. 2007, "Reversal of methylation silencing of Apo2L/TRAIL receptor 1 (DR4) expression overcomes resistance of SK-MEL-3 and SK-MEL-28 melanoma cells to interferons (IFNs) or Apo2L/TRAIL", *Oncogene*, .
- Baeg, G.-., Zhou, R. & Perrimon, N. 2005, "Genome-wide RNAi analysis of JAK/STAT signaling components in *Drosophila*", *Genes and Development*, vol. 19, no. 16, pp. 1861-1870.

- Bagga, S., Bracht, J., Hunter, S., Massirer, K., Holtz, J., Eachus, R. & Pasquinelli, A.E. 2005, "Regulation by let-7 and lin-4 miRNAs results in target mRNA degradation", *Cell*, vol. 122, no. 4, pp. 553-563.
- Bailey, S.N., Ali, S.M., Carpenter, A.E., Higgins, C.O. & Sabatini, D.M. 2006, "Microarrays of lentiviruses for gene function screens in immortalized and primary cells", *Nature methods*, vol. 3, no. 2, pp. 117-122.
- Behm-Ansmant, I., Rehwinkel, J., Doerks, T., Stark, A., Bork, P. & Izaurralde, E. 2006, "mRNA degradation by miRNAs and GW182 requires both CCR4:NOT deadenylase and DCP1:DCP2 decapping complexes", *Genes & development*, vol. 20, no. 14, pp. 1885-1898.
- Bellen, H.J., Levis, R.W., Liao, G., He, Y., Carlson, J.W., Tsang, G., Evans-Holm, M., Hiesinger, P.R., Schulze, K.L., Rubin, G.M., Hoskins, R.A. & Spradling, A.C. 2004, "The BDGP gene disruption project: single transposon insertions associated with 40% of *Drosophila* genes", *Genetics*, vol. 167, no. 2, pp. 761-781.
- Berns, K., Hijmans, E.M., Mullenders, J., Brummelkamp, T.R., Velds, A., Heimerikx, M., Kerkhoven, R.M., Madiredjo, M., Nijkamp, W., Weigelt, B., Agami, R., Ge, W., Cavet, G., Linsley, P.S., Beijersbergen, R.L. & Bernards, R. 2004, "A large-scale RNAi screen in human cells identifies new components of the p53 pathway", *Nature*, vol. 428, no. 6981, pp. 431-437.
- Bernstein, E., Caudy, A.A., Hammond, S.M. & Hannon, G.J. 2001, "Role for a bidentate ribonuclease in the initiation step of RNA interference", *Nature*, vol. 409, no. 6818, pp. 363-366.
- Bild, A.H., Yao, G., Chang, J.T., Wang, Q., Potti, A., Chasse, D., Joshi, M.B., Harpole, D., Lancaster, J.M., Berchuck, A., Olson, J.A., Jr., Marks, J.R., Dressman, H.K., West, M. & Nevins, J.R. 2006, "Oncogenic pathway signatures in human cancers as a guide to targeted therapies", *Nature*, vol. 439, no. 7074, pp. 353-357.
- Birmingham, A., Anderson, E.M., Reynolds, A., Ilsley-Tyree, D., Leake, D., Fedorov, Y., Baskerville, S., Maksimova, E., Robinson, K., Karpilow, J., Marshall, W.S. & Khvorova, A. 2006, "3' UTR seed matches, but not overall identity, are associated with RNAi off-targets", *Nature methods*, vol. 3, no. 3, pp. 199-204.
- Boehm, J.S., Zhao, J.J., Yao, J., Kim, S.Y., Firestein, R., Dunn, I.F., Sjostrom, S.K., Garraway, L.A., Weremowicz, S., Richardson, A.L., Greulich, H., Stewart, C.J., Mulvey, L.A., Shen, R.R., Ambrogio, L., Hirozane-Kishikawa, T., Hill, D.E., Vidal, M., Meyerson, M., Grenier, J.K., Hinkle, G., Root, D.E., Roberts, T.M., Lander, E.S., Polyak, K. & Hahn, W.C. 2007, "Integrative Genomic Approaches Identify IKBKE as a Breast Cancer Oncogene", *Cell*, vol. 129, no. 6, pp. 1065-1079.

- Boutros, M., Brás, L.P. & Huber, W. 2006, "Analysis of cell-based RNAi screens", *Genome Biology*, vol. 7, no. 7.
- Boutros, M., Kiger, A.A., Armknecht, S., Kerr, K., Hild, M., Koch, B., Haas, S.A., Paro, R., Perrimon, N. & Heidelberg Fly Array Consortium 2004, "Genome-wide RNAi analysis of growth and viability in Drosophila cells", *Science (New York, N.Y.)*, vol. 303, no. 5659, pp. 832-835.
- Brasch, M.A., Hartley, J.L. & Vidal, M. 2004, "ORFeome Cloning and Systems Biology: Standardized Mass Production of the Parts From the Parts-List", *Genome Research*, vol. 14, no. 10b, pp. 2001-2009.
- Brennecke, J., Stark, A., Russell, R.B. & Cohen, S.M. 2005, "Principles of microRNA-target recognition", *PLoS biology*, vol. 3, no. 3, pp. e85.
- Brenner, S. 1974, "The genetics of *Caenorhabditis elegans*", *Genetics*, vol. 77, no. 1, pp. 71-94.
- Bridge, A.J., Pebernard, S., Ducraux, A., Nicoulaz, A. & Iggo, R. 2003, "Induction of an interferon response by RNAi vectors in mammalian cells", *Nat Genet*, vol. 34, no. 3, pp. 263-264.
- Burns, T.F. & El-Deiry, W.S. 2001, "Identification of Inhibitors of TRAIL-induced Death (ITIDs) in the TRAIL-sensitive Colon Carcinoma Cell Line SW480 Using a Genetic Approach", *Journal of Biological Chemistry*, vol. 276, no. 41, pp. 37879-37886.
- Casselton, L. & Zolan, M. 2002, "The art and design of genetic screens: Filamentous fungi", *Nature Reviews Genetics*, vol. 3, no. 9, pp. 683-697.
- Chen, X., Thakkar, H., Tyan, F., Gim, S., Robinson, H., Lee, C., Pandey, S.K., Nwokorie, C., Onwudiwe, N. & Srivastava, R.K. 2001, "Constitutively active Akt is an important regulator of TRAIL sensitivity in prostate cancer", *Oncogene*, vol. 20, no. 42, pp. 6073-6083.
- Chendrimada, T.P., Gregory, R.I., Kumaraswamy, E., Norman, J., Cooch, N., Nishikura, K. & Shiekhattar, R. 2005, "TRBP recruits the Dicer complex to Ago2 for microRNA processing and gene silencing", *Nature*, vol. 436, no. 7051, pp. 740-744.
- Chi, J., Chang, H.Y., Wang, N.N., Chang, D.S., Dunphy, N. & Brown, P.O. 2003, "Genomewide view of gene silencing by small interfering RNAs", *PNAS*, vol. 100, no. 11, pp. 6343-6346.
- Chinnaiyan, A.M., Prasad, U., Shankar, S., Hamstra, D.A., Shanaiah, M., Chenevert, T.L., Ross, B.D. & Rehemtulla, A. 2000, "Combined effect of tumor necrosis factor-related

- apoptosis-inducing ligand and ionizing radiation in breast cancer therapy", *Proceedings of the National Academy of Sciences of the United States of America*, vol. 97, no. 4, pp. 1754-1759.
- Clemens, J.C., Worby, C.A., Simonson-Leff, N., Muda, M., Maehama, T., Hemmings, B.A. & Dixon, J.E. 2000, "Use of double-stranded RNA interference in Drosophila cell lines to dissect signal transduction pathways", *Proceedings of the National Academy of Sciences of the United States of America*, vol. 97, no. 12, pp. 6499-6503.
- Collins, J.E., Goward, M.E., Cole, C.G., Smink, L.J., Huckle, E.J., Knowles, S., Bye, J.M., Beare, D.M. & Dunham, I. 2003, "Reevaluating human gene annotation: a second-generation analysis of chromosome 22", *Genome research*, vol. 13, no. 1, pp. 27-36.
- Collins, J.E., Wright, C.L., Edwards, C.A., Davis, M.P., Grinham, J.A., Cole, C.G., Goward, M.E., Aguado, B., Mallya, M., Mokrab, Y., Huckle, E.J., Beare, D.M. & Dunham, I. 2004, "A genome annotation-driven approach to cloning the human ORFeome", *Genome biology*, vol. 5, no. 10, pp. R84.
- Cretney, E., Takeda, K., Yagita, H., Glaccum, M., Peschon, J.J. & Smyth, M.J. 2002, "Increased Susceptibility to Tumor Initiation and Metastasis in TNF-Related Apoptosis-Inducing Ligand-Deficient Mice", *The Journal of Immunology*, vol. 168, no. 3, pp. 1356-1361.
- Croft, D. & Olson, M. 2006, "The Rho GTPase Effector ROCK Regulates Cyclin A, Cyclin D1, and p27Kip1 Levels by Distinct Mechanisms", *Molecular and Cellular Biology*, vol. 26, no. 12, pp. 4612-4627.
- D'Andrea, M.R., Qiu, Y., Haynes-Johnson, D., Bhattacharjee, S., Kraft, P. & Lundein, S. 2005, "Expression of PDE11A in normal and malignant human tissues", *The journal of histochemistry and cytochemistry : official journal of the Histochemistry Society*, vol. 53, no. 7, pp. 895-903.
- Degli-Esposti, M.A., Dougall, W.C., Smolak, P.J., Waugh, J.Y., Smith, C.A. & Goodwin, R.G. 1997a, "The novel receptor TRAIL-R4 induces NF-kappaB and protects against TRAIL-mediated apoptosis, yet retains an incomplete death domain", *Immunity*, vol. 7, no. 6, pp. 813-820.
- Degli-Esposti, M.A., Smolak, P.J., Walczak, H., Waugh, J., Huang, C.P., DuBose, R.F., Goodwin, R.G. & Smith, C.A. 1997b, "Cloning and characterization of TRAIL-R3, a novel member of the emerging TRAIL receptor family", *The Journal of experimental medicine*, vol. 186, no. 7, pp. 1165-1170.
- Deng, Y.B., Lin, Y.H. & Wu, X.W. 2002, "TRAIL-induced apoptosis requires Bax-dependent mitochondria release of Smac/DIABLO", *Genes & Development*, vol. 16, no. 1, pp. 33-45.

- Denli, A.M., Tops, B.B., Plasterk, R.H., Ketting, R.F. & Hannon, G.J. 2004, "Processing of primary microRNAs by the Microprocessor complex", *Nature*, vol. 432, no. 7014, pp. 231-235.
- Deveraux, Q.L., Takahashi, R., Salvesen, G.S. & Reed, J.C. 1997, "X-linked IAP is a direct inhibitor of cell-death proteases", *Nature*, vol. 388, no. 6639, pp. 300-304.
- Diehl, G.E., Yue, H.H., Hsieh, K., Kuang, A.A., Ho, M., Morici, L.A., Lenz, L.L., Cado, D., Riley, L.W. & Winoto, A. 2004, "TRAIL-R as a negative regulator of innate immune cell responses", *Immunity*, vol. 21, no. 6, pp. 877-889.
- Doench, J.G. & Sharp, P.A. 2004, "Specificity of microRNA target selection in translational repression", *Genes & development*, vol. 18, no. 5, pp. 504-511.
- Drews, J. 2000, "Drug discovery: a historical perspective", *Science (New York, N.Y.)*, vol. 287, no. 5460, pp. 1960-1964.
- Du, Q., Thonberg, H., Wang, J., Wahlestedt, C. & Liang, Z. 2005, "A systematic analysis of the silencing effects of an active siRNA at all single-nucleotide mismatched target sites", *Nucleic acids research*, vol. 33, no. 5, pp. 1671-1677.
- Duiker, E.W., Mom, C.H., de Jong, S., Willemse, P.H., Gietema, J.A., van der Zee, A.G. & de Vries, E.G. 2006, "The clinical trial of TRAIL", *European journal of cancer (Oxford, England : 1990)*, vol. 42, no. 14, pp. 2233-2240.
- Echeverri, C.J., Beachy, P.A., Baum, B., Boutros, M., Buchholz, F., Chanda, S.K., Downward, J., Ellenberg, J., Fraser, A.G., Hacohen, N., Hahn, W.C., Jackson, A.L., Kiger, A., Linsley, P.S., Lum, L., Ma, Y., Mathey-Prévôt, B., Root, D.E., Sabatini, D.M., Taipale, J., Perrimon, N. & Bernards, R. 2006, "Minimizing the risk of reporting false positives in large-scale RNAi screens", *Nature Methods*, vol. 3, no. 10, pp. 777-779.
- Echeverri, C.J. & Perrimon, N. 2006, "High-throughput RNAi screening in cultured cells: a user's guide", *Nature reviews Genetics*, vol. 7, no. 5, pp. 373-384.
- Ehrhardt, H., Fulda, S., Schmid, I., Hiscott, J., Debatin, K.-. & Jeremias, I. 2003, "TRAIL induced survival and proliferation in cancer cells resistant towards TRAIL-induced apoptosis mediated by NF- κ B", *Oncogene*, vol. 22, no. 25, pp. 3842-3852.
- Ehrlich, S., Infante-Duarte, C., Seeger, B. & Zipp, F. 2003, "Regulation of soluble and surface-bound TRAIL in human T cells, B cells, and monocytes", *Cytokine*, vol. 24, no. 6, pp. 244-253.
- Eis, P.S., Tam, W., Sun, L., Chadburn, A., Li, Z., Gomez, M.F., Lund, E. & Dahlberg, J.E. 2005, "Accumulation of miR-155 and BIC RNA in human B cell lymphomas",

- Proceedings of the National Academy of Sciences of the United States of America*, vol. 102, no. 10, pp. 3627-3632.
- Elbashir, S.M., Harborth, J., Lendeckel, W., Yalcin, A., Weber, K. & Tuschl, T. 2001, "Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells", *Nature*, vol. 411, no. 6836, pp. 494-498.
- Elbashir, S.M., Harborth, J., Weber, K. & Tuschl, T. 2002, "Analysis of gene function in somatic mammalian cells using small interfering RNAs", *Methods (San Diego, Calif.)*, vol. 26, no. 2, pp. 199-213.
- Elbashir, S.M., Lendeckel, W. & Tuschl, T. 2001, "RNA interference is mediated by 21- and 22-nucleotide RNAs", *Genes & development*, vol. 15, no. 2, pp. 188-200.
- Elbashir, S.M., Martinez, J., Patkaniowska, A., Lendeckel, W. & Tuschl, T. 2001, "Functional anatomy of siRNAs for mediating efficient RNAi in Drosophila melanogaster embryo lysate", *The EMBO journal*, vol. 20, no. 23, pp. 6877-6888.
- Ellis, H.M. & Horvitz, H.R. 1986, "Genetic control of programmed cell death in the nematode *C. elegans*", *Cell*, vol. 44, no. 6, pp. 817-829.
- Emery, J.G., McDonnell, P., Burke, M.B., Deen, K.C., Lyn, S., Silverman, C., Dul, E., Appelbaum, E.R., Eichman, C., DiPrinzio, R., Dodds, R.A., James, I.E., Rosenberg, M., Lee, J.C. & Young, P.R. 1998, "Osteoprotegerin is a receptor for the cytotoxic ligand TRAIL", *The Journal of biological chemistry*, vol. 273, no. 23, pp. 14363-14367.
- Erfle, H., Neumann, B., Liebel, U., Rogers, P., Held, M., Walter, T., Ellenberg, J. & Pepperkok, R. 2007, "Reverse transfection on cell arrays for high content screening microscopy", *Nature Protocols*, vol. 2, no. 2, pp. 392-399.
- Fawcett, L., Baxendale, R., Stacey, P., McGrouther, C., Harrow, I., Soderling, S., Hetman, J., Beavo, J.A. & Phillips, S.C. 2000, "Molecular cloning and characterization of a distinct human phosphodiesterase gene family: PDE11A", *Proceedings of the National Academy of Sciences*, vol. 97, no. 7, pp. 3702-3707.
- Finn, R., Mistry, J., Schuster-Bockler, B., Griffiths-Jones, S., Hollich, V., Lassmann, T., Moxon, S., Marshall, M., Khanna, A., Durbin, R., Eddy, S., Sonnhammer, E.L. & Bateman, A. 2006, "Pfam: clans, web tools and services", *Nucleic Acids Research*, vol. 34, no. suppl_1, pp. D247-251.
- Finnberg, N., Gruber, J.J., Fei, P., Rudolph, D., Bric, A., Kim, S.H., Burns, T.F., Ajuha, H., Page, R., Wu, G.S., Chen, Y., McKenna, W.G., Bernhard, E., Lowe, S., Mak, T. & El-Deiry, W.S. 2005, "DR5 knockout mice are compromised in radiation-induced apoptosis", *Molecular and cellular biology*, vol. 25, no. 5, pp. 2000-2013.

- Fire, A., Xu, S., Montgomery, M.K., Kostas, S.A., Driver, S.E. & Mello, C.C. 1998, "Potent and specific genetic interference by double-stranded RNA in *Caenorhabditis elegans*", *Nature*, vol. 391, no. 6669, pp. 806-811.
- Fitzgerald, K.A., McWhirter, S.M., Faia, K.L., Rowe, D.C., Latz, E., Golenbock, D.T., Coyle, A.J., Liao, S.M. & Maniatis, T. 2003, "IKKepsilon and TBK1 are essential components of the IRF3 signaling pathway", *Nature immunology*, vol. 4, no. 5, pp. 491-496.
- Forsburg, S.L. 2001, "The art and design of genetic screens: Yeast", *Nature Reviews Genetics*, vol. 2, no. 9, pp. 659-668.
- Fraser, A.G., James, C., Evan, G.I. & Hengartner, M.O. 1999, "Caenorhabditis elegans inhibitor of apoptosis protein (IAP) homologue BIR-1 plays a conserved role in cytokinesis", *Current biology : CB*, vol. 9, no. 6, pp. 292-301.
- Fraser, A.G., Kamath, R.S., Zipperlen, P., Martinez-Campos, M., Sohrmann, M. & Ahringer, J. 2000, "Functional genomic analysis of *C. elegans* chromosome I by systematic RNA interference", *Nature*, vol. 408, no. 6810, pp. 325-330.
- Frese, S., Pirnia, F., Miescher, D., Krajewski, S., Borner, M.M., Reed, J.C. & Schmid, R.A. 2003, "PG490-mediated sensitization of lung cancer cells to Apo2l/TRAIL-induced apoptosis requires activation of ERK2", *Oncogene*, vol. 22, no. 35, pp. 5427-5435.
- Friedman, A. & Perrimon, N. 2007, "Genetic Screening for Signal Transduction in the Era of Network Biology", *Cell*, vol. 128, no. 2, pp. 225-231.
- Ganten, T.M., Haas, T.L., Sykora, J., Stahl, H., Sprick, M.R., Fas, S.C., Krueger, A., Weigand, M.A., Grosse-Wilde, A., Stremmel, W., Krammer, P.H. & Walczak, H. 2004, "Enhanced caspase-8 recruitment to and activation at the DISC is critical for sensitisation of human hepatocellular carcinoma cells to TRAIL-induced apoptosis by chemotherapeutic drugs", *Cell death and differentiation*, vol. 11 Suppl 1, pp. S86-96.
- Ganten, T.M., Koschny, R., Haas, T.L., Sykora, J., Li-Weber, M., Herzer, K. & Walczak, H. 2005, "Proteasome inhibition sensitizes hepatocellular carcinoma cells, but not human hepatocytes, to TRAIL", *Hepatology (Baltimore, Md.)*, vol. 42, no. 3, pp. 588-597.
- Gazitt, Y., Shaughnessy, P. & Montgomery, W. 1999, "Apoptosis-induced by TRAIL AND TNF-alpha in human multiple myeloma cells is not blocked by BCL-2", *Cytokine*, vol. 11, no. 12, pp. 1010-1019.
- Gibson, S.B., Oyer, R., Spalding, A.C., Anderson, S.M. & Johnson, G.L. 2000, "Increased expression of death receptors 4 and 5 synergizes the apoptosis response to combined treatment with etoposide and TRAIL", *Molecular and cellular biology*, vol. 20, no. 1, pp. 205-212.

- Golks, A., Brenner, D., Fritsch, C., Krammer, P.H. & Lavrik, I.N. 2005, "c-FLIPR, a new regulator of death receptor-induced apoptosis", *The Journal of biological chemistry*, vol. 280, no. 15, pp. 14507-14513.
- Gonczy, P., Echeverri, C., Oegema, K., Coulson, A., Jones, S.J., Copley, R.R., Duperon, J., Oegema, J., Brehm, M., Cassin, E., Hannak, E., Kirkham, M., Pichler, S., Flohrs, K., Goessen, A., Leidel, S., Alleaume, A.M., Martin, C., Ozlu, N., Bork, P. & Hyman, A.A. 2000, "Functional genomic analysis of cell division in *C. elegans* using RNAi of genes on chromosome III", *Nature*, vol. 408, no. 6810, pp. 331-336.
- Gregory, R., Chendrimada, T., Cooch, N. & Shiekhattar, R. 2005, "Human RISC Couples MicroRNA Biogenesis and Posttranscriptional Gene Silencing", *Cell*, .
- Griffith, T.S., Fialkov, J.M., Scott, D.L., Azuhata, T., Williams, R.D., Wall, N.R., Altieri, D.C. & Sandler, A.D. 2002, "Induction and Regulation of Tumor Necrosis Factor-related Apoptosis-inducing Ligand/Apo-2 Ligand-mediated Apoptosis in Renal Cell Carcinoma", *Cancer Research*, vol. 62, no. 11, pp. 3093-3099.
- Grimm, D., Streetz, K.L., Jopling, C.L., Storm, T.A., Pandey, K., Davis, C.R., Marion, P., Salazar, F. & Kay, M.A. 2006, "Fatality in mice due to oversaturation of cellular microRNA/short hairpin RNA pathways", *Nature*, vol. 441, no. 7092, pp. 537-541.
- Grimm, S. 2004, "The art and design of genetic screens: Mammalian culture cells", *Nature Reviews Genetics*, vol. 5, no. 3, pp. 179-189.
- Grimson, A., Farh, K.K., Johnston, W.K., Garrett-Engele, P., Lim, L.P. & Bartel, D.P. 2007, "MicroRNA targeting specificity in mammals: determinants beyond seed pairing", *Molecular cell*, vol. 27, no. 1, pp. 91-105.
- Grzmil, M., Kaulfuss, S., Thelen, P., Hemmerlein, B., Schweyer, S., Obenauer, S., Kang, T.W. & Burfeind, P. 2006, "Expression and functional analysis of Bax inhibitor-1 in human breast cancer cells", *The Journal of pathology*, vol. 208, no. 3, pp. 340-349.
- Guo, S. & Kemphues, K.J. 1995, "par-1, a gene required for establishing polarity in *C. elegans* embryos, encodes a putative Ser/Thr kinase that is asymmetrically distributed", *Cell*, vol. 81, no. 4, pp. 611-620.
- Harper, N., Hughes, M.A., Farrow, S.N., Cohen, G.M. & MacFarlane, M. 2003, "Protein kinase C modulates tumor necrosis factor-related apoptosis-inducing ligand-induced apoptosis by targeting the apical events of death receptor signaling", *The Journal of biological chemistry*, vol. 278, no. 45, pp. 44338-44347.

- Harris, J., Oliere, S., Sharma, S., Sun, Q., Lin, R., Hiscott, J. & Grandvaux, N. 2006, "Nuclear accumulation of cRel following C-terminal phosphorylation by TBK1/IKK epsilon", *Journal of immunology (Baltimore, Md.: 1950)*, vol. 177, no. 4, pp. 2527-2535.
- Hartwell, L.H., Culotti, J. & Reid, B. 1970, "Genetic control of the cell-division cycle in yeast. I. Detection of mutants", *Proceedings of the National Academy of Sciences of the United States of America*, vol. 66, no. 2, pp. 352-359.
- Hattori, H., Zhang, X., Jia, Y., Subramanian, K.K., Jo, H., Loison, F., Newburger, P.E. & Luo, H.R. 2007, "RNAi screen identifies UBE2D3 as a mediator of all-trans retinoic acid-induced cell growth arrest in human acute promyelocytic NB4 cells", *Blood*, vol. 110, no. 2, pp. 640-650.
- Hellemans, J., Mortier, G., De Paepe, A., Speleman, F. & Vandesompele, J. 2007, "qBase relative quantification framework and software for management and automated analysis of real-time quantitative PCR data", *Genome biology*, vol. 8, no. 2, pp. R19.
- Hemann, M.T., Fridman, J.S., Zilfou, J.T., Hernando, E., Paddison, P.J., Cordon-Cardo, C., Hannon, G.J. & Lowe, S.W. 2003, "An epi-allelic series of p53 hypomorphs created by stable RNAi produces distinct tumor phenotypes in vivo", *Nature genetics*, vol. 33, no. 3, pp. 396-400.
- Hilliard, B., Wilmen, A., Seidel, C., Liu, T.T., Goke, R. & Chen, Y. 2001, "Roles of TNF-Related Apoptosis-Inducing Ligand in Experimental Autoimmune Encephalomyelitis", *The Journal of Immunology*, vol. 166, no. 2, pp. 1314-1319.
- Hoebe, K., Du, X., Georgel, P., Janssen, E., Tabeta, K., Kim, S.O., Goode, J., Lin, P., Mann, N., Mudd, S., Crozat, K., Sovath, S., Han, J. & Beutler, B. 2003, "Identification of Lps2 as a key transducer of MyD88-independent TIR signalling", *Nature*, vol. 424, no. 6950, pp. 743-748.
- Holen, T. 2006, "Efficient prediction of siRNAs with siRNArules 1.0: An open-source JAVA approach to siRNA algorithms", *RNA*, vol. 12, no. 9, pp. 1620-1625.
- Holler, N., Zaru, R., Micheau, O., Thome, M., Attinger, A., Valitutti, S., Bodmer, J.L., Schneider, P., Seed, B. & Tschoopp, J. 2000, "Fas triggers an alternative, caspase-8-independent cell death pathway using the kinase RIP as effector molecule", *Nature immunology*, vol. 1, no. 6, pp. 489-495.
- Hopkins, A.L. & Groom, C.R. 2002, "The druggable genome", *Nature reviews.Drug discovery*, vol. 1, no. 9, pp. 727-730.
- Hornung, V., Guenthner-Biller, M., Bourquin, C., Ablasser, A., Schlee, M., Uematsu, S., Noronha, A., Manoharan, M., Akira, S., de Fougerolles, A., Endres, S. & Hartmann, G.

- 2005, "Sequence-specific potent induction of IFN-alpha by short interfering RNA in plasmacytoid dendritic cells through TLR7", *Nature medicine*, vol. 11, no. 3, pp. 263-270.
- Huerta, S., Goulet, E.J., Huerta-Yepez, S. & Livingston, E.H. 2007, "Screening and Detection of Apoptosis", *Journal of Surgical Research*, vol. 139, no. 1, pp. 143-156.
- Huesken, D., Lange, J., Mickanin, C., Weiler, J., Asselbergs, F., Warner, J., Meloon, B., Engel, S., Rosenberg, A., Cohen, D., Labow, M., Reinhardt, M., Natt, F. & Hall, J. 2005, "Design of a genome-wide siRNA library using an artificial neural network", *Nature biotechnology*, vol. 23, no. 8, pp. 995-1001.
- Hutvagner, G., McLachlan, J., Pasquinelli, A.E., Balint, E., Tuschl, T. & Zamore, P.D. 2001, "A Cellular Function for the RNA-Interference Enzyme Dicer in the Maturation of the let-7 Small Temporal RNA", *Science*, vol. 293, no. 5531, pp. 834-838.
- Ikeda, F., Hecker, C.M., Rozenknop, A., Nordmeier, R.D., Rogov, V., Hofmann, K., Akira, S., Dotsch, V. & Dikic, I. 2007, "Involvement of the ubiquitin-like domain of TBK1/IKK-i kinases in regulation of IFN-inducible genes", *The EMBO journal*, vol. 26, no. 14, pp. 3451-3462.
- Irmler, M., Thome, M., Hahne, M., Schneider, P., Hofmann, K., Steiner, V., Bodmer, J.L., Schroter, M., Burns, K., Mattmann, C., Rimoldi, D., French, L.E. & Tschoopp, J. 1997, "Inhibition of death receptor signals by cellular FLIP", *Nature*, vol. 388, no. 6638, pp. 190-195.
- Jackson, A.L., Burchard, J., Leake, D., Reynolds, A., Schelter, J., Guo, J., Johnson, J.M., Lim, L., Karpilow, J., Nichols, K., Marshall, W., Khvorova, A. & Linsley, P.S. 2006, "Position-specific chemical modification of siRNAs reduces "off-target" transcript silencing", *RNA*, vol. 12, no. 7, pp. 1197-1205.
- Jackson, A.L. & Linsley, P.S. 2004, "Noise amidst the silence: off-target effects of siRNAs?", *Trends Genet*, vol. 20, no. 11, pp. 521-4.
- Jackson, A.L., Bartz, S.R., Schelter, J., Kobayashi, S.V., Burchard, J., Mao, M., Li, B., Cavet, G. & Linsley, P.S. 2003, "Expression profiling reveals off-target gene regulation by RNAi", *Nat Biotech*, vol. 21, no. 6, pp. 635-637.
- JACOB, F. & MONOD, J. 1961, "Genetic regulatory mechanisms in the synthesis of proteins", *Journal of Molecular Biology*, vol. 3, pp. 318-356.
- Janssen, E.M., Droin, N.M., Lemmens, E.E., Pinkoski, M.J., Bensinger, S.J., Ehst, B.D., Griffith, T.S., Green, D.R. & Schoenberger, S.P. 2005, "CD4+ T-cell help controls CD8+ T-cell memory via TRAIL-mediated activation-induced cell death", *Nature*, vol. 434, no. 7029, pp. 88-93.

- Jia, P., Shi, T., Cai, Y. & Li, Y. 2006, "Demonstration of two novel methods for predicting functional siRNA efficiency", *BMC bioinformatics*, vol. 7, pp. 271.
- Jo, M., Kim, T.H., Seol, D.W., Esplen, J.E., Dorko, K., Billiar, T.R. & Strom, S.C. 2000, "Apoptosis induced in normal human hepatocytes by tumor necrosis factor-related apoptosis-inducing ligand", *Nature medicine*, vol. 6, no. 5, pp. 564-567.
- Jorgensen, E.M. & Mango, S.E. 2002, "The art and design of genetic screens: *Caenorhabditis elegans*", *Nature Reviews Genetics*, vol. 3, no. 5, pp. 356-369.
- Joza, N., Susin, S.A., Daugas, E., Stanford, W.L., Cho, S.K., Li, C.Y., Sasaki, T., Elia, A.J., Cheng, H.Y., Ravagnan, L., Ferri, K.F., Zamzami, N., Wakeham, A., Hakem, R., Yoshida, H., Kong, Y.Y., Mak, T.W., Zuniga-Pflucker, J.C., Kroemer, G. & Penninger, J.M. 2001, "Essential role of the mitochondrial apoptosis-inducing factor in programmed cell death", *Nature*, vol. 410, no. 6828, pp. 549-554.
- Judge, A. & MacLachlan, I. 2008, "Overcoming the innate immune response to small interfering RNA", *Human Gene Therapy*, vol. 19, no. 2, pp. 111-124.
- Judge, A.D., Sood, V., Shaw, J.R., Fang, D., McClintock, K. & MacLachlan, I. 2005, "Sequence-dependent stimulation of the mammalian innate immune response by synthetic siRNA", *Nature biotechnology*, vol. 23, no. 4, pp. 457-462.
- Kamath, R.S., Fraser, A.G., Dong, Y., Poulin, G., Durbin, R., Gotta, M., Kanapin, A., Le Bot, N., Moreno, S., Sohrmann, M., Welchman, D.P., Zipperlen, P. & Ahringer, J. 2003, "Systematic functional analysis of the *Caenorhabditis elegans* genome using RNAi", *Nature*, vol. 421, no. 6920, pp. 231-237.
- Kawasaki, H. & Taira, K. 2004, "Induction of DNA methylation and gene silencing by short interfering RNAs in human cells", *Nature*, vol. 431, no. 7005, pp. 211-217.
- Kayagaki, N., Yamaguchi, N., Nakayama, M., Eto, H., Okumura, K. & Yagita, H. 1999, "Type I Interferons (IFNs) Regulate Tumor Necrosis Factor-related Apoptosis-inducing Ligand (TRAIL) Expression on Human T Cells: A Novel Mechanism for the Antitumor Effects of Type I IFNs", *The Journal of Experimental Medicine*, vol. 189, no. 9, pp. 1451-1460.
- Kelley, R.F., Totpal, K., Lindstrom, S.H., Mathieu, M., Billeci, K., DeForge, L., Pai, R., Hymowitz, S.G. & Ashkenazi, A. 2005, "Receptor-selective Mutants of Apoptosis-inducing Ligand 2/Tumor Necrosis Factor-related Apoptosis-inducing Ligand Reveal a Greater Contribution of Death Receptor (DR) 5 than DR4 to Apoptosis Signaling", *Journal of Biological Chemistry*, vol. 280, no. 3, pp. 2205-2212.

- Kemp, T.J., Elzey, B.D. & Griffith, T.S. 2003, "Plasmacytoid Dendritic Cell-Derived IFN- α Induces TNF-Related Apoptosis-Inducing Ligand/Apo-2L-Mediated Antitumor Activity by Human Monocytes Following CpG Oligodeoxynucleotide Stimulation", *The Journal of Immunology*, vol. 171, no. 1, pp. 212-218.
- Kennerdell, J. & Carthew, R. 1998, "Use of dsRNA-Mediated Genetic Interference to Demonstrate that frizzled and frizzled 2 Act in the Wingless Pathway", *Cell*, vol. 95, no. 7, pp. 1017-1026.
- Kiger, A.A., Baum, B., Jones, S., Jones, M.R., Coulson, A., Echeverri, C. & Perrimon, N. 2003, "A functional genomic analysis of cell morphology using RNA interference", *J Biol*, vol. 2, no. 4, pp. 27.
- Kile, B.T., Hentges, K.E., Clark, A.T., Nakamura, H., Salinger, A.P., Liu, B., Box, N., Stockton, D.W., Johnson, R.L., Behringer, R.R., Bradley, A. & Justice, M.J. 2003, "Functional genetic analysis of mouse chromosome 11", *Nature*, vol. 425, no. 6953, pp. 81-86.
- Kile, B.T. & Hilton, D.J. 2005, "The art and design of genetic screens: Mouse", *Nature Reviews Genetics*, vol. 6, no. 7, pp. 557-567.
- Kim, D.H., Longo, M., Han, Y., Lundberg, P., Cantin, E. & Rossi, J.J. 2004, "Interferon induction by siRNAs and ssRNAs synthesized by phage polymerase", *Nat Biotechnol*, vol. 22, no. 3, pp. 321-5.
- Kim, D.H., Villeneuve, L.M., Morris, K.V. & Rossi, J.J. 2006, "Argonaute-1 directs siRNA-mediated transcriptional gene silencing in human cells", *Nature Structural and Molecular Biology*, vol. 13, no. 9, pp. 793-797.
- Kim, J.K., Gabel, H.W., Kamath, R.S., Tewari, M., Pasquinelli, A., Rual, J.F., Kennedy, S., Dybbs, M., Bertin, N., Kaplan, J.M., Vidal, M. & Ruvkun, G. 2005, "Functional genomic analysis of RNA interference in *C. elegans*", *Science (New York, N.Y.)*, vol. 308, no. 5725, pp. 1164-1167.
- Kim, K., Fisher, M.J., Xu, S.Q. & el-Deiry, W.S. 2000, "Molecular determinants of response to TRAIL in killing of normal and cancer cells", *Clinical cancer research : an official journal of the American Association for Cancer Research*, vol. 6, no. 2, pp. 335-346.
- Kin, H.K., Ng, M.-J., Ching, Y.-. & Jin, D.-. 2007, "Human TRBP and PACT directly interact with each other and associate with dicer to facilitate the production of small interfering RNA", *Journal of Biological Chemistry*, vol. 282, no. 24, pp. 17649-17657.
- Kittler, R., Pelletier, L., Ma, C., Poser, I., Fischer, S., Hyman, A.A. & Buchholz, F. 2005, "RNA interference rescue by bacterial artificial chromosome transgenesis in mammalian

- tissue culture cells", *Proceedings of the National Academy of Sciences of the United States of America*, vol. 102, no. 7, pp. 2396-2401.
- Kittler, R., Putz, G., Pelletier, L., Poser, I., Heninger, A., Drechsel, D., Fischer, S., Konstantinova, I., Habermann, B., Grabner, H., Yaspo, M., Himmelbauer, H., Korn, B., Neugebauer, K., Pisabarro, M.T. & Buchholz, F. 2004, "An endoribonuclease-prepared siRNA screen in human cells identifies genes essential for cell division", *Nature*, vol. 432, no. 7020, pp. 1036-1040.
- Kolfschoten, I.G., van Leeuwen, B., Berns, K., Mullenders, J., Beijersbergen, R.L., Bernards, R., Voorhoeve, P.M. & Agami, R. 2005, "A genetic screen identifies PITX1 as a suppressor of RAS activity and tumorigenicity", *Cell*, vol. 121, no. 6, pp. 849-58.
- Kuang, A.A., Diehl, G.E., Zhang, J.K. & Winoto, A. 2000, "FADD is required for DR4-and DR5-mediated apoptosis - Lack of trail-induced apoptosis in FADD-deficient mouse embryonic fibroblasts", *Journal of Biological Chemistry*, vol. 275, no. 33, pp. 25065-25068.
- Lackner, M.R., Kornfeld, K., Miller, L.M., Horvitz, H.R. & Kim, S.K. 1994, "A MAP kinase homolog, mpk-1, is involved in ras-mediated induction of vulval cell fates in *Caenorhabditis elegans*", *Genes & development*, vol. 8, no. 2, pp. 160-173.
- Lamhamdi-Cherradi, S.E., Zheng, S.J., Maguschak, K.A., Peschon, J. & Chen, Y.H. 2003, "Defective thymocyte apoptosis and accelerated autoimmune diseases in TRAIL-/- mice", *Nature immunology*, vol. 4, no. 3, pp. 255-260.
- Lawrence, D., Shahrokh, Z., Marsters, S., Achilles, K., Shih, D., Mounho, B., Hillan, K., Totpal, K., DeForge, L., Schow, P., Hooley, J., Sherwood, S., Pai, R., Leung, S., Khan, L., Gliniak, B., Bussiere, J., Smith, C.A., Strom, S.S., Kelley, S., Fox, J.A., Thomas, D. & Ashkenazi, A. 2001, "Differential hepatocyte toxicity of recombinant Apo2L/TRAIL versions", *Nature medicine*, vol. 7, no. 4, pp. 383-385.
- Lee 2002, "MicroRNA maturation: stepwise processing and subcellular localization", *The EMBO Journal*, vol. 21, no. 17, pp. 4663.
- Lee, Y., Hur, I., Park, S.Y., Kim, Y.K., Suh, M.R. & Kim, V.N. 2006, "The role of PACT in the RNA silencing pathway", *The EMBO journal*, vol. 25, no. 3, pp. 522-532.
- Lee, Y., Nakahara, K., Pham, J., Kim, K., He, Z., Sontheimer, E. & Carthew, R. 2004 Apr 2, "Distinct roles for Drosophila Dicer-1 and Dicer-2 in the siRNA/miRNA silencing pathways.", *Cell*, vol. 117, no. 1, pp. 69-81.
- Lejeune, F.J., Lienard, D., Matter, M. & Ruegg, C. 2006, "Efficiency of recombinant human TNF in human cancer therapy", *Cancer immunity : a journal of the Academy of Cancer Immunology*, vol. 6, pp. 6.

- Lemmers, C., Medina, E., Delgrossi, M.H., Michel, D., Arsanto, J.P. & Le Bivic, A. 2002, "hINADl/PATJ, a homolog of discs lost, interacts with crumbs and localizes to tight junctions in human epithelial cells", *The Journal of biological chemistry*, vol. 277, no. 28, pp. 25408-25415.
- Lewis, B., Burge, C. & Bartel, D. 2005, "Conserved Seed Pairing, Often Flanked by Adenosines, Indicates that Thousands of Human Genes are MicroRNA Targets", *Cell*, vol. 120, no. 1, pp. 15-20.
- Li, F., Ambrosini, G., Chu, E.Y., Plescia, J., Tognin, S., Marchisio, P.C. & Altieri, D.C. 1998, "Control of apoptosis and mitotic spindle checkpoint by survivin", *Nature*, vol. 396, no. 6711, pp. 580-584.
- Li, Y.X., Farrell, M.J., Liu, R., Mohanty, N. & Kirby, M.L. 2000, "Double-stranded RNA injection produces null phenotypes in zebrafish", *Developmental biology*, vol. 217, no. 2, pp. 394-405.
- Lim, S., Sala, C., Yoon, J., Park, S., Kuroda, S., Sheng, M. & Kim, E. 2001, "Sharpin, a novel postsynaptic density protein that directly interacts with the shank family of proteins", *Molecular and cellular neurosciences*, vol. 17, no. 2, pp. 385-397.
- Lin, X., Morgan-Lappe, S., Huang, X., Li, L., Zakula, D.M., Vernetti, L.A., Fesik, S.W. & Shen, Y. 2007, "'Seed' analysis of off-target siRNAs reveals an essential role of Mcl-1 in resistance to the small-molecule Bcl-2/Bcl-XL inhibitor ABT-737", *Oncogene*, vol. 26, no. 27, pp. 3972-3979.
- Lin, X., Ruan, X., Anderson, M.G., McDowell, J.A., Kroeger, P.E., Fesik, S.W. & Shen, Y. 2005, "siRNA-mediated off-target gene silencing triggered by a 7 nt complementation", *Nucleic acids research*, vol. 33, no. 14, pp. 4527-4535.
- Lin, Y., Devin, A., Rodriguez, Y. & Liu, Z.-. 1999, "Cleavage of the death domain kinase RIP by Caspase-8 prompts TNF-induced apoptosis", *Genes and Development*, vol. 13, no. 19, pp. 2514-2526.
- Lippa, M.S., Strockbine, L.D., Le, T.T., Branstetter, D.G., Strathdee, C.A. & Holland, P.M. 2007, "Expression of anti-apoptotic factors modulates Apo2L/TRAIL resistance in colon carcinoma cells", *Apoptosis : An International Journal on Programmed Cell Death*, vol. 12, no. 8, pp. 1465-1478.
- Liu, J.D., Carmell, M.A., Rivas, F.V., Marsden, C.G., Thomson, J.M., Song, J.J., Hammond, S.M., Joshua-Tor, L. & Hannon, G.J. 2004, "Argonaute2 is the catalytic engine of mammalian RNAi", *Science*, vol. 305, no. 5689, pp. 1437-1441.

- Liu, S., Yu, Y., Zhang, M., Wang, W. & Cao, X. 2001, "The involvement of TNF-alpha-related apoptosis-inducing ligand in the enhanced cytotoxicity of IFN-beta-stimulated human dendritic cells to tumor cells", *Journal of immunology* (Baltimore, Md.: 1950), vol. 166, no. 9, pp. 5407-5415.
- Longman, D., Plasterk, R.H., Johnstone, I.L. & Caceres, J.F. 2007, "Mechanistic insights and identification of two novel factors in the C. elegans NMD pathway", *Genes & development*, vol. 21, no. 9, pp. 1075-1085.
- Lum, J.J., Pilon, A.A., Sanchez-Dardon, J., Phenix, B.N., Kim, J.E., Mihowich, J., Jamison, K., Hawley-Foss, N., Lynch, D.H. & Badley, A.D. 2001, "Induction of Cell Death in Human Immunodeficiency Virus-Infected Macrophages and Resting Memory CD4 T Cells by TRAIL/Apo2L", *The Journal of Virology*, vol. 75, no. 22, pp. 11128-11136.
- Lum, L., Yao, S., Mozer, B., Rovescalli, A., Von Kessler, D., Nirenberg, M. & Beachy, P.A. 2003, "Identification of Hedgehog pathway components by RNAi in Drosophila cultured cells", *Science (New York, N.Y.)*, vol. 299, no. 5615, pp. 2039-2045.
- Luscher, B. 2001, "Function and regulation of the transcription factors of the Myc/Max/Mad network", *Gene*, vol. 277, no. 1-2, pp. 1-14.
- MacFarlane, M., Kohlhaas, S.L., Sutcliffe, M.J., Dyer, M.J. & Cohen, G.M. 2005, "TRAIL receptor-selective mutants signal to apoptosis via TRAIL-R1 in primary lymphoid malignancies", *Cancer research*, vol. 65, no. 24, pp. 11265-11270.
- Machida, Y.J., Chen, Y., Machida, Y., Malhotra, A., Sarkar, S. & Dutta, A. 2006, "Targeted comparative RNA interference analysis reveals differential requirement of genes essential for cell proliferation", *Molecular Biology of the Cell*, vol. 17, no. 11, pp. 4837-4845.
- MacKeigan, J.P., Murphy, L.O. & Blenis, J. 2005, "Sensitized RNAi screen of human kinases and phosphatases identifies new regulators of apoptosis and chemoresistance", *Nature Cell Biology*, vol. 7, no. 6, pp. 591-600.
- Maeda, I., Kohara, Y., Yamamoto, M. & Sugimoto, A. 2001, "Large-scale analysis of gene function in *Caenorhabditis elegans* by high-throughput RNAi", *Current Biology*, vol. 11, no. 3, pp. 171-176.
- Manche, L., Green, S.R., Schmedt, C. & Mathews, M.B. 1992, "Interactions between double-stranded RNA regulators and the protein kinase DAI", *Molecular and cellular biology*, vol. 12, no. 11, pp. 5238-5248.
- Marques, J.T., Devosse, T., Wang, D., Zamanian-Daryoush, M., Serbinowski, P., Hartmann, R., Fujita, T., Behlke, M.A. & Williams, B.R. 2006, "A structural basis for discriminating

- between self and nonself double-stranded RNAs in mammalian cells", *Nature biotechnology*, vol. 24, no. 5, pp. 559-565.
- Martin, S.J., Amarante-Mendes, G.P., Shi, L., Chuang, T.H., Casiano, C.A., O'Brien, G.A., Fitzgerald, P., Tan, E.M., Bokoch, G.M., Greenberg, A.H. & Green, D.R. 1996, "The cytotoxic cell protease granzyme B initiates apoptosis in a cell-free system by proteolytic processing and activation of the ICE/CED-3 family protease, CPP32, via a novel two-step mechanism", *The EMBO journal*, vol. 15, no. 10, pp. 2407-2416.
- Matranga, C., Tomari, Y., Shin, C., Bartel, D.P. & Zamore, P.D. 2005, "Passenger-Strand Cleavage Facilitates Assembly of siRNA into Ago2-Containing RNAi Enzyme Complexes", *Cell*, vol. 123, no. 4, pp. 607-620.
- Matsuyama, A., Arai, R., Yashiroda, Y., Shirai, A., Kamata, A., Sekido, S., Kobayashi, Y., Hashimoto, A., Hamamoto, M., Hiraoka, Y., Horinouchi, S. & Yoshida, M. 2006, "ORFeome cloning and global analysis of protein localization in the fission yeast Schizosaccharomyces pombe", *Nature biotechnology*, vol. 24, no. 7, pp. 841-847.
- Meister, G., Landthaler, M., Peters, L., Chen, P.Y., Urlaub, H., Lührmann, R. & Tuschl, T. 2005, "Identification of Novel Argonaute-Associated Proteins", *Current Biology*, vol. 15, no. 23, pp. 2149-2155.
- Merino, D., Lalaoui, N., Morizot, A., Schneider, P., Solary, E. & Micheau, O. 2006, "Differential inhibition of TRAIL-mediated DR5-DISC formation by decoy receptors 1 and 2", *Molecular and cellular biology*, vol. 26, no. 19, pp. 7046-7055.
- Michael, M.Z., O'Connor, S.M., van Holst Pellekaan, N.G., Young, G.P. & James, R.J. 2003, "Reduced accumulation of specific microRNAs in colorectal neoplasia", *Molecular cancer research : MCR*, vol. 1, no. 12, pp. 882-891.
- Micheau, O., Thome, M., Schneider, P., Holler, N., Tschoopp, J., Nicholson, D.W., Briand, C. & Grutter, M.G. 2002, "The long form of FLIP is an activator of caspase-8 at the Fas death-inducing signaling complex", *The Journal of biological chemistry*, vol. 277, no. 47, pp. 45162-45171.
- Michl, P., Ramjaun, A.R., Pardo, O.E., Warne, P.H., Wagner, M., Poulsom, R., D'Arrigo, C., Ryder, K., Menke, A., Gress, T. & Downward, J. 2005, "CUTL1 is a target of TGF(beta) signaling that enhances cancer cell motility and invasiveness", *Cancer cell*, vol. 7, no. 6, pp. 521-532.
- Mirandola, P., Ponti, C., Gobbi, G., Sponzilli, I., Vaccarezza, M., Cocco, L., Zauli, G., Secchiero, P., Manzoli, F.A. & Vitale, M. 2004, "Activated human NK and CD8+ T cells express both TNF-related apoptosis-inducing ligand (TRAIL) and TRAIL

receptors but are resistant to TRAIL-mediated cytotoxicity", *Blood*, vol. 104, no. 8, pp. 2418-2424.

Moffat, J., Grueneberg, D.A., Yang, X., Kim, S.Y., Kloepfer, A.M., Hinkle, G., Piqani, B., Eisenhaure, T.M., Luo, B., Grenier, J.K., Carpenter, A.E., Foo, S.Y., Stewart, S.A., Stockwell, B.R., Hacohen, N., Hahn, W.C., Lander, E.S., Sabatini, D.M. & Root, D.E. 2006, "A Lentiviral RNAi Library for Human and Mouse Genes Applied to an Arrayed Viral High-Content Screen", *Cell*, vol. 124, no. 6, pp. 1283-1298.

Morgan-Lappe, S.E., Tucker, L.A., Huang, X., Zhang, Q., Sarthy, A.V., Zakula, D., Vernetti, L., Schurdak, M., Wang, J. & Fesik, S.W. 2007, "Identification of Ras-related nuclear protein, targeting protein for Xenopus kinesin-like protein 2, and stearoyl-CoA desaturase 1 as promising cancer targets from an RNAi-based screen", *Cancer Research*, vol. 67, no. 9, pp. 4390-4398.

Morris, K.V., Chan, S.W.L., Jacobsen, S.E. & Looney, D.J. 2004, "Small interfering RNA-induced transcriptional gene silencing in human cells", *Science*, vol. 305, no. 5688, pp. 1289-1292.

Moubarak, R., Yuste, V., Artus, C., Bouharrour, A., Greer, P., Menissier-de Murcia & Susin, S. "Sequential Activation of PARP-1, Calpains, and Bax is Essential in AIF-Mediated Programmed Necrosis", *Mol Cell Biol*.

Mukherji, M., Bell, R., Supekova, L., Wang, Y., Orth, A.P., Batalov, S., Miraglia, L., Huesken, D., Lange, J., Martin, C., Sahasrabudhe, S., Reinhardt, M., Natt, F., Hall, J., Mickanin, C., Labow, M., Chanda, S.K., Cho, C.Y. & Schultz, P.G. 2006, "Genome-wide functional analysis of human cell-cycle regulators", *Proceedings of the National Academy of Sciences of the United States of America*, vol. 103, no. 40, pp. 14819-14824.

Müller, P., Kuttenkeuler, D., Gesellchen, V., Zeidler, M.P. & Boutros, M. 2005, "Identification of JAK/STAT signalling components by genome-wide RNA interference", *Nature*, vol. 436, no. 7052, pp. 871-875.

Napoli, C., Lemieux, C. & Jorgensen, R. 1990, "Introduction of a Chimeric Chalcone Synthase Gene into Petunia Results in Reversible Co-Suppression of Homologous Genes in trans", *The Plant Cell*, vol. 2, no. 4, pp. 279-289.

Nesterov, A., Nikrad, M., Johnson, T. & Kraft, A.S. 2004, "Oncogenic Ras Sensitizes Normal Human Cells to Tumor Necrosis Factor- α -Related Apoptosis-Inducing Ligand-Induced Apoptosis", *Cancer Research*, vol. 64, no. 11, pp. 3922-3927.

Nicke, B., Bastien, J., Khanna, S.J., Warne, P.H., Cowling, V., Cook, S.J., Peters, G., Delpuech, O., Schulze, A., Berns, K., Mullenders, J., Beijersbergen, R.L., Bernards, R., Ganesan, T.S., Downward, J. & Hancock, D.C. 2005, "Involvement of MINK, a Ste20

- family kinase, in Ras oncogene-induced growth arrest in human ovarian surface epithelial cells", *Molecular cell*, vol. 20, no. 5, pp. 673-685.
- Nielsen, C.B., Shomron, N., Sandberg, R., Hornstein, E., Kitzman, J. & Burge, C.B. 2007, "Determinants of targeting by endogenous and exogenous microRNAs and siRNAs", *RNA (New York, N.Y.)*, vol. 13, no. 11, pp. 1894-1910.
- Nieminen, A.I., Partanen, J.I. & Klefstrom, J. 2007, "c-Myc blazing a trail of death: coupling of the mitochondrial and death receptor apoptosis pathways by c-Myc", *Cell cycle (Georgetown, Tex.)*, vol. 6, no. 20, pp. 2464-2472.
- Nilsson, J.A. & Cleveland, J.L. 2003, "Myc pathways provoking cell suicide and cancer", *Oncogene*, vol. 22, no. 56, pp. 9007-9021.
- Nollen, E.A., Garcia, S.M., van Haaften, G., Kim, S., Chavez, A., Morimoto, R.I. & Plasterk, R.H. 2004, "Genome-wide RNA interference screen identifies previously undescribed regulators of polyglutamine aggregation", *Proc Natl Acad Sci U S A*, vol. 101, no. 17, pp. 6403-8.
- Nosseri, C., Coppola, S. & Ghibelli, L. 1994, "Possible involvement of poly(ADP-ribosyl) polymerase in triggering stress-induced apoptosis", *Experimental cell research*, vol. 212, no. 2, pp. 367-373.
- Nurse, P., Thuriaux, P. & Nasmyth, K. 1976, "Genetic control of the cell division cycle in the fission yeast *Schizosaccharomyces pombe*", *Molecular & general genetics : MGG*, vol. 146, no. 2, pp. 167-178.
- Nusslein-Volhard, C. & Wieschaus, E. 1980, "Mutations affecting segment number and polarity in *Drosophila*", *Nature*, vol. 287, no. 5785, pp. 795-801.
- Nykanen, A., Haley, B. & Zamore, P.D. 2001, "ATP requirements and small interfering RNA structure in the RNA interference pathway", *Cell*, vol. 107, no. 3, pp. 309-321.
- Ogasawara, J., Watanabe-Fukunaga, R., Adachi, M., Matsuzawa, A., Kasugai, T., Kitamura, Y., Itoh, N., Suda, T. & Nagata, S. 1993, "Lethal effect of the anti-Fas antibody in mice", *Nature*, vol. 364, no. 6440, pp. 806-809.
- Ohta, T., Michel, J.J., Schottelius, A.J. & Xiong, Y. 1999, "ROC1, a homolog of APC11, represents a family of cullin partners with an associated ubiquitin ligase activity", *Molecular cell*, vol. 3, no. 4, pp. 535-541.
- Ovcharenko, D., Kelnar, K., Johnson, C., Leng, N. & Brown, D. 2007, "Genome-Scale MicroRNA and Small Interfering RNA Screens Identify Small RNA Modulators of TRAIL-Induced Apoptosis Pathway", *Cancer Research*, vol. 67, no. 22, pp. 10782-10788.

- Paddison, P.J., Caudy, A.A., Bernstein, E., Hannon, G.J. & Conklin, D.S. 2002, "Short hairpin RNAs (shRNAs) induce sequence-specific silencing in mammalian cells", *Genes & development*, vol. 16, no. 8, pp. 948-958.
- Paddison, P.J., Cleary, M., Silva, J.M., Chang, K., Sheth, N., Sachidanandam, R. & Hannon, G.J. 2004a, "Cloning of short hairpin RNAs for gene knockdown in mammalian cells.", *Nat Methods*, vol. 1, no. 2, pp. 163-167.
- Paddison, P.J., Silva, J.M., Conklin, D.S., Schlabach, M., Li, M., Aruleba, S., Balija, V., O'Shaughnessy, A., Gnoj, L., Scobie, K., Chang, K., Westbrook, T., Cleary, M., Sachidanandam, R., McCombie, W.R., Elledge, S.J. & Hannon, G.J. 2004b, "A resource for large-scale RNA-interference-based screens in mammals", *Nature*, vol. 428, no. 6981, pp. 427-431.
- Pak, J. & Fire, A. 2007, "Distinct populations of primary and secondary effectors during RNAi in *C. elegans*", *Science (New York, N.Y.)*, vol. 315, no. 5809, pp. 241-244.
- Palmer, E. & Freeman, T. 2004, "Investigation into the use of C- and N-terminal GFP fusion proteins for subcellular localization studies using reverse transfection microarrays", *Comparative and Functional Genomics*, vol. 5, no. 4, pp. 342-353.
- Pan, G., Ni, J., Wei, Y.F., Yu, G., Gentz, R. & Dixit, V.M. 1997a, "An antagonist decoy receptor and a death domain-containing receptor for TRAIL", *Science (New York, N.Y.)*, vol. 277, no. 5327, pp. 815-818.
- Pan, G., O'Rourke, K., Chinnaiyan, A.M., Gentz, R., Ebner, R., Ni, J. & Dixit, V.M. 1997b, "The receptor for the cytotoxic ligand TRAIL", *Science (New York, N.Y.)*, vol. 276, no. 5309, pp. 111-113.
- Panner, A., Nakamura, J.L., Parsa, A.T., Rodriguez-Viciiana, P., Berger, M.S., Stokoe, D. & Pieper, R.O. 2006, "mTOR-independent translational control of the extrinsic cell death pathway by RalA", *Molecular and Cellular Biology*, vol. 26, no. 20, pp. 7345-7357.
- Paradis, S., Harrar, D.B., Lin, Y., Koon, A.C., Hauser, J.L., Griffith, E.C., Zhu, L., Brass, L.F., Chen, C. & Greenberg, M.E. 2007, "An RNAi-Based Approach Identifies Molecules Required for Glutamatergic and GABAergic Synapse Development", *Neuron*, vol. 53, no. 2, pp. 217-232.
- Park, C.W., Chen, Z., Kren, B.T., Steer, C.J. & Steer, C.J. 2004, "Double-stranded siRNA targeted to the huntingtin gene does not induce DNA methylation", *Biochemical and Biophysical Research Communications*, vol. 323, no. 1, pp. 275-280.
- Patton, E.E. & Zon, L.I. 2001, "The art and design of genetic screens: Zebrafish", *Nature Reviews Genetics*, vol. 2, no. 12, pp. 956-966.

- Pattyn, F., Robbrecht, P., De Paepe, A., Speleman, F. & Vandesompele, J. 2006, "RTPrimerDB: the real-time PCR primer and probe database, major update 2006", *Nucleic acids research*, vol. 34, no. Database issue, pp. D684-8.
- Patzel, V. 2007, "In silico selection of active siRNA", *Drug Discovery Today*, vol. 12, no. 3-4, pp. 139-148.
- Pebernard, S. & Iggo, R.D. 2004, "Determinants of interferon-stimulated gene induction by RNAi vectors", *Differentiation; research in biological diversity*, vol. 72, no. 2-3, pp. 103-111.
- Peters, L. & Meister, G. 2007, "Argonaute proteins: mediators of RNA silencing", *Molecular cell*, vol. 26, no. 5, pp. 611-623.
- Pfaffl, M.W. 2001, "A new mathematical model for relative quantification in real-time RT-PCR", *Nucleic Acids Res*, vol. 29, no. 9, pp. e45.
- Phillips, T.A., Ni, J., Pan, G., Ruben, S.M., Wei, Y.F., Pace, J.L. & Hunt, J.S. 1999, "TRAIL (Apo-2L) and TRAIL receptors in human placentas: implications for immune privilege", *Journal of immunology (Baltimore, Md.: 1950)*, vol. 162, no. 10, pp. 6053-6059.
- Pitti, R.M., Marsters, S.A., Ruppert, S., Donahue, C.J., Moore, A. & Ashkenazi, A. 1996, "Induction of apoptosis by Apo-2 ligand, a new member of the tumor necrosis factor cytokine family", *The Journal of biological chemistry*, vol. 271, no. 22, pp. 12687-12690.
- Pothof, J., van Haaften, G., Thijssen, K., Kamath, R.S., Fraser, A.G., Ahringer, J., Plasterk, R.H.A. & Tijsterman, M. 2003, "Identification of genes that protect the *C. elegans* genome against mutations by genome-wide RNAi", *Genes Dev.*, vol. 17, no. 4, pp. 443-448.
- Pugazhenthi, S., Nesterova, A., Sable, C., Heidenreich, K.A., Boxer, L.M., Heasley, L.E. & Reusch, J.E. 2000, "Akt/protein kinase B up-regulates Bcl-2 expression through cAMP-response element-binding protein", *The Journal of biological chemistry*, vol. 275, no. 15, pp. 10761-10766.
- Qin, J., Chaturvedi, V., Bonish, B. & Nickoloff, B.J. 2001, "Avoiding premature apoptosis of normal epidermal cells", *Nature medicine*, vol. 7, no. 4, pp. 385-386.
- Ramet, M., Manfruelli, P., Pearson, A., Mathey-Prevot, B. & Ezekowitz, R.A.B. 2002, "Functional genomic analysis of phagocytosis and identification of a *Drosophila* receptor for *E. coli*", *Nature*, vol. 416, no. 6881, pp. 644-648.
- Rand, T.A., Ginalski, K., Grishin, N.V. & Wang, X. 2004, "Biochemical identification of Argonaute 2 as the sole protein required for RNA-induced silencing complex activity",

Proceedings of the National Academy of Sciences of the United States of America, vol. 101, no. 40, pp. 14385-14389.

Rand, T.A., Petersen, S., Du, F. & Wang, X. 2005, "Argonaute2 Cleaves the Anti-Guide Strand of siRNA during RISC Activation", *Cell*, vol. 123, no. 4, pp. 621-629.

Rasper, D.M., Vaillancourt, J.P., Hadano, S., Houtzager, V.M., Seiden, I., Keen, S.L., Tawa, P., Xanthoudakis, S., Nasir, J., Martindale, D., Koop, B.F., Peterson, E.P., Thornberry, N.A., Huang, J., MacPherson, D.P., Black, S.C., Hornung, F., Lenardo, M.J., Hayden, M.R., Roy, S. & Nicholson, D.W. 1998, "Cell death attenuation by 'Usurpin', a mammalian DED-caspase homologue that precludes caspase-8 recruitment and activation by the CD-95 (Fas, APO-1) receptor complex", *Cell death and differentiation*, vol. 5, no. 4, pp. 271-288.

Ravi, R., Bedi, G.C., Engstrom, L.W., Zeng, Q., Mookerjee, B., Gélinas, C., Fuchs, E.J. & Bedi, A. 2001, "Regulation of death receptor expression and TRAIL/Apo2L-induced apoptosis by NF- κ B", *Nature Cell Biology*, vol. 3, no. 4, pp. 409-416.

Remacle-Bonnet, M., Garrouste, F., Baillat, G., Andre, F., Marvaldi, J. & Pommier, G. 2005, "Membrane rafts segregate pro- from anti-apoptotic insulin-like growth factor-I receptor signaling in colon carcinoma cells stimulated by members of the tumor necrosis factor superfamily", *The American journal of pathology*, vol. 167, no. 3, pp. 761-773.

Ren, Y., Wagner, K.W., Knee, D.A., Aza-Blanc, P., Nasoff, M. & Devereaux, Q.L. 2004, "Differential Regulation of the TRAIL Death Receptors DR4 and DR5 by the Signal Recognition Particle", *Mol. Biol. Cell*, vol. 15, no. 11, pp. 5064-5074.

Reynolds, A., Leake, D., Boese, Q., Scaringe, S., Marshall, W.S. & Khvorova, A. 2004, "Rational siRNA design for RNA interference", *Nature biotechnology*, vol. 22, no. 3, pp. 326-330.

Ricci, M.S., Kim, S.H., Ogi, K., Plastaras, J.P., Ling, J., Wang, W., Jin, Z., Liu, Y.Y., Dicker, D.T., Chiao, P.J., Flaherty, K.T., Smith, C.D. & El-Deiry, W.S. 2007, "Reduction of TRAIL-induced Mcl-1 and cIAP2 by c-Myc or sorafenib sensitizes resistant human cancer cells to TRAIL-induced death", *Cancer cell*, vol. 12, no. 1, pp. 66-80.

Ricci, M.S., Jin, Z., Dews, M., Yu, D., Thomas-Tikhonenko, A., Dicker, D.T. & El-Deiry, W.S. 2004, "Direct Repression of FLIP Expression by c-myc Is a Major Determinant of TRAIL Sensitivity", *Molecular and Cellular Biology*, vol. 24, no. 19, pp. 8541-8555.

Rinchik, E., Carpenter, D. & Selby, P. 1990, "A Strategy for Fine-Structure Functional Analysis of a 6- to 11-Centimorgan Region of Mouse Chromosome 7 by High-Efficiency Mutagenesis", *Proceedings of the National Academy of Sciences*, vol. 87, no. 3, pp. 896-900.

- Robb, G.B. & Rana, T.M. 2007, "RNA Helicase A Interacts with RISC in Human Cells and Functions in RISC Loading", *Molecular Cell*, vol. 26, no. 4, pp. 523-537.
- Rottmann, S., Wang, Y., Nasoff, M., Deveraux, Q.L. & Quon, K.C. 2005, "A TRAIL receptor-dependent synthetic lethal relationship between MYC activation and GSK3beta/FBW7 loss of function", *Proceedings of the National Academy of Sciences of the United States of America*, vol. 102, no. 42, pp. 15195-15200.
- Roy, N., Deveraux, Q.L., Takahashi, R., Salvesen, G.S. & Reed, J.C. 1997, "The c-IAP-1 and c-IAP-2 proteins are direct inhibitors of specific caspases", *The EMBO journal*, vol. 16, no. 23, pp. 6914-6925.
- Rozen, S. & Skaletsky, H. 2000, "Primer3 on the WWW for general users and for biologist programmers", *Methods in molecular biology (Clifton, N.J.)*, vol. 132, pp. 365-386.
- Sætrom, P., Heale, B.S.E., Snøve Jr., O., Aagaard, L., Alluin, J. & Rossi, J.J. 2007, "Distance constraints between microRNA target sites dictate efficacy and cooperativity", *Nucleic Acids Research*, vol. 35, no. 7, pp. 2333-2342.
- Sarov, M. & Stewart, A.F. 2005, "The best control for the specificity of RNAi", *Trends in biotechnology*, vol. 23, no. 9, pp. 446-448.
- Sato, K., Hida, S., Takayanagi, H., Yokochi, T., Kayagaki, N., Takeda, K., Yagita, H., Okumura, K., Tanaka, N., Taniguchi, T. & Ogasawara, K. 2001, "Antiviral response by natural killer cells through TRAIL gene induction by IFN-alpha/beta", *European journal of immunology*, vol. 31, no. 11, pp. 3138-3146.
- Saxena, S., Jonsson, Z.O. & Dutta, A. 2003, "Small RNAs with Imperfect Match to Endogenous mRNA Repress Translation: IMPLICATIONS FOR OFF-TARGET ACTIVITY OF SMALL INHIBITORY RNA IN MAMMALIAN CELLS", *J. Biol. Chem.*, vol. 278, no. 45, pp. 44312-44319.
- Schmitz, C., Kinge, P. & Hutter, H. 2007, "Axon guidance genes identified in a large-scale RNAi screen using the RNAi-hypersensitive *Caenorhabditis elegans* strain nre-1(hd20) lin-15b(hd126)", *Proceedings of the National Academy of Sciences of the United States of America*, vol. 104, no. 3, pp. 834-839.
- Schwarz, D.S., Hutvagner, G., Du, T., Xu, Z., Aronin, N. & Zamore, P.D. 2003, "Asymmetry in the assembly of the RNAi enzyme complex", *Cell*, vol. 115, no. 2, pp. 199-208.
- Schwarz, D.S., Hutvagner, G., Haley, B. & Zamore, P.D. 2002, "Evidence that siRNAs function as guides, not primers, in the Drosophila and human RNAi pathways", *Mol Cell*, vol. 10, no. 3, pp. 537-48.

- Scott, R.W. & Olson, M.F. 2007, "LIM kinases: function, regulation and association with human disease", *Journal of Molecular Medicine (Berlin, Germany)*, vol. 85, no. 6, pp. 555-568.
- Sedger, L.M., Glaccum, M.B., Schuh, J.C., Kanaly, S.T., Williamson, E., Kayagaki, N., Yun, T., Smolak, P., Le, T., Goodwin, R. & Gliniak, B. 2002, "Characterization of the in vivo function of TNF-alpha-related apoptosis-inducing ligand, TRAIL/Apo2L, using TRAIL/Apo2L gene-deficient mice", *European journal of immunology*, vol. 32, no. 8, pp. 2246-2254.
- Semizarov, D., Frost, L., Sarthy, A., Kroeger, P., Halbert, D.N. & Fesik, S.W. 2003, "Specificity of short interfering RNA determined through gene expression signatures", *PNAS*, vol. 100, no. 11, pp. 6347-6352.
- Seymour, R.E., Hasham, M.G., Cox, G.A., Shultz, L.D., Hogenesch, H., Roopenian, D.C. & Sundberg, J.P. 2007, "Spontaneous mutations in the mouse Sharpin gene result in multiorgan inflammation, immune system dysregulation and dermatitis", *Genes and immunity*, .
- Sharma, S., tenOever, B., Grandvaux, N., Zhou, G., Lin, R. & Hiscott, J. 2003, "Triggering the Interferon Antiviral Response Through an IKK-Related Pathway", *Science*, vol. 300, no. 5622, pp. 1148-1151.
- Shimada, T., Kawai, T., Takeda, K., Matsumoto, M., Inoue, J., Tatsumi, Y., Kanamaru, A. & Akira, S. 1999, "IKK-i, a novel lipopolysaccharide-inducible kinase that is related to IkappaB kinases", *International immunology*, vol. 11, no. 8, pp. 1357-1362.
- Shin, K., Wang, Q. & Margolis, B. 2007, "PATJ regulates directional migration of mammalian epithelial cells", *EMBO reports*, vol. 8, no. 2, pp. 158-164.
- Shuman, H.A. & Silhavy, T.J. 2003, "The art and design of genetic screens: Escherichia coli", *Nature Reviews Genetics*, vol. 4, no. 6, pp. 419-431.
- Sijen, T., Fleenor, J., Simmer, F., Thijssen, K.L., Parrish, S., Timmons, L., Plasterk, R.H. & Fire, A. 2001, "On the role of RNA amplification in dsRNA-triggered gene silencing", *Cell*, vol. 107, no. 4, pp. 465-476.
- Silva, J.M., Li, M.Z., Chang, K., Ge, W., Golding, M.C., Rickles, R.J., Siolas, D., Hu, G., Paddison, P.J., Schlabach, M.R., Sheth, N., Bradshaw, J., Burchard, J., Kulkarni, A., Cavet, G., Sachidanandam, R., McCombie, W.R., Cleary, M.A., Elledge, S.J. & Hannon, G.J. 2005, "Second-generation shRNA libraries covering the mouse and human genomes", *Nature Genetics*, vol. 37, no. 11, pp. 1281-1288.

- Silva, J.M., Mizuno, H., Brady, A., Lucito, R. & Hannon, G.J. 2004, "RNA interference microarrays: High-throughput loss-of-function genetics in mammalian cells", *PNAS*, vol. 101, no. 17, pp. 6548-6552.
- Simon, M.A., Bowtell, D.D., Dodson, G.S., Laverty, T.R. & Rubin, G.M. 1991, "Ras1 and a putative guanine nucleotide exchange factor perform crucial steps in signaling by the sevenless protein tyrosine kinase", *Cell*, vol. 67, no. 4, pp. 701-716.
- Simpson, J.C., Cetin, C., Erfle, H., Joggerst, B., Liebel, U., Ellenberg, J. & Pepperkok, R. 2007, "An RNAi screening platform to identify secretion machinery in mammalian cells", *Journal of Biotechnology*, vol. 129, no. 2, pp. 352-365.
- Simpson, J.C., Wellenreuther, R., Poustka, A., Pepperkok, R. & Wiemann, S. 2000, "Systematic subcellular localization of novel proteins identified by large-scale cDNA sequencing", *EMBO Reports*, vol. 1, no. 3, pp. 287-292.
- Siolas, D., Lerner, C., Burchard, J., Ge, W., Linsley, P.S., Paddison, P.J., Hannon, G.J. & Cleary, M.A. 2005, "Synthetic shRNAs as potent RNAi triggers", *Nat Biotechnol*, vol. 23, no. 2, pp. 227-31.
- Sledz, C.A., Holko, M., de Veer, M.J., Silverman, R.H. & Williams, B.R.G. 2003, "Activation of the interferon system by short-interfering RNAs", *Nat Cell Biol*, vol. 5, no. 9, pp. 834-839.
- Speliotes, E.K., Uren, A., Vaux, D. & Horvitz, H.R. 2000, "The survivin-like *C. elegans* BIR-1 protein acts with the Aurora-like kinase AIR-2 to affect chromosomes and the spindle midzone", *Molecular cell*, vol. 6, no. 2, pp. 211-223.
- St Johnston, D. 2002, "The art and design of genetic screens: *Drosophila melanogaster*", *Nature Reviews Genetics*, vol. 3, no. 3, pp. 176-188.
- Stephens, P., Edkins, S., Davies, H., Greenman, C., Cox, C., Hunter, C., Bignell, G., Teague, J., Smith, R., Stevens, C., O'Meara, S., Parker, A., Tarpey, P., Avis, T., Bartherope, A., Brackenbury, L., Buck, G., Butler, A., Clements, J., Cole, J., Dicks, E., Edwards, K., Forbes, S., Gorton, M., Gray, K., Halliday, K., Harrison, R., Hills, K., Hinton, J., Jones, D., Kosmidou, V., Laman, R., Lugg, R., Menzies, A., Perry, J., Petty, R., Raine, K., Shepherd, R., Small, A., Solomon, H., Stephens, Y., Tofts, C., Varian, J., Webb, A., West, S., Widaa, S., Yates, A., Brasseur, F., Cooper, C.S., Flanagan, A.M., Green, A., Knowles, M., Leung, S.Y., Looijenga, L.H., Malkowicz, B., Pierotti, M.A., Teh, B., Yuen, S.T., Nicholson, A.G., Lakhani, S., Easton, D.F., Weber, B.L., Stratton, M.R., Futreal, P.A. & Wooster, R. 2005, "A screen of the complete protein kinase gene family identifies diverse patterns of somatic mutations in human breast cancer", *Nature genetics*, vol. 37, no. 6, pp. 590-592.

- Streisinger, G., Walker, C., Dower, N., Knauber, D. & Singer, F. 1981, "Production of clones of homozygous diploid zebra fish (*Brachydanio rerio*)", *Nature*, vol. 291, no. 5813, pp. 293-296.
- Subramanian, A., Tamayo, P., Mootha, V.K., Mukherjee, S., Ebert, B.L., Gillette, M.A., Paulovich, A., Pomeroy, S.L., Golub, T.R., Lander, E.S. & Mesirov, J.P. 2005, "Gene set enrichment analysis: a knowledge-based approach for interpreting genome-wide expression profiles", *Proceedings of the National Academy of Sciences of the United States of America*, vol. 102, no. 43, pp. 15545-15550.
- Suliman, A., Lam, A., Datta, R. & Srivastava, R.K. 2001, "Intracellular mechanisms of TRAIL: apoptosis through mitochondrial-dependent and -independent pathways", *Oncogene*, vol. 20, no. 17, pp. 2122-2133.
- Sulston, J.E. & Horvitz, H.R. 1977, "Post-embryonic cell lineages of the nematode, *Caenorhabditis elegans*", *Developmental Biology*, vol. 56, no. 1, pp. 110-156.
- Sumi, T., Hashigasako, A., Matsumoto, K. & Nakamura, T. 2006, "Different activity regulation and subcellular localization of LIMK1 and LIMK2 during cell cycle transition", *Experimental cell research*, vol. 312, no. 7, pp. 1021-1030.
- Sun, L., Gu, S., Li, X., Sun, Y., Zheng, D., Yu, K., Ji, C., Tang, R., Xie, Y. & Mao, Y. 2006, "Identification of a novel human MAST4 gene, a new member of the microtubule associated serine-threonine kinase family", *Molekuliarnaia biologija*, vol. 40, no. 5, pp. 808-815.
- Suter, T., Biollaz, G., Gatto, D., Bernasconi, L., Herren, T., Reith, W. & Fontana, A. 2003, "The brain as an immune privileged site: dendritic cells of the central nervous system inhibit T cell activation", *European journal of immunology*, vol. 33, no. 11, pp. 2998-3006.
- Suzuki, Y., Nakabayashi, Y. & Takahashi, R. 2001, "Ubiquitin-protein ligase activity of X-linked inhibitor of apoptosis protein promotes proteasomal degradation of caspase-3 and enhances its anti-apoptotic effect in Fas-induced cell death", *Proceedings of the National Academy of Sciences*, vol. 98, no. 15, pp. 8662-8667.
- Svoboda, P., Stein, P., Hayashi, H. & Schultz, R.M. 2000, "Selective reduction of dormant maternal mRNAs in mouse oocytes by RNA interference", *Development (Cambridge, England)*, vol. 127, no. 19, pp. 4147-4156.
- Takeda, K., Smyth, M.J., Cretney, E., Hayakawa, Y., Yamaguchi, N., Yagita, H. & Okumura, K. 2001, "Involvement of Tumor Necrosis Factor-Related Apoptosis-Inducing Ligand in NK Cell-Mediated and IFN- γ -Dependent Suppression of Subcutaneous Tumor Growth", *Cellular Immunology*, vol. 214, no. 2, pp. 194-200.

- Takimoto, R. & El-Deiry, W.S. 2000, "Wild-type p53 transactivates the KILLER/DR5 gene through an intronic sequence-specific DNA-binding site", *Oncogene*, vol. 19, no. 14, pp. 1735-1743.
- Tan, M., Gallegos, J.R., Gu, Q., Huang, Y., Li, J., Jin, Y., Lu, H. & Sun, Y. 2006, "SAG/ROC-SCF beta-TrCP E3 ubiquitin ligase promotes pro-caspase-3 degradation as a mechanism of apoptosis protection", *Neoplasia (New York, N.Y.)*, vol. 8, no. 12, pp. 1042-1054.
- Tanji, C., Yamamoto, H., Yorioka, N., Kohno, N., Kikuchi, K. & Kikuchi, A. 2002, "A-kinase anchoring protein AKAP220 binds to glycogen synthase kinase-3beta (GSK-3beta) and mediates protein kinase A-dependent inhibition of GSK-3beta", *The Journal of biological chemistry*, vol. 277, no. 40, pp. 36955-36961.
- Tao, Y., Pinzi, V., Bourhis, J. & Deutsch, E. 2007, "Mechanisms of Disease: Signaling of the insulin-like growth factor 1 receptor pathway - Therapeutic perspectives in cancer", *Nature Clinical Practice Oncology*, vol. 4, no. 10, pp. 591-602.
- Thakkar, H., Chen, X., Tyan, F., Gim, S., Robinson, H., Lee, C., Pandey, S.K., Nwokorie, C., Onwudiwe, N. & Srivastava, R.K. 2001, "Pro-survival function of Akt/protein kinase B in prostate cancer cells. Relationship with TRAIL resistance", *The Journal of biological chemistry*, vol. 276, no. 42, pp. 38361-38369.
- Thon, L., Mathieu, S., Kabelitz, D. & Adam, D. 2006, "The murine TRAIL receptor signals caspase-independent cell death through ceramide", *Experimental cell research*, vol. 312, no. 19, pp. 3808-3821.
- Timmons, L. & Fire, A. 1998, "Specific interference by ingested dsRNA", *Nature*, vol. 395, no. 6705, pp. 854.
- Ting, A.T., Pimentel-Muinos, F.X. & Seed, B. 1996, "RIP mediates tumor necrosis factor receptor 1 activation of NF-kappaB but not Fas/APO-1-initiated apoptosis", *The EMBO journal*, vol. 15, no. 22, pp. 6189-6196.
- Tomari, Y., Du, T., Haley, B., Schwarz, D.S., Bennett, R., Cook, H.A., Koppetsch, B.S., Theurkauf, W.E. & Zamore, P.D. 2004a, "RISC assembly defects in the Drosophila RNAi mutant armitage", *Cell*, vol. 116, no. 6, pp. 831-41.
- Tomari, Y., Matranga, C., Haley, B., Martinez, N. & Zamore, P.D. 2004b, "A Protein Sensor for siRNA Asymmetry", *Science*, vol. 306, no. 5700, pp. 1377-1380.
- Tomiyoshi, G., Horita, Y., Nishita, M., Ohashi, K. & Mizuno, K. 2004, "Caspase-mediated cleavage and activation of LIM-kinase 1 and its role in apoptotic membrane blebbing", *Genes to cells : devoted to molecular & cellular mechanisms*, vol. 9, no. 6, pp. 591-600.

- Tong, A.H., Evangelista, M., Parsons, A.B., Xu, H., Bader, G.D., Page, N., Robinson, M., Raghibizadeh, S., Hogue, C.W., Bussey, H., Andrews, B., Tyers, M. & Boone, C. 2001, "Systematic genetic analysis with ordered arrays of yeast deletion mutants", *Science (New York, N.Y.)*, vol. 294, no. 5550, pp. 2364-2368.
- Trauzold, A., Siegmund, D., Schniewind, B., Sipos, B., Egberts, J., Zorenkov, D., Emme, D., Roder, C., Kalthoff, H. & Wajant, H. 2006, "TRAIL promotes metastasis of human pancreatic ductal adenocarcinoma", *Oncogene*, vol. 25, no. 56, pp. 7434-7439.
- Tsai, S.F., Martin, D.I., Zon, L.I., D'Andrea, A.D., Wong, G.G. & Orkin, S.H. 1989, "Cloning of cDNA for the major DNA-binding protein of the erythroid lineage through expression in mammalian cells", *Nature*, vol. 339, no. 6224, pp. 446-451.
- Tsunoda, S. & Zuker, C.S. 1999, "The organization of INAD-signaling complexes by a multivalent PDZ domain protein in Drosophila photoreceptor cells ensures sensitivity and speed of signaling", *Cell Calcium*, vol. 26, no. 5, pp. 165-171.
- Ui-Tei, K., Naito, Y., Takahashi, F., Haraguchi, T., Ohki-Hamazaki, H., Juni, A., Ueda, R. & Saigo, K. 2004, "Guidelines for the selection of highly effective siRNA sequences for mammalian and chick RNA interference", *Nucleic acids research*, vol. 32, no. 3, pp. 936-948.
- Urbano, A., Lakshmanan, U., Choo, P.H., Kwan, J.C., Ng, P.Y., Guo, K., Dhakshinamoorthy, S. & Porter, A. 2005, "AIF suppresses chemical stress-induced apoptosis and maintains the transformed state of tumor cells", *The EMBO journal*, vol. 24, no. 15, pp. 2815-2826.
- Uren, A.G., Wong, L., Pakusch, M., Fowler, K.J., Burrows, F.J., Vaux, D.L. & Choo, K.H. 2000, "Survivin and the inner centromere protein INCENP show similar cell-cycle localization and gene knockout phenotype", *Current biology : CB*, vol. 10, no. 21, pp. 1319-1328.
- Valiente, M., Andres-Pons, A., Gomar, B., Torres, J., Gil, A., Tapparel, C., Antonarakis, S. & Pulido, R. 2005, "Binding of PTEN to specific PDZ domains contributes to PTEN protein stability and phosphorylation by MAST kinases", *Journal of Biological Chemistry*, .
- Walczak, H., Bouchon, A., Stahl, H. & Krammer, P.H. 2000, "Tumor necrosis factor-related apoptosis-inducing ligand retains its apoptosis-inducing capacity on Bcl-2- or Bcl-xL-overexpressing chemotherapy-resistant tumor cells", *Cancer research*, vol. 60, no. 11, pp. 3051-3057.
- Walczak, H., Degli-Esposti, M.A., Johnson, R.S., Smolak, P.J., Waugh, J.Y., Boiani, N., Timour, M.S., Gerhart, M.J., Schooley, K.A., Smith, C.A., Goodwin, R.G. & Rauch,

- C.T. 1997, "TRAIL-R2: a novel apoptosis-mediating receptor for TRAIL", *The EMBO journal*, vol. 16, no. 17, pp. 5386-5397.
- Walczak, H., Miller, R.E., Arial, K., Gliniak, B., Griffith, T.S., Kubin, M., Chin, W., Jones, J., Woodward, A., Le, T., Smith, C., Smolak, P., Goodwin, R.G., Rauch, C.T., Schuh, J.C.L. & Lynch, D.H. 1999, "Tumoricidal activity of tumor necrosis factor-related apoptosis-inducing ligand in vivo", *Nature Medicine*, vol. 5, no. 2, pp. 157-163.
- Walter, L., Dirks, B., Rothermel, E., Heyens, M., Szpirer, C., Levan, G. & Gunther, E. 1994, "A novel, conserved gene of the rat that is developmentally regulated in the testis", *Mammalian genome : official journal of the International Mammalian Genome Society*, vol. 5, no. 4, pp. 216-221.
- Walter, L., Marynen, P., Szpirer, J., Levan, G. & Gunther, E. 1995, "Identification of a novel conserved human gene, TEGT", *Genomics*, vol. 28, no. 2, pp. 301-304.
- Wang, Y., Engels, I.H., Knee, D.A., Nasoff, M., Deveraux, Q.L. & Quon, K.C. 2004/5, "Synthetic lethal targeting of MYC by activation of the DR5 death receptor pathway", *Cancer Cell*, vol. 5, no. 5, pp. 501-512.
- Wang, Y., Quon, K.C., Knee, D.A., Nesterov, A. & Kraft, A.S. 2005, "RAS, MYC, and Sensitivity to Tumor Necrosis Factor- α -Related Apoptosis-Inducing Ligand-Induced Apoptosis", *Cancer Research*, vol. 65, no. 4, pp. 1615-1617.
- Wassmer, T., Attar, N., Bujny, M.V., Oakley, J., Traer, C.J. & Cullen, P.J. 2007, "A loss-of-function screen reveals SNX5 and SNX6 as potential components of the mammalian retromer", *Journal of Cell Science*, vol. 120, no. 1, pp. 45-54.
- Westbrook, T.F., Martin, E.S., Schlabach, M.R., Leng, Y., Liang, A.C., Feng, B., Zhao, J.J., Roberts, T.M., Mandel, G., Hannon, G.J., DePinho, R.A., Chin, L. & Elledge, S.J. 2005, "A genetic screen for candidate tumor suppressors identifies REST", *Cell*, vol. 121, no. 6, pp. 837-848.
- Whitehurst, A.W., Bodenmann, B.O., Cardenas, J., Ferguson, D., Girard, L., Peyton, M., Minna, J.D., Michnoff, C., Hao, W., Roth, M.G., Xie, X.- & White, M.A. 2007, "Synthetic lethal screen identification of chemosensitizer loci in cancer cells", *Nature*, vol. 446, no. 7137, pp. 815-819.
- Wiley, S.R., Schooley, K., Smolak, P.J., Din, W.S., Huang, C.P., Nicholl, J.K., Sutherland, G.R., Smith, T.D., Rauch, C. & Smith, C.A. 1995, "Identification and characterization of a new member of the TNF family that induces apoptosis", *Immunity*, vol. 3, no. 6, pp. 673-682.

- Winzeler, E.A., Shoemaker, D.D., Astromoff, A., Liang, H., Anderson, K., Andre, B., Bangham, R., Benito, R., Boeke, J.D., Bussey, H., Chu, A.M., Connelly, C., Davis, K., Dietrich, F., Dow, S.W., El Bakkoury, M., Foury, F., oise, Friend, S.H., Gentalen, E., Giaever, G., Hegemann, J.H., Jones, T., Laub, M., Liao, H., Liebundguth, N., Lockhart, D.J., Lucau-Danila, A., Lussier, M., M'Rabet, N., Menard, P., Mittmann, M., Pai, C., Reischung, C., Revuelta, J.L., Riles, L., Roberts, C.J., Ross-MacDonald, P., Scherens, B., Snyder, M., Sookhai-Mahadeo, S., Storms, R.K., Véronneau, S., Voet, M., Volckaert, G., Ward, T.R., Wysocki, R., Yen, G.S., Yu, K., Zimmermann, K., Philippsen, P., Johnston, M. & Davis, R.W. 1999, "Functional Characterization of the *S. cerevisiae* Genome by Gene Deletion and Parallel Analysis", *Science*, vol. 285, no. 5429, pp. 901-906.
- Wu, L., Fan, J. & Belasco, J.G. 2006, "MicroRNAs direct rapid deadenylation of mRNA", *Proceedings of the National Academy of Sciences of the United States of America*, vol. 103, no. 11, pp. 4034-4039.
- Wu, X.X., Ogawa, O. & Kakehi, Y. 2004, "Sensitization of human renal cell carcinoma cell lines to TRAIL-induced apoptosis by anthracyclines", *International journal of urology : official journal of the Japanese Urological Association*, vol. 11, no. 3, pp. 164-170.
- Xie, Q., Lin, T., Zhang, Y., Zheng, J. & Bonanno, J.A. 2005, "Molecular cloning and characterization of a human AIF-like gene with ability to induce apoptosis", *The Journal of biological chemistry*, vol. 280, no. 20, pp. 19673-19681.
- Xiong, H., Li, H., Chen, Y., Zhao, J. & Unkeless, J.C. 2004, "Interaction of TRAF6 with MAST205 regulates NF-kappaB activation and MAST205 stability", *The Journal of biological chemistry*, vol. 279, no. 42, pp. 43675-43683.
- Xu, Q. & Reed, J.C. 1998, "Bax inhibitor-1, a mammalian apoptosis suppressor identified by functional screening in yeast", *Molecular cell*, vol. 1, no. 3, pp. 337-346.
- Xu, T., Wang, W., Zhang, S., Stewart, R.A. & Yu, W. 1995, "Identifying tumor suppressors in genetic mosaics: the Drosophila lats gene encodes a putative protein kinase", *Development (Cambridge, England)*, vol. 121, no. 4, pp. 1053-1063.
- Yi, C.H., Sogah, D.K., Boyce, M., Degterev, A., Christofferson, D.E. & Yuan, J. 2007, "A genome-wide RNAi screen reveals multiple regulators of caspase activation", *The Journal of cell biology*.
- Yi, R., Qin, Y., Macara, I.G. & Cullen, B.R. 2003, "Exportin-5 mediates the nuclear export of pre-microRNAs and short hairpin RNAs", *Genes & development*, vol. 17, no. 24, pp. 3011-3016.

- Yoo, J.W., Hong, S.W., Kim, S. & Lee, D.-. 2006, "Inflammatory cytokine induction by siRNAs is cell type- and transfection reagent-specific", *Biochemical and Biophysical Research Communications*, vol. 347, no. 4, pp. 1053-1058.
- Yu, L.H., Kawai-Yamada, M., Naito, M., Watanabe, K., Reed, J.C. & Uchimiya, H. 2002, "Induction of mammalian cell death by a plant Bax inhibitor", *FEBS letters*, vol. 512, no. 1-3, pp. 308-312.
- Zerafa, N., Westwood, J.A., Cretney, E., Mitchell, S., Waring, P., Iezzi, M. & Smyth, M.J. 2005, "Cutting edge: TRAIL deficiency accelerates hematological malignancies", *Journal of immunology (Baltimore, Md.: 1950)*, vol. 175, no. 9, pp. 5586-5590.
- Zhang, J.-., Chung, T.D.Y. & Oldenburg, K.R. 1999, "A simple statistical parameter for use in evaluation and validation of high throughput screening assays", *Journal of Biomolecular Screening*, vol. 4, no. 2, pp. 67-73.
- Zhang, X.D. 2007, "A pair of new statistical parameters for quality control in RNA interference high-throughput screening assays", *Genomics*, vol. 89, no. 4, pp. 552-561.
- Zhang, X.D., Franco, A., Myers, K., Gray, C., Nguyen, T. & Hersey, P. 1999, "Relation of TNF-related apoptosis-inducing ligand (TRAIL) receptor and FLICE-inhibitory protein expression to TRAIL-induced apoptosis of melanoma", *Cancer Research*, vol. 59, no. 11, pp. 2747-2753.
- Zhao, Y. & Ding, S. 2007, "A high-throughput siRNA library screen identifies osteogenic suppressors in human mesenchymal stem cells", *Proceedings of the National Academy of Sciences of the United States of America*, vol. 104, no. 23, pp. 9673-9678.
- Zheng, L., Liu, J., Batalov, S., Zhou, D., Orth, A., Ding, S. & Schultz, P.G. 2004, "An approach to genomewide screens of expressed small interfering RNAs in mammalian cells", *PNAS*, vol. 101, no. 1, pp. 135-140.