6. References

Abrahante, J. E., Daul, A. L., Li, M., Volk, M. L., Tennessen, J. M., Miller, E. A., and Rougvie, A. E. (2003). The Caenorhabditis elegans hunchback-like gene lin-57/hbl-1 controls developmental time and is regulated by microRNAs. Dev Cell *4*, 625-637.

Abrahante, J. E., Miller, E. A., and Rougvie, A. E. (1998). Identification of heterochronic mutants in Caenorhabditis elegans. Temporal misexpression of a collagen::green fluorescent protein fusion gene. Genetics *149*, 1335-1351.

Altschul, S. F., Madden, T. L., Schaffer, A. A., Zhang, J., Zhang, Z., Miller, W., and Lipman, D. J. (1997). Gapped BLAST and PSI-BLAST: a new generation of protein database search programs. Nucleic Acids Res *25*, 3389-3402.

Ambros, V. (1989). A hierarchy of regulatory genes controls a larva-to-adult developmental switch in C. elegans. Cell *57*, 49-57.

Ambros, V. (2000). Control of developmental timing in Caenorhabditis elegans. Curr Opin Genet Dev *10*, 428-433.

Ambros, V. (2001). microRNAs: tiny regulators with great potential. Cell *107*, 823-826.

Ambros, V. (2003). MicroRNA pathways in flies and worms: growth, death, fat, stress, and timing. Cell *113*, 673-676.

Ambros, V., and Horvitz, H. R. (1984). Heterochronic mutants of the nematode Caenorhabditis elegans. Science *226*, 409-416.

Ambros, V., and Horvitz, H. R. (1987). The lin-14 locus of Caenorhabditis elegans controls the time of expression of specific postembryonic developmental events. Genes Dev *1*, 398-414.

Ambros, V., Lee, R. C., Lavanway, A., Williams, P. T., and Jewell, D. (2003). MicroRNAs and other tiny endogenous RNAs in C. elegans. Curr Biol *13*, 807-818.

Ambros, V., and Moss, E. G. (1994). Heterochronic genes and the temporal control of C. elegans development. Trends Genet *10*, 123-127.

Antebi, A., Culotti, J. G., and Hedgecock, E. M. (1998). *daf-12* regulates developmental age and the dauer alternative in *C. elegans*. Development *125*, 1191-1205.

Antebi, A., Yeh, W. H., Tait, D., Hedgecock, E. M., and Riddle, D. L. (2000). daf-12 encodes a nuclear receptor that regulates the dauer diapause and developmental age in C. elegans. Genes Dev *14*, 1512-1527.

Arasu, P., Wightman, B., and Ruvkun, G. (1991). Temporal regulation of lin-14 by the antagonistic action of two other heterochronic genes, lin-4 and lin-28. Genes Dev *5*, 1825-1833.

Asahina, M., Ishihara, T., Jindra, M., Kohara, Y., Katsura, I., and Hirose, S. (2000). The conserved nuclear receptor Ftz-F1 is required for embryogenesis, moulting and reproduction in Caenorhabditis elegans. Genes Cells *5*, 711-723.

Asai, K., Satoh, N., Sasaki, H., Satoh, H., and Nagato, Y. (2002). A rice heterochronic mutant, mori1, is defective in the juvenile-adult phase change. Development *129*, 265-273.

Bai, C., Sen, P., Hofmann, K., Ma, L., Goebl, M., Harper, J. W., and Elledge, S. J. (1996). SKP1 connects cell cycle regulators to the ubiquitin proteolysis machinery through a novel motif, the F-box. Cell *86*, 263-274.

Banerjee, D., and Slack, F. (2002). Control of developmental timing by small temporal RNAs: a paradigm for RNA-mediated regulation of gene expression. Bioessays *24*, 119-129.

Barral, Y., Jentsch, S., and Mann, C. (1995). G1 cyclin turnover and nutrient uptake are controlled by a common pathway in yeast. Genes Dev *9*, 399-409.

Bender, M., Imam, F. B., Talbot, W. S., Ganetzky, B., and Hogness, D. S. (1997). Drosophila ecdysone receptor mutations reveal functional differences among receptor isoforms. Cell *91*, 777-788.

Berardini, T. Z., Bollman, K., Sun, H., and Poethig, R. S. (2001). Regulation of vegetative phase change in Arabidopsis thaliana by cyclophilin 40. Science *291*, 2405-2407.

Bernstein, E., Caudy, A. A., Hammond, S. M., and Hannon, G. J. (2001). Role for a bidentate ribonuclease in the initiation step of RNA interference. Nature *409*, 363-366.

Bettinger, J. C., Euling, S., and Rougvie, A. E. (1997). The terminal differentiation factor LIN-29 is required for proper vulval morphogenesis and egg laying in Caenorhabditis elegans. Development *124*, 4333-4342.

Bettinger, J. C., Lee, K., and Rougvie, A. E. (1996). Stage-specific accumulation of the terminal differentiation factor LIN-29 during Caenorhabditis elegans development. Development *122*, 2517-2527.

Bialecki, M., Shilton, A., Fichtenberg, C., Segraves, W. A., and Thummel, C. S. (2002). Loss of the ecdysteroid-inducible E75A orphan nuclear receptor uncouples molting from metamorphosis in Drosophila. Dev Cell *3*, 209-220.

Blondel, M., Galan, J. M., Chi, Y., Lafourcade, C., Longaretti, C., Deshaies, R. J., and Peter, M. (2000). Nuclear-specific degradation of Far1 is controlled by the localization of the F-box protein Cdc4. Embo J *19*, 6085-6097.

Brennecke, J., Hipfner, D. R., Stark, A., Russell, R. B., and Cohen, S. M. (2003). bantam encodes a developmentally regulated microRNA that controls cell proliferation and regulates the proapoptotic gene hid in Drosophila. Cell *113*, 25-36.

Brenner, S. (1974). The genetics of Caenorhabditis elegans. Genetics *77*, 71-94.

Carrano, A. C., Eytan, E., Hershko, A., and Pagano, M. (1999). SKP2 is required for ubiquitin-mediated degradation of the CDK inhibitor p27. Nat Cell Biol *1*, 193-199.

Carrington, J. C., and Ambros, V. (2003). Role of microRNAs in plant and animal development. Science *301*, 336-338.

Cassada, R., and Russell, R. (1975). The Dauer-Larva: A Post-Embryonic Developmental Variant of the Nematode *C. elegans*. Dev Biol *46*, 326-342.

C. elegans Sequencing Consortium (1998). Genome sequence of the nematode C. elegans: a platform for investigating biology. Science *282*, 2012-2018.

Cenciarelli, C., Chiaur, D. S., Guardavaccaro, D., Parks, W., Vidal, M., and Pagano, M. (1999). Identification of a family of human F-box proteins. Curr Biol *9*, 1177-1179.

Chalfie, M., Horvitz, H. R., and Sulston, J. E. (1981). Mutations that lead to reiterations in the cell lineages of C. elegans. Cell *24*, 59-69.

Ciccarelli, F. D., Copley, R. R., Doerks, T., Russell, R. B., and Bork, P. (2002). CASH--a beta-helix domain widespread among carbohydrate-binding proteins. Trends Biochem Sci *27*, 59-62.

Clifford, R., Lee, M. H., Nayak, S., Ohmachi, M., Giorgini, F., and Schedl, T. (2000). FOG-2, a novel F-box containing protein, associates with the GLD-1 RNA binding protein and directs male sex determination in the C. elegans hermaphrodite germline. Development *127*, 5265-5276.

Cox, G. N., and Hirsh, D. (1985). Stage-specific patterns of collagen gene expression during development of Caenorhabditis elegans. Mol Cell Biol *5*, 363-372.

Cox, G. N., Kusch, M., and Edgar, R. S. (1981). Cuticle of Caenorhabditis elegans: its isolation and partial characterization. J Cell Biol *90*, 7-17.

Craig, K. L., and Tyers, M. (1999). The F-box: a new motif for ubiquitin dependent proteolysis in cell cycle regulation and signal transduction. Prog Biophys Mol Biol *72*, 299-328.

Davy, A., Bello, P., Thierry-Mieg, N., Vaglio, P., Hitti, J., Doucette-Stamm, L., Thierry-Mieg, D., Reboul, J., Boulton, S., Walhout, A. J.*, et al.* (2001). A protein-protein interaction map of the Caenorhabditis elegans 26S proteasome. EMBO Rep *2*, 821-828.

de Beer, G. (1958). Embryos and Ancestors. Oxford: Clarendon.

del Pozo, J. C., and Estelle, M. (2000). F-box proteins and protein degradation: an emerging theme in cellular regulation. Plant Mol Biol *44*, 123-128.

Deshaies, R. J. (1999). SCF and Cullin/Ring H2-based ubiquitin ligases. Annu Rev Cell Dev Biol *15*, 435-467.

Doherty, F. J., Dawson, S., and Mayer, R. J. (2002). The ubiquitin-proteasome pathway of intracellular proteolysis. Essays Biochem *38*, 51-63.

Drury, L. S., Perkins, G., and Diffley, J. F. (1997). The Cdc4/34/53 pathway targets Cdc6p for proteolysis in budding yeast. Embo J *16*, 5966-5976.

Dudley, M., and Poethig, R. S. (1991). The effect of a heterochronic mutation, Teopod2, on the cell lineage of the maize shoot. Development *111*, 733-739.

Dudley, M., and Poethig, R. S. (1993). The heterochronic Teopod1 and Teopod2 mutations of maize are expressed non-cell-autonomously. Genetics *133*, 389-399.

Durfee, T., Roe, J. L., Sessions, R. A., Inouye, C., Serikawa, K., Feldmann, K. A., Weigel, D., and Zambryski, P. C. (2003). The F-box-containing protein UFO and AGAMOUS participate in antagonistic pathways governing early petal development in Arabidopsis. Proc Natl Acad Sci U S A *100*, 8571-8576.

Ebens, A. J., Garren, H., Cheyette, B. N., and Zipursky, S. L. (1993). The Drosophila anachronism locus: a glycoprotein secreted by glia inhibits neuroblast proliferation. Cell *74*, 15-27.

Edwards, M. K., and Wood, W. B. (1983). Location of specific messenger RNAs in Caenorhabditis elegans by cytological hybridization. Dev Biol *97*, 375-390.

Epstein, H. F., Shakes, D.C. (eds.) (1995). Caenorhabditis elegans: Modern biological analysis of an organism, Vol. 48, Academic Press.

Erhardt, J. A., Hynicka, W., DiBenedetto, A., Shen, N., Stone, N., Paulson, H., and Pittman, R. N. (1998). A novel F box protein, NFB42, is highly enriched in neurons and induces growth arrest. J Biol Chem *273*, 35222-35227.

Euling, S., and Ambros, V. (1996). Heterochronic genes control cell cycle progress and developmental competence of C. elegans vulva precursor cells. Cell *84*, 667-676.

Euling, S., Bettinger, J. C., and Rougvie, A. E. (1999). The LIN-29 transcription factor is required for proper morphogenesis of the Caenorhabditis elegans male tail. Dev Biol *206*, 142-156.

Evans, M. M., Passas, H. J., and Poethig, R. S. (1994). Heterochronic effects of glossy15 mutations on epidermal cell identity in maize. Development *120*, 1971-1981.

Evans, M. M., and Poethig, R. S. (1995). Gibberellins promote vegetative phase change and reproductive maturity in maize. Plant Physiol *108*, 475-487.

Fay, D. S., Stanley, H. M., Han, M., and Wood, W. B. (1999). A Caenorhabditis elegans homologue of hunchback is required for late stages of development but not early embryonic patterning. Dev Biol *205*, 240-253.

Feinbaum, R., and Ambros, V. (1999). The timing of lin-4 RNA accumulation controls the timing of postembryonic developmental events in Caenorhabditis elegans. Dev Biol *210*, 87-95.

Feldman, R. M., Correll, C. C., Kaplan, K. B., and Deshaies, R. J. (1997). A complex of Cdc4p, Skp1p, and Cdc53p/cullin catalyzes ubiquitination of the phosphorylated CDK inhibitor Sic1p. Cell *91*, 221-230.

Feng, S., Ma, L., Wang, X., Xie, D., Dinesh-Kumar, S. P., Wei, N., and Deng, X. W. (2003). The COP9 signalosome interacts physically with SCF COI1 and modulates jasmonate responses. Plant Cell *15*, 1083-1094.

Fire, A., Xu, S., Montgomery, M. K., Kostas, S. A., Driver, S. E., and Mello, C. C. (1998). Potent and specific genetic interference by double-stranded RNA in Caenorhabditis elegans. Nature *391*, 806-811.

Flick, K. M., Spielewoy, N., Kalashnikova, T. I., Guaderrama, M., Zhu, Q., Chang, H. C., and Wittenberg, C. (2003). Grr1-dependent inactivation of Mth1 mediates glucose-induced dissociation of Rgt1 from HXT gene promoters. Mol Biol Cell *14*, 3230-3241.

Frieden, E. (1981). The dual role of thyroid hormones in vertebrate development and calorigenesis. Metamorphosis: A Problem in Developmental Biology. New York: Plenum, pp. 545-564.

Galan, J. M., and Peter, M. (1999). Ubiquitin-dependent degradation of multiple F-box proteins by an autocatalytic mechanism. Proc Natl Acad Sci U S A *96*, 9124-9129.

Gellon, G., and McGinnis, W. (1998). Shaping animal body plans in development and evolution by modulation of Hox expression patterns. Bioessays *20*, 116-125.

Gems, D., Sutton, A. J., Sundermeyer, M. L., Albert, P. S., King, K. V., Edgley, M. L., Larsen, P. L., and Riddle, D. L. (1998). Two pleiotropic classes of daf-2 mutation affect larval arrest, adult behavior, reproduction and longevity in Caenorhabditis elegans. Genetics *150*, 129-155.

Gerisch, B., and Antebi, A. (2004). Hormonal signals produced by DAF-9/cytochrome P450 regulate C. elegans dauer diapause in response to environmental cues. Development *131* 1765-1776.

Gerisch, B., Weitzel, C., Kober-Eisermann, C., Rottiers, V., and Antebi, A. (2001). A hormonal signaling pathway influencing C. elegans metabolism, reproductive development, and life span. Dev Cell *1*, 841-851.

Gissendanner, C. R., and Sluder, A. E. (2000). nhr-25, the Caenorhabditis elegans ortholog of ftz-f1, is required for epidermal and somatic gonad development. Dev Biol *221*, 259-272.

Goh, P. Y., and Surana, U. (1999). Cdc4, a protein required for the onset of S phase, serves an essential function during G(2)/M transition in Saccharomyces cerevisiae. Mol Cell Biol *19*, 5512-5522.

Gould, S. (1977). Ontogeny and Phylogeny. Cambridre, MA: Harvard Univ Press.

Grima, B., Lamouroux, A., Chelot, E., Papin, C., Limbourg-Bouchon, B., and Rouyer, F. (2002). The F-box protein slimb controls the levels of clock proteins period and timeless. Nature *420*, 178-182.

Grishok, A., Pasquinelli, A. E., Conte, D., Li, N., Parrish, S., Ha, I., Baillie, D. L., Fire, A., Ruvkun, G., and Mello, C. C. (2001). Genes and mechanisms related to RNA interference regulate expression of the small temporal RNAs that control C. elegans developmental timing. Cell *106*, 23-34.

Grumbach, M. M., Styne, D. M. (1998). Puberty: ontogeny, neuroendocrinology, physiology and disorders (Philadelphia, Wilson JD, Foster DW, Kronenberg HM, Larsen PR (eds). Philadelphia, PA, WB Saunders, 1998, pp 1509-1625, 1998.).

Gupta-Rossi, N., Le Bail, O., Gonen, H., Brou, C., Logeat, F., Six, E., Ciechanover, A., and Israel, A. (2001). Functional interaction between SEL-10, an F-box protein, and the nuclear form of activated Notch1 receptor. J Biol Chem *276*, 34371-34378.

Haas, A. L., Warms, J. V., Hershko, A., and Rose, I. A. (1982). Ubiquitin-activating enzyme. Mechanism and role in protein-ubiquitin conjugation. J Biol Chem *257*, 2543-2548.

Hallam, S. J., and Jin, Y. (1998). lin-14 regulates the timing of synaptic remodelling in Caenorhabditis elegans. Nature *395*, 78-82.

Harris, T. W., Lee, R., Schwarz, E., Bradnam, K., Lawson, D., Chen, W., Blasier, D., Kenny, E., Cunningham, F., Kishore, R*., et al.* (2003). WormBase: a cross-species database for comparative genomics. Nucleic Acids Res *31*, 133-137.

Hedgecock, E. M., and White, J. G. (1985). Polyploid tissues in the nematode Caenorhabditis elegans. Dev Biol *107*, 128-133.

Henchoz, S., Chi, Y., Catarin, B., Herskowitz, I., Deshaies, R. J., and Peter, M. (1997). Phosphorylation- and ubiquitin-dependent degradation of the cyclin-dependent kinase inhibitor Far1p in budding yeast. Genes Dev *11*, 3046-3060.

Heriche, J. K., Ang, D., Bier, E., and O'Farrell, P. H. (2003). Involvement of an SCFSlmb complex in timely elimination of E2F upon initiation of DNA replication in Drosophila. BMC Genet *4*, 9.

Hershko, A., and Ciechanover, A. (1998). The ubiquitin system. Annu Rev Biochem *67*, 425-479.

Hishida, R., Ishihara, T., Kondo, K., and Katsura, I. (1996). hch-1, a gene required for normal hatching and normal migration of a neuroblast in C. elegans, encodes a protein related to TOLLOID and BMP-1. Embo J *15*, 4111-4122.

Hochstrasser, M. (2000). Biochemistry. All in the ubiquitin family. Science *289*, 563-564.

Hodin, J., and Riddiford, L. M. (1998). The ecdysone receptor and ultraspiracle regulate the timing and progression of ovarian morphogenesis during Drosophila metamorphosis. Dev Genes Evol *208*, 304-317.

Hodin, J., and Riddiford, L. M. (2000). Different mechanisms underlie phenotypic plasticity and interspecific variation for a reproductive character in drosophilids (Insecta: Diptera). Evolution Int J Org Evolution *54*, 1638-1653.

Holloway, P., McCormick, W., Watson, R. J., and Chan, Y. K. (1996). Identification and analysis of the dissimilatory nitrous oxide reduction genes, nosRZDFY, of Rhizobium meliloti. J Bacteriol *178*, 1505-1514.

Hong, Y., Lee, R. C., and Ambros, V. (2000). Structure and function analysis of LIN-14, a temporal regulator of postembryonic developmental events in Caenorhabditis elegans. Mol Cell Biol *20*, 2285-2295.

Horton, P., and Nakai, K. (1996). A probabilistic classification system for predicting the cellular localization sites of proteins. Proc Int Conf Intell Syst Mol Biol *4*, 109-115.

Huhtaniemi, I. (2000). The Parkes lecture. Mutations of gonadotrophin and gonadotrophin receptor genes: what do they teach us about reproductive physiology? J Reprod Fertil *119*, 173-186.

Huhtaniemi, I. T. (2002). The role of mutations affecting gonadotrophin secretion and action in disorders of pubertal development. Best Pract Res Clin Endocrinol Metab *16*, 123-138.

Huibregtse, J. M., Scheffner, M., Beaudenon, S., and Howley, P. M. (1995). A family of proteins structurally and functionally related to the E6-AP ubiquitin-protein ligase. Proc Natl Acad Sci U S A *92*, 5249.

Hutvagner, G., McLachlan, J., Pasquinelli, A. E., Balint, E., Tuschl, T., and Zamore, P. D. (2001). A cellular function for the RNA-interference enzyme Dicer in the maturation of the let-7 small temporal RNA. Science *293*, 834-838.

Hutvagner, G., and Zamore, P. D. (2002). A microRNA in a multiple-turnover RNAi enzyme complex. Science *297*, 2056-2060.

Huxely, J. (1920). Metamorphosis of axolotl caused by thyroid feeding. Nature *104:436*.

Isshiki, T., Pearson, B., Holbrook, S., and Doe, C. Q. (2001). Drosophila neuroblasts sequentially express transcription factors which specify the temporal identity of their neuronal progeny. Cell *106*, 511-521.

Jackson, P. K., and Eldridge, A. G. (2002). The SCF ubiquitin ligase: an extended look. Mol Cell *9*, 923-925.

Jenkins, J., Mayans, O., and Pickersgill, R. (1998). Structure and evolution of parallel beta-helix proteins. J Struct Biol *122*, 236-246.

Jentsch, S., and Pyrowolakis, G. (2000). Ubiquitin and its kin: how close are the family ties? Trends Cell Biol *10*, 335-342.

Jeon, M., Gardner, H. F., Miller, E. A., Deshler, J., and Rougvie, A. E. (1999). Similarity of the C. elegans developmental timing protein LIN-42 to circadian rhythm proteins. Science *286*, 1141-1146.

Jia, K., Albert, P. S., and Riddle, D. L. (2002). DAF-9, a cytochrome P450 regulating C. elegans larval development and adult longevity. Development *129*, 221-231.

Jiang, J., and Struhl, G. (1998). Regulation of the Hedgehog and Wingless signalling pathways by the F-box/WD40-repeat protein Slimb. Nature *391*, 493-496.

Joazeiro, C. A., and Weissman, A. M. (2000). RING finger proteins: mediators of ubiquitin ligase activity. Cell *102*, 549-552.

Johnson, S. M., Lin, S. Y., and Slack, F. J. (2003). The time of appearance of the C. elegans let-7 microRNA is transcriptionally controlled utilizing a temporal regulatory element in its promoter. Dev Biol *259*, 364-379.

Johnstone, I. L., and Barry, J. D. (1996). Temporal reiteration of a precise gene expression pattern during nematode development. Embo J *15*, 3633-3639.

Jones, D., and Candido, E. P. (2000). The NED-8 conjugating system in Caenorhabditis elegans is required for embryogenesis and terminal differentiation of the hypodermis. Dev Biol *226*, 152-165.

Jones, D., Crowe, E., Stevens, T. A., and Candido, E. P. (2002). Functional and phylogenetic analysis of the ubiquitylation system in Caenorhabditis elegans: ubiquitin-conjugating enzymes, ubiquitin-activating enzymes, and ubiquitin-like proteins. Genome Biol *3*, RESEARCH0002.

Kaiser, P., Flick, K., Wittenberg, C., and Reed, S. I. (2000). Regulation of transcription by ubiquitination without proteolysis: Cdc34/SCF(Met30)-mediated inactivation of the transcription factor Met4. Cell *102*, 303-314.

Kaiser, P., Sia, R. A., Bardes, E. G., Lew, D. J., and Reed, S. I. (1998). Cdc34 and the F-box protein Met30 are required for degradation of the Cdk-inhibitory kinase Swe1. Genes Dev *12*, 2587-2597.

Kamath, R. S., and Ahringer, J. (2003). Genome-wide RNAi screening in Caenorhabditis elegans. Methods *30*, 313-321.

Kamath, R. S., Martinez-Campos, M., Zipperlen, P., Fraser, A. G., and Ahringer, J. (2001). Effectiveness of specific RNA-mediated interference through ingested double-stranded RNA in Caenorhabditis elegans. Genome Biol *2*, RESEARCH0002.

Kamura, T., Conrad, M. N., Yan, Q., Conaway, R. C., and Conaway, J. W. (1999). The Rbx1 subunit of SCF and VHL E3 ubiquitin ligase activates Rub1 modification of cullins Cdc53 and Cul2. Genes Dev *13*, 2928-2933.

Kamura, T., Hara, T., Kotoshiba, S., Yada, M., Ishida, N., Imaki, H., Hatakeyama, S., Nakayama, K., and Nakayama, K. I. (2003). Degradation of p57Kip2 mediated by SCFSkp2-dependent ubiquitylation. Proc Natl Acad Sci U S A *100*, 10231-10236.

Kamura, T., Sato, S., Haque, D., Liu, L., Kaelin, W. G., Jr., Conaway, R. C., and Conaway, J. W. (1998). The Elongin BC complex interacts with the conserved SOCS-box motif present in members of the SOCS, ras, WD-40 repeat, and ankyrin repeat families. Genes Dev *12*, 3872-3881.

Kaplan, K. B., Hyman, A. A., and Sorger, P. K. (1997). Regulating the yeast kinetochore by ubiquitin-dependent degradation and Skp1p-mediated phosphorylation. Cell *91*, 491-500.

Kennerdell, J. R., and Carthew, R. W. (2000). Heritable gene silencing in Drosophila using double-stranded RNA. Nat Biotechnol *18*, 896-898.

Ketting, R. F., Fischer, S. E., Bernstein, E., Sijen, T., Hannon, G. J., and Plasterk, R. H. (2001). Dicer functions in RNA interference and in synthesis of small RNA involved in developmental timing in C. elegans. Genes Dev *15*, 2654-2659.

Kim, J., Krichevsky, A., Grad, Y., Hayes, G. D., Kosik, K. S., Church, G. M., and Ruvkun, G. (2004). Identification of many microRNAs that copurify with polyribosomes in mammalian neurons. Proc Natl Acad Sci U S A *101*, 360-365.

Kimble, J., and Hirsh, D. (1979). The postembryonic cell lineages of the hermaphrodite and male gonads in Caenorhabditis elegans. Dev Biol *70*, 396-417.

King, D. P., and Takahashi, J. S. (2000). Molecular genetics of circadian rhythms in mammals. Annu Rev Neurosci *23*, 713-742.

Kipreos, E. T., Gohel, S. P., and Hedgecock, E. M. (2000). The C. elegans F-box/WD-repeat protein LIN-23 functions to limit cell division during development. Development *127*, 5071-5082.

Kipreos, E. T., and Pagano, M. (2000). The F-box protein family. Genome Biol *1*, REVIEWS3002.

Ko, H. W., Jiang, J., and Edery, I. (2002). Role for Slimb in the degradation of Drosophila Period protein phosphorylated by Doubletime. Nature *420*, 673-678.

Koelle, M. R., Segraves, W. A., and Hogness, D. S. (1992). DHR3: a Drosophila steroid receptor homolog. Proc Natl Acad Sci U S A *89*, 6167-6171.

Kornitzer, D., Raboy, B., Kulka, R. G., and Fink, G. R. (1994). Regulated degradation of the transcription factor Gcn4. Embo J *13*, 6021-6030.

Kostrouchova, M., Krause, M., Kostrouch, Z., and Rall, J. E. (1998). CHR3: a Caenorhabditis elegans orphan nuclear hormone receptor required for proper epidermal development and molting. Development *125*, 1617-1626.

Kostrouchova, M., Krause, M., Kostrouch, Z., and Rall, J. E. (2001). Nuclear hormone receptor CHR3 is a critical regulator of all four larval molts of the nematode Caenorhabditis elegans. Proc Natl Acad Sci U S A *98*, 7360-7365.

Krause, M. (1995). Techniques for analyzing transcription and translation. Methods Cell Biol *48*, 513-529.

Kumar, A., and Paietta, J. V. (1995). The sulfur controller-2 negative regulatory gene of Neurospora crassa encodes a protein with beta-transducin repeats. Proc Natl Acad Sci U S A *92*, 3343-3347.

Kumar, A., and Paietta, J. V. (1998). An additional role for the F-box motif: gene regulation within the Neurospora crassa sulfur control network. Proc Natl Acad Sci U S A *95*, 2417-2422.

Kwon, Y. T., Reiss, Y., Fried, V. A., Hershko, A., Yoon, J. K., Gonda, D. K., Sangan, P., Copeland, N. G., Jenkins, N. A., and Varshavsky, A. (1998). The mouse and human genes encoding the recognition component of the N-end rule pathway. Proc Natl Acad Sci U S A *95*, 7898-7903.

Kyriacou, C. P., Oldroyd, M., Wood, J., Sharp, M., and Hill, M. (1990). Clock mutations alter developmental timing in Drosophila. Heredity *64 (Pt 3)*, 395-401.

Lagos-Quintana, M., Rauhut, R., Lendeckel, W., and Tuschl, T. (2001). Identification of novel genes coding for small expressed RNAs. Science *294*, 853-858.

Lagos-Quintana, M., Rauhut, R., Yalcin, A., Meyer, J., Lendeckel, W., and Tuschl, T. (2002). Identification of tissue-specific microRNAs from mouse. Curr Biol *12*, 735-739.

Lander, E. S., Linton, L. M., Birren, B., Nussbaum, C., Zody, M.C., Baldwin, J., Devon, K., Dewar, K., Doyle, M., FitzHugh, W., *et al.* (2001). Initial Sequencing and analysis of the human genome. Nature *409*, 860-921

Laney, J. D., and Hochstrasser, M. (1999). Substrate targeting in the ubiquitin system. Cell *97*, 427-430.

Lau, N. C., Lim, L. P., Weinstein, E. G., and Bartel, D. P. (2001). An abundant class of tiny RNAs with probable regulatory roles in Caenorhabditis elegans. Science *294*, 858-862.

Lawson, E. J., and Poethig, R. S. (1995). Shoot development in plants: time for a change. Trends Genet *11*, 263-268.

Le Poole, I. C., Sarangarajan, R., Zhao, Y., Stennett, L. S., Brown, T. L., Sheth, P., Miki, T., and Boissy, R. E. (2001). 'VIT1', a novel gene associated with vitiligo. Pigment Cell Res *14*, 475-484.

Lee, I., Aukerman, M. J., Gore, S. L., Lohman, K. N., Michaels, S. D., Weaver, L. M., John, M. C., Feldmann, K. A., and Amasino, R. M. (1994). Isolation of LUMINIDEPENDENS: a gene involved in the control of flowering time in Arabidopsis. Plant Cell *6*, 75-83.

Lee, R. C., and Ambros, V. (2001). An extensive class of small RNAs in Caenorhabditis elegans. Science *294*, 862-864.

Lee, R. C., Feinbaum, R. L., and Ambros, V. (1993). The C. elegans heterochronic gene lin-4 encodes small RNAs with antisense complementarity to lin-14. Cell *75*, 843-854.

Lehmann, R., and Nusslein-Volhard, C. (1987). hunchback, a gene required for segmentation of an anterior and posterior region of the Drosophila embryo. Dev Biol *119*, 402-417.

Li, F. N., and Johnston, M. (1997). Grr1 of Saccharomyces cerevisiae is connected to the ubiquitin proteolysis machinery through Skp1: coupling glucose sensing to gene expression and the cell cycle. Embo J *16*, 5629-5638.

Li, S., Armstrong, C. M., Bertin, N., Ge, H., Milstein, S., Boxem, M., Vidalain, P. O., Han, J. D., Chesneau, A., Hao, T.*, et al.* (2004). A map of the interactome network of the metazoan C. elegans. Science *303*, 540-543.

Lim, L. P., Lau, N. C., Weinstein, E. G., Abdelhakim, A., Yekta, S., Rhoades, M. W., Burge, C. B., and Bartel, D. P. (2003). The microRNAs of Caenorhabditis elegans. Genes Dev *17*, 991-1008.

Lin, S. Y., Johnson, S. M., Abraham, M., Vella, M. C., Pasquinelli, A., Gamberi, C., Gottlieb, E., and Slack, F. J. (2003). The C elegans hunchback homolog, hbl-1, controls temporal patterning and is a probable microRNA target. Dev Cell *4*, 639-650.

Liu, Z., Kirch, S., and Ambros, V. (1995). The Caenorhabditis elegans heterochronic gene pathway controls stage-specific transcription of collagen genes. Development *121*, 2471-2478.

Liu, Z. C., and Ambros, V. (1989). Heterochronic genes control the stage-specific initiation and expression of the dauer larva developmental program in Caenorhabditis elegans. Genes Dev *3*, 2039-2049.

Llave, C., Xie, Z., Kasschau, K. D., and Carrington, J. C. (2002). Cleavage of Scarecrow-like mRNA targets directed by a class of Arabidopsis miRNA. Science *297*, 2053-2056.

Ludewig, A. H., Kober-Eisermann, C., Weitzel, C., Bethke, A., Neubert, K., Hutter, H., and Antebi, A. (2004). A novel nuclear receptor/coregulator complex regulates C. elegans lipid metabolism, larval development and aging. Genes and Development, submitted.

Macknight, R., Bancroft, I., Page, T., Lister, C., Schmidt, R., Love, K., Westphal, L., Murphy, G., Sherson, S., Cobbett, C., and Dean, C. (1997). FCA, a gene controlling flowering time in Arabidopsis, encodes a protein containing RNA-binding domains. Cell *89*, 737-745.

Maniatis, T. (1999). A ubiquitin ligase complex essential for the NF-kappaB, Wnt/Wingless, and Hedgehog signaling pathways. Genes Dev *13*, 505-510.

Margottin, F., Bour, S. P., Durand, H., Selig, L., Benichou, S., Richard, V., Thomas, D., Strebel, K., and Benarous, R. (1998). A novel human WD protein, h-beta TrCp, that interacts

with HIV-1 Vpu connects CD4 to the ER degradation pathway through an F-box motif. Mol Cell *1*, 565-574.

Margottin-Goguet, F., Hsu, J. Y., Loktev, A., Hsieh, H. M., Reimann, J. D., and Jackson, P. K. (2003). Prophase destruction of Emi1 by the SCF(betaTrCP/Slimb) ubiquitin ligase activates the anaphase promoting complex to allow progression beyond prometaphase. Dev Cell *4*, 813-826.

Martinez, J., Patkaniowska, A., Urlaub, H., Luhrmann, R., and Tuschl, T. (2002). Single-stranded antisense siRNAs guide target RNA cleavage in RNAi. Cell *110*, 563-574.

Mathias, N., Johnson, S. L., Winey, M., Adams, A. E., Goetsch, L., Pringle, J. R., Byers, B., and Goebl, M. G. (1996). Cdc53p acts in concert with Cdc4p and Cdc34p to control the G1-to-S-phase transition and identifies a conserved family of proteins. Mol Cell Biol *16*, 6634-6643.

McKay, S. J., and Jones, S. J. (2002). AcePrimer: automation of PCR primer design based on gene structure. Bioinformatics *18*, 1538-1539.

Meimoun, A., Holtzman, T., Weissman, Z., McBride, H. J., Stillman, D. J., Fink, G. R., and Kornitzer, D. (2000). Degradation of the transcription factor Gcn4 requires the kinase Pho85 and the SCF(CDC4) ubiquitin-ligase complex. Mol Biol Cell *11*, 915-927.

Mello, C. C., Kramer, J. M., Stinchcomb, D., and Ambros, V. (1991). Efficient gene transfer in C.elegans: extrachromosomal maintenance and integration of transforming sequences. Embo J *10*, 3959-3970.

Miletich, I., and Limbourg-Bouchon, B. (2000). Drosophila null slimb clones transiently deregulate Hedgehog-independent transcription of wingless in all limb discs, and induce decapentaplegic transcription linked to imaginal disc regeneration. Mech Dev *93*, 15-26.

Moss, E. G., Lee, R. C., and Ambros, V. (1997). The cold shock domain protein LIN-28 controls developmental timing in C. elegans and is regulated by the lin-4 RNA. Cell *88*, 637-646.

Moss, E. G., and Tang, L. (2003). Conservation of the heterochronic regulator Lin-28, its developmental expression and microRNA complementary sites. Dev Biol *258*, 432-442.

Natorff, R., Piotrowska, M., and Paszewski, A. (1998). The Aspergillus nidulans sulphur regulatory gene sconB encodes a protein with WD40 repeats and an F-box. Mol Gen Genet *257*, 255-263.

Newman, A. P., Inoue, T., Wang, M., and Sternberg, P. W. (2000). The Caenorhabditis elegans heterochronic gene lin-29 coordinates the vulval-uterine-epidermal connections. Curr Biol *10*, 1479-1488.

Norris, D. O., Jones, R. E., and Cohen, D. C. (1973). Effects of mammalian gonadotropins (LH, FSH, HCG) and gonadal steroids on TSH-induced metamorphosis of Ambystoma tigrinum (Amphibia: Caudata). Gen Comp Endocrinol *20*, 467-473.

Olsen, P. H., and Ambros, V. (1999). The lin-4 regulatory RNA controls developmental timing in Caenorhabditis elegans by blocking LIN-14 protein synthesis after the initiation of translation. Dev Biol *216*, 671-680.

Orlicky, S., Tang, X., Willems, A., Tyers, M., and Sicheri, F. (2003). Structural basis for phosphodependent substrate selection and orientation by the SCFCdc4 ubiquitin ligase. Cell *112*, 243-256.

Ou, C. Y., Pi, H., and Chien, C. T. (2003). Control of protein degradation by E3 ubiquitin ligases in Drosophila eye development. Trends Genet *19*, 382-389.

Pasquinelli, A. E., Reinhart, B. J., Slack, F., Martindale, M. Q., Kuroda, M. I., Maller, B., Hayward, D. C., Ball, E. E., Degnan, B., Muller, P.*, et al.* (2000). Conservation of the sequence and temporal expression of let-7 heterochronic regulatory RNA. Nature *408*, 86-89.

Pasquinelli, A. E., and Ruvkun, G. (2002). Control of developmental timing by micrornas and their targets. Annu Rev Cell Dev Biol *18*, 495-513.

Passmore, L. A., and Barford, D. (2004). Getting into position: The catalytic mechanisms of protein ubiquitylation. Biochem J *Pt 379*, 513-525.

Patton, E. E., Peyraud, C., Rouillon, A., Surdin-Kerjan, Y., Tyers, M., and Thomas, D. (2000). SCF(Met30)-mediated control of the transcriptional activator Met4 is required for the G(1)-S transition. Embo J *19*, 1613-1624.

Patton, E. E., Willems, A. R., Sa, D., Kuras, L., Thomas, D., Craig, K. L., and Tyers, M. (1998). Cdc53 is a scaffold protein for multiple Cdc34/Skp1/F-box proteincomplexes that regulate cell division and methionine biosynthesis in yeast. Genes Dev *12*, 692-705.

Pickart, C. M. (2001). Mechanisms underlying ubiquitination. Annu Rev Biochem *70*, 503-533.

Pintard, L., Willis, J. H., Willems, A., Johnson, J. L., Srayko, M., Kurz, T., Glaser, S., Mains, P. E., Tyers, M., Bowerman, B., and Peter, M. (2003). The BTB protein MEL-26 is a substrate-specific adaptor of the CUL-3 ubiquitin-ligase. Nature *425*, 311-316.

Poethig, S. (1989). Genetic mosaics and cell lineage analysis in plants. Trends Genet *5*, 273-277.

Prahlad, K. V., and DeLanney, L. E. (1965). A study of induced metamorphosis in the axolotl. J Exp Zool *160*, 137-145.

Putterill, J., Robson, F., Lee, K., Simon, R., and Coupland, G. (1995). The CONSTANS gene of Arabidopsis promotes flowering and encodes a protein showing similarities to zinc finger transcription factors. Cell *80*, 847-857.

Raff, R. A. (1987). Constraint, flexibility, and phylogenetic history in the evolution of direct development in sea urchins. Dev Biol *119*, 6-19.

Reinhart, B. J., and Bartel, D. P. (2002). Small RNAs correspond to centromere heterochromatic repeats. Science *297*, 1831.

Reinhart, B. J., and Ruvkun, G. (2001). Isoform-specific mutations in the Caenorhabditis elegans heterochronic gene lin-14 affect stage-specific patterning. Genetics *157*, 199-209.

Reinhart, B. J., Slack, F. J., Basson, M., Pasquinelli, A. E., Bettinger, J. C., Rougvie, A. E., Horvitz, H. R., and Ruvkun, G. (2000). The 21-nucleotide let-7 RNA regulates developmental timing in Caenorhabditis elegans. Nature *403*, 901-906.

Rhoades, M. W., Reinhart, B. J., Lim, L. P., Burge, C. B., Bartel, B., and Bartel, D. P. (2002). Prediction of plant microRNA targets. Cell *110*, 513-520.

Riddiford, L. M. (1993). Hormone receptors and the regulation of insect metamorphosis. Receptor *3*, 203-209.

Riddiford, L. M., Cherbas, P., and Truman, J. W. (2000). Ecdysone receptors and their biological actions. Vitam Horm *60*, 1-73.

Riddiford, L. M., Hiruma, K., Zhou, X., and Nelson, C. A. (2003). Insights into the molecular basis of the hormonal control of molting and metamorphosis from Manduca sexta and Drosophila melanogaster. Insect Biochem Mol Biol *33*, 1327-1338.

Riddle, D. L., and Albert, P. S. (1997). Genetic and Environmental Regulation of Dauer Larva Development. In *C. elegans* II, T. Blumenthal, ed. (Cold Spring Harbor, N.Y., Cold Spring Harbor Laboratory Press).

Rottiers, V. (2003) Endocrine regulation of development and aging in Caenorhabditis elegans. PhD thesis.

Rougvie, A. E. (2001). Control of developmental timing in animals. Nat Rev Genet *2*, 690-701.

Rougvie, A. E., and Ambros, V. (1995). The heterochronic gene lin-29 encodes a zinc finger protein that controls a terminal differentiation event in Caenorhabditis elegans. Development *121*, 2491-2500.

Ruegger, M., Dewey, E., Gray, W. M., Hobbie, L., Turner, J., and Estelle, M. (1998). The TIR1 protein of Arabidopsis functions in auxin response and is related to human SKP2 and yeast grr1p. Genes Dev *12*, 198-207.

Ruvkun, G., Ambros, V., Coulson, A., Waterston, R., Sulston, J., and Horvitz, H. R. (1989). Molecular genetics of the Caenorhabditis elegans heterochronic gene lin-14. Genetics *121*, 501-516.

Ruvkun, G., and Giusto, J. (1989). The Caenorhabditis elegans heterochronic gene lin-14 encodes a nuclear protein that forms a temporal developmental switch. Nature *338*, 313-319.

Ruvkun, G., Wightman, B., Burglin, T., and Arasu, P. (1991). Dominant gain-of-function mutations that lead to misregulation of the C. elegans heterochronic gene lin-14, and the

evolutionary implications of dominant mutations in pattern-formation genes. Dev Suppl *1*, 47-54.

Scheffner, M., Nuber, U., and Huibregtse, J. M. (1995). Protein ubiquitination involving an E1-E2-E3 enzyme ubiquitin thioester cascade. Nature *373*, 81-83.

Seggerson, K., Tang, L., and Moss, E. G. (2002). Two genetic circuits repress the Caenorhabditis elegans heterochronic gene lin-28 after translation initiation. Dev Biol *243*, 215-225.

Sempere, L. F., Dubrovsky, E. B., Dubrovskaya, V. A., Berger, E. M., and Ambros, V. (2002). The expression of the let-7 small regulatory RNA is controlled by ecdysone during metamorphosis in Drosophila melanogaster. Dev Biol *244*, 170-179.

Sempere, L. F., Freemantle, S., Pitha-Rowe, I., Moss, E., Dmitrovsky, E., and Ambros, V. (2004). Expression profiling of mammalian microRNAs uncovers a subset of brain-expressed microRNAs with possible roles in murine and human neuronal differentiation. Genome Biol *5*, R13.

Sempere, L. F., Sokol, N. S., Dubrovsky, E. B., Berger, E. M., and Ambros, V. (2003). Temporal regulation of microRNA expression in Drosophila melanogaster mediated by hormonal signals and broad-Complex gene activity. Dev Biol *259*, 9-18.

Shostak, Y. (2002) Molecular Mechanisms of C. elegans Intracellular Receptor DAF-12 Action. PhD thesis.

Siegmund, T., and Korge, G. (2001). Innervation of the ring gland of Drosophila melanogaster. J Comp Neurol *431*, 481-491.

Simon, M. N., Pelegrini, O., Veron, M., and Kay, R. R. (1992). Mutation of protein kinase A causes heterochronic development of Dictyostelium. Nature *356*, 171-172.

Singh, R. N., Sulston J.E. (1978). Some observations on molting in C. elegans. Nematologica *24*, 63-71.

Sizemore, S. T., and Paietta, J. V. (2002). Cloning and characterization of scon-3+, a new member of the Neurospora crassa sulfur regulatory system. Eukaryot Cell *1*, 875-883.

Skowyra, D., Craig, K. L., Tyers, M., Elledge, S. J., and Harper, J. W. (1997). F-box proteins are receptors that recruit phosphorylated substrates to the SCF ubiquitin-ligase complex. Cell *91*, 209-219.

Skowyra, D., Koepp, D. M., Kamura, T., Conrad, M. N., Conaway, R. C., Conaway, J. W., Elledge, S. J., and Harper, J. W. (1999). Reconstitution of G1 cyclin ubiquitination with complexes containing SCFGrr1 and Rbx1. Science *284*, 662-665.

Slack, F., and Ruvkun, G. (1997). Temporal pattern formation by heterochronic genes. Annu Rev Genet *31*, 611-634.

Slack, F. J., Basson, M., Liu, Z., Ambros, V., Horvitz, H. R., and Ruvkun, G. (2000). The lin-41 RBCC gene acts in the C. elegans heterochronic pathway between the let-7 regulatory RNA and the LIN-29 transcription factor. Mol Cell *5*, 659-669.

Somers, D. E., Schultz, T. F., Milnamow, M., and Kay, S. A. (2000). ZEITLUPE encodes a novel clock-associated PAS protein from Arabidopsis. Cell *101*, 319-329.

Sonoda, J., and Wharton, R. P. (1999). Recruitment of Nanos to hunchback mRNA by Pumilio. Genes Dev *13*, 2704-2712.

Sonoda, J., and Wharton, R. P. (2001). Drosophila Brain Tumor is a translational repressor. Genes Dev *15*, 762-773.

Spencer, E., Jiang, J., and Chen, Z. J. (1999). Signal-induced ubiquitination of IkappaBalpha by the F-box protein Slimb/beta-TrCP. Genes Dev *13*, 284-294.

Sulston, J., and Hodgkin, J. (1988). Methods. In The nematode, Caenorhabditis elegans, W. B. Wood, ed. (Cold Spring Harbor, N.Y., Cold Spring Harbor Laboratory Press), pp. 587-606.

Sulston, J. E. (1983). Neuronal cell lineages in the nematode Caenorhabditis elegans. Cold Spring Harb Symp Quant Biol *48 Pt 2*, 443-452.

Sulston, J. E., Albertson, D. G., and Thomson, J. N. (1980). The Caenorhabditis elegans male: postembryonic development of nongonadal structures. Dev Biol *78*, 542-576.

Sulston, J. E., and Horvitz, H. R. (1977). Post-embryonic cell lineages of the nematode, Caenorhabditis elegans. Dev Biol *56*, 110-156.

Sutterluty, H., Chatelain, E., Marti, A., Wirbelauer, C., Senften, M., Muller, U., and Krek, W. (1999). p45SKP2 promotes p27Kip1 degradation and induces S phase in quiescent cells. Nat Cell Biol *1*, 207-214.

Tang, G., Reinhart, B. J., Bartel, D. P., and Zamore, P. D. (2003). A biochemical framework for RNA silencing in plants. Genes Dev *17*, 49-63.

Taurog, A., Oliver, C., Eskay, R. L., Porter, J. C., and McKenzie, J. M. (1974). The role of TRH in the neoteny of the Mexican axolotl (Ambystoma mexicanum). Gen Comp Endocrinol *24*, 267-279.

Telfer, A., and Poethig, R. S. (1998). HASTY: a gene that regulates the timing of shoot maturation in Arabidopsis thaliana. Development *125*, 1889-1898.

Theodosiou, N. A., Zhang, S., Wang, W. Y., and Xu, T. (1998). slimb coordinates wg and dpp expression in the dorsal-ventral and anterior-posterior axes during limb development. Development *125*, 3411-3416.

Thomas, D., Kuras, L., Barbey, R., Cherest, H., Blaiseau, P. L., and Surdin-Kerjan, Y. (1995). Met30p, a yeast transcriptional inhibitor that responds to S-adenosylmethionine, is an essential protein with WD40 repeats. Mol Cell Biol *15*, 6526-6534.

Thummel, C. S. (1996). Files on steroids-Drosophila metamorphosis and the mechanisms of steroid hormone action. Trends Genet *12*, 306-310.

Thummel, C. S. (2001). Molecular mechanisms of developmental timing in C. elegans and Drosophila. Dev Cell *1*, 453-465.

Tongaonkar, P., Chen, L., Lambertson, D., Ko, B., and Madura, K. (2000). Evidence for an interaction between ubiquitin-conjugating enzymes and the 26S proteasome. Mol Cell Biol *20*, 4691-4698.

Tsvetkov, L. M., Yeh, K. H., Lee, S. J., Sun, H., and Zhang, H. (1999). p27(Kip1) ubiquitination and degradation is regulated by the SCF(Skp2) complex through phosphorylated Thr187 in p27. Curr Biol *9*, 661-664.

Tyers, M., and Jorgensen, P. (2000). Proteolysis and the cell cycle: with this RING I do thee destroy. Curr Opin Genet Dev *10*, 54-64.

Vella, M. C., Choi, E. Y., Lin, S. Y., Reinert, K., and Slack, F. J. (2004). The C. elegans microRNA let-7 binds to imperfect let-7 complementary sites from the lin-41 3'UTR. Genes Dev *18*, 132-137.

Verma, R., Chen, S., Feldman, R., Schieltz, D., Yates, J., Dohmen, J., and Deshaies, R. J. (2000). Proteasomal proteomics: identification of nucleotide-sensitive proteasome-interacting proteins by mass spectrometric analysis of affinity-purified proteasomes. Mol Biol Cell *11*, 3425-3439.

Verma, R., Feldman, R. M., and Deshaies, R. J. (1997). SIC1 is ubiquitinated in vitro by a pathway that requires CDC4, CDC34, and cyclin/CDK activities. Mol Biol Cell *8*, 1427-1437.

Volpe, T. A., Kidner, C., Hall, I. M., Teng, G., Grewal, S. I., and Martienssen, R. A. (2002). Regulation of heterochromatic silencing and histone H3 lysine-9 methylation by RNAi. Science *297*, 1833-1837.

von Arnim, A. G. (2001). A hitchhiker's guide to the proteasome. Sci STKE *2001*, PE2.

Wang, G., Wang, B., and Jiang, J. (1999). Protein kinase A antagonizes Hedgehog signaling by regulating both the activator and repressor forms of Cubitus interruptus. Genes Dev *13*, 2828-2837.

Wang, X., Feng, S., Nakayama, N., Crosby, W. L., Irish, V., Deng, X. W., and Wei, N. (2003). The COP9 signalosome interacts with SCF UFO and participates in Arabidopsis flower development. Plant Cell *15*, 1071-1082.

Wanker, E. E., Rovira, C., Scherzinger, E., Hasenbank, R., Walter, S., Tait, D., Colicelli, J., and Lehrach, H. (1997). HIP-I: a huntingtin interacting protein isolated by the yeast two-hybrid system. Hum Mol Genet *6*, 487-495.

Weiss, J., Axelrod, L., Whitcomb, R. W., Harris, P. E., Crowley, W. F., and Jameson, J. L. (1992). Hypogonadism caused by a single amino acid substitution in the beta subunit of luteinizing hormone. N Engl J Med *326*, 179-183.

White, J. G. (1988). The Anatomy In The Nematode Caenorhabditis. elegans, W. B. Wood, ed. (Cold Spring Harbor, Cold Spring Habor Laboratory Press).

White, K. P., Hurban, P., Watanabe, T., and Hogness, D. S. (1997). Coordination of Drosophila metamorphosis by two ecdysone-induced nuclear receptors. Science *276*, 114-117.

Wicks, S. R., Yeh, R. T., Gish, W. R., Waterston, R. H., and Plasterk, R. H. (2001). Rapid gene mapping in Caenorhabditis elegans using a high density polymorphism map. Nat Genet *28*, 160-164.

Wightman, B., Burglin, T. R., Gatto, J., Arasu, P., and Ruvkun, G. (1991). Negative regulatory sequences in the lin-14 3'-untranslated region are necessary to generate a temporal switch during Caenorhabditis elegans development. Genes Dev *5*, 1813-1824.

Wightman, B., Ha, I., and Ruvkun, G. (1993). Posttranscriptional regulation of the heterochronic gene lin-14 by lin-4 mediates temporal pattern formation in C. elegans. Cell *75*, 855-862.

Winston, J. T., Koepp, D. M., Zhu, C., Elledge, S. J., and Harper, J. W. (1999a). A family of mammalian F-box proteins. Curr Biol *9*, 1180-1182.

Winston, J. T., Strack, P., Beer-Romero, P., Chu, C. Y., Elledge, S. J., and Harper, J. W. (1999b). The SCFbeta-TRCP-ubiquitin ligase complex associates specifically with phosphorylated destruction motifs in IkappaBalpha and beta-catenin and stimulates IkappaBalpha ubiquitination in vitro. Genes Dev *13*, 270-283.

Wirbelauer, C., Sutterluty, H., Blondel, M., Gstaiger, M., Peter, M., Reymond, F., and Krek, W. (2000). The F-box protein Skp2 is a ubiquitylation target of a Cul1-based core ubiquitin ligase complex: evidence for a role of Cul1 in the suppression of Skp2 expression in quiescent fibroblasts. Embo J *19*, 5362-5375.

Wood, W. B. (1988). Introduction to C. elegans Biology. In The Nematode C. elegans, W. B. Wood, ed. (Cold Spring Harbor, N.Y., Cold Spring Harbor Laboratory Press).

Wu, G., Lyapina, S., Das, I., Li, J., Gurney, M., Pauley, A., Chui, I., Deshaies, R. J., and Kitajewski, J. (2001). SEL-10 is an inhibitor of notch signaling that targets notch for ubiquitin-mediated protein degradation. Mol Cell Biol *21*, 7403-7415.

Wu, S. M., Leschek, E. W., Rennert, O. M., and Chan, W. Y. (2000). Luteinizing hormone receptor mutations in disorders of sexual development and cancer. Front Biosci *5*, D343-352.

Xie, D. X., Feys, B. F., James, S., Nieto-Rostro, M., and Turner, J. G. (1998). COI1: an Arabidopsis gene required for jasmonate-regulated defense and fertility. Science *280*, 1091-1094.

Xie, Y., and Varshavsky, A. (1999). The E2-E3 interaction in the N-end rule pathway: the RING-H2 finger of E3 is required for the synthesis of multiubiquitin chain. Embo J *18*, 6832-6844.

Xie, Y., and Varshavsky, A. (2000). Physical association of ubiquitin ligases and the 26S proteasome. Proc Natl Acad Sci U S A *97*, 2497-2502.

Xu, L., Wei, Y., Reboul, J., Vaglio, P., Shin, T. H., Vidal, M., Elledge, S. J., and Harper, J. W. (2003a). BTB proteins are substrate-specific adaptors in an SCF-like modular ubiquitin ligase containing CUL-3. Nature *425*, 316-321.

Xu, P., Vernooy, S. Y., Guo, M., and Hay, B. A. (2003b). The Drosophila microRNA Mir-14 suppresses cell death and is required for normal fat metabolism. Curr Biol *13*, 790-795.

Yamada, M., Murata, T., Hirose, S., Lavorgna, G., Suzuki, E., and Ueda, H. (2000). Temporally restricted expression of transcription factor betaFTZ-F1: significance for embryogenesis, molting and metamorphosis in Drosophila melanogaster. Development *127*, 5083-5092.

Yan, F., Gao, X., Lonard, D. M., and Nawaz, Z. (2003). Specific ubiquitin-conjugating enzymes promote degradation of specific nuclear receptor coactivators. Mol Endocrinol *17*, 1315-1331.

Yochem, J., Gu, T., and Han, M. (1998). A new marker for mosaic analysis in Caenorhabditis elegans indicates a fusion between hyp6 and hyp7, two major components of the hypodermis. Genetics *149*, 1323-1334.

Young, M. W. (2000). Life's 24-hour clock: molecular control of circadian rhythms in animal cells. Trends Biochem Sci *25*, 601-606.

Zheng, N., Schulman, B. A., Song, L., Miller, J. J., Jeffrey, P. D., Wang, P., Chu, C., Koepp, D. M., Elledge, S. J., Pagano, M.*, et al.* (2002). Structure of the Cul1-Rbx1-Skp1-F boxSkp2 SCF ubiquitin ligase complex. Nature *416*, 703-709.

Zhou, P., and Howley, P. M. (1998). Ubiquitination and degradation of the substrate recognition subunits of SCF ubiquitin-protein ligases. Mol Cell *2*, 571-580.