

Review

Nature Reviews Genetics 3, 356-369 (May 2002) | doi:10.1038/nrg794

ARTICLE SERIES: [The Art and Design of Genetic Screens](#)

[\(/nrg/series/screens/index.html\)](/nrg/series/screens/index.html)

The art and design of genetic screens: *Caenorhabditis elegans*

Erik M. Jorgensen [1 \(#a1\)](#) & Susan E. Mango [2 \(#a2\)](#) [About the authors](#)

[\(/nrg/journal/v3/n5/authors/nrg794.html\)](/nrg/journal/v3/n5/authors/nrg794.html)

[top \(#top\)](#)

The nematode *Caenorhabditis elegans* was chosen as a model genetic organism because its attributes, chiefly its hermaphroditic lifestyle and rapid generation time, make it suitable for the isolation and characterization of genetic mutants. The most important challenge for the geneticist is to design a genetic screen that will identify mutations that specifically disrupt the biological process of interest. Since 1974, when Sydney Brenner published his pioneering genetic screen, researchers have developed increasingly powerful methods for identifying genes and genetic pathways in *C. elegans*.

View [At a Glance \(/nrg/journal/v3/n5/execsumm/nrg794.html\)](#)

In 1963, Sydney Brenner realized that the central dogma of molecular biology — that DNA makes RNA makes protein — had been outlined in form, and was casting about for the next big problem to tackle. Brenner concluded that the organizing principles of multicellular organisms were the mysteries that scientists must confront in the future. Specifically, he believed that the nervous system and embryonic development were the most exciting areas to study in biology. Brenner decided that a new experimental organism was needed for a genetic approach to these problems (reviewed in Ref. [1 \(#B1\)](#)). He chose the nematode *Caenorhabditis elegans* ([Fig. 1 \(#f1\)](#)).

Figure 1 | Scanning electron micrograph of a *Caenorhabditis elegans* hermaphrodite. [\(/nrg/journal/v3/n5/fig_tab/nrg794_F1.html\)](/nrg/journal/v3/n5/fig_tab/nrg794_F1.html)



[\(/nrg/journal/v3/n5/fig_tab/nrg794_F1.html\)](/nrg/journal/v3/n5/fig_tab/nrg794_F1.html)

(Photo courtesy of Juergen Berger and Ralf Sommer, Max Planck Institute, Tuebingen, Germany.)

[High resolution image and legend \(87 KB\)](/nrg/journal/v3/n5/fig_tab/nrg794_F1.html)[\(/nrg/journal/v3/n5/fig_tab/nrg794_F1.html\)](/nrg/journal/v3/n5/fig_tab/nrg794_F1.html)[Figures and tables index](/nrg/journal/v3/n5/fig_tab/nrg794_ft.html)[\(/nrg/journal/v3/n5/fig_tab/nrg794_ft.html\)](/nrg/journal/v3/n5/fig_tab/nrg794_ft.html)

One criterion for selecting a genetic organism is that it should be the simplest organism that has the traits of interest. Brenner thought that the simplicity of *C. elegans* ([Box 1 \(/nrg/journal/v3/n5/box/nrg794_BX1.html\)](/nrg/journal/v3/n5/box/nrg794_BX1.html)) would make the worm the T4 phage of metazoan studies. A second guideline in the selection of model organisms is ease of manipulation. *C. elegans* is small, and can be grown either in small Petri dishes or in liquid culture if large numbers are required. It has a three-day generation time at room temperature, and strains can be kept as frozen stocks. In 1967, Brenner carried out his first mutagenesis and, in 1974, he published the characterization of ~100 genes that generated viable, visible phenotypes² ([#B2](#)). The screening approaches that are described in this landmark paper remain a guide for the design of simple genetic screens, as well as for the more elaborate ones that have since been developed.

[Box 1 | Morphology and life cycle of *Caenorhabditis elegans*](/nrg/journal/v3/n5/box/nrg794_BX1.html)[\(/nrg/journal/v3/n5/box/nrg794_BX1.html\)](/nrg/journal/v3/n5/box/nrg794_BX1.html)[Full box \(/nrg/journal/v3/n5/box/nrg794_BX1.html\)](/nrg/journal/v3/n5/box/nrg794_BX1.html)

In this review, we first discuss simple screens that are used routinely in worm laboratories. These simple screens can be conducted in a mutant strain to identify suppressor or enhancer mutations and, thereby, genes that are involved in a specific process. Second, we discuss screens that are designed to identify mutations in a particular biological process. Some of these have used selection procedures to accelerate the identification of mutants, whereas others have required a great deal of labour to identify the relevant mutants. Finally, we discuss screens that are likely to be used more often in the future; specifically, sensitized screens and screens for redundant genes.

Simple screens

Most of the mutations that were identified in Brenner's paper were visible, recessive mutations. Such mutations can be identified using a simple F₂ screen ([Fig. 2 \(#f2\)](#)). In these screens, a mutagen, such as ethyl methane sulphonate (EMS), is used to induce mutations in the sperm and oocytes of wild-type hermaphrodites (how this is done in practice is outlined in [Box 2 \(/nrg/journal/v3/n5/box/nrg794_BX2.html\)](/nrg/journal/v3/n5/box/nrg794_BX2.html)). The mutagenized worms are placed on Petri dishes and grown for two generations to produce homozygous mutants. Worms that show a mutant phenotype are then

transferred individually to new plates to determine whether their phenotype is transmitted to the next generation. In a typical screen that lasts about two weeks, 12,000 copies of any particular gene can be assayed. Using standard concentrations of mutagen, the frequency at which mutations at any particular locus are recovered is about one null mutation for every 2,000 copies of the gene that is analysed in the screen. So, in a typical screen of 12,000 haploid genomes, we would expect to recover six mutations in a particular gene.

Figure 2 | A simple F₂ screen. (/nrg/journal/v3/n5/fig_tab/nrg794_F2.html)



(/nrg/journal/v3/n5/fig_tab/nrg794_F2.html)

a | A population of wild-type hermaphrodites is exposed to a mutagen and genes are randomly mutated in the germ cells (mutated germ cells are indicated in red). For example, one sperm could be mutated for the gene *unc-32*, which is required for the correct functioning of the nervous system. Fertilization of an egg by this sperm will result in a heterozygous F₁ individual. Because this animal is a self-fertilizing hermaphrodite, it will produce eggs and sperm that bear this mutated gene; one-quarter of its F₂ progeny will be homozygous for the mutation and result in a coiled phenotype (shown in **b**). Such an animal can be transferred to a plate, and in three days, its F₃ progeny can be inspected to determine whether the mutant phenotype breeds true. **b** | An *unc-32(f131)* mutant. *unc-32* encodes the *a* subunit of the Vo complex of the vacuolar ATPase [119 \(#B119\)](#) — a proton pump that generates the energy that is required for transporting neurotransmitter into synaptic vesicles. Animals that lack the proton pump do not release normal levels of neurotransmitter at the synapse and therefore have uncoordinated movement.

[High resolution image and legend \(80 KB\)](#)

(/nrg/journal/v3/n5/fig_tab/nrg794_F2.html)

[Figures and tables index](#)

(/nrg/journal/v3/n5/fig_tab/nrg794_ft.html)

Box 2 | Protocol for EMS mutagenesis in worms

(/nrg/journal/v3/n5/box/nrg794_BX2.html)

Full box (/nrg/journal/v3/n5/box/nrg794_BX2.html)

Using this approach, Brenner identified 619 mutants with visible phenotypes. Of

particular interest was the uncoordinated class, which failed to move normally. Movement is largely dispensable for the worm under laboratory conditions because food is plentiful and sex is superfluous. Therefore, this kind of screen is perfectly suited for identifying proteins, such as the homeodomain transcription factor UNC-30 (uncoordinated 30) that regulate neuronal fate³ (#B3). [UNC-30](http://www.wormbase.org/db/gene/locus?name=unc-30;class=Locus) (<http://www.wormbase.org/db/gene/locus?name=unc-30;class=Locus>) is required for several aspects of the differentiation of certain [GABA NEURONS](http://nrg/journal/v3/n5/glossary/nrg794.html#df1) ([/nrg/journal/v3/n5/glossary/nrg794.html#df1](http://nrg/journal/v3/n5/glossary/nrg794.html#df1)); the muscles of these mutants can contract, but have difficulty relaxing owing to the lack of inhibitory neurotransmission. Brenner also identified worms with defects in neuronal pathfinding — for example, those caused by loss of the graded extracellular signal [UNC-6](http://www.wormbase.org/db/gene/locus?name=unc-6;class=Locus) (<http://www.wormbase.org/db/gene/locus?name=unc-6;class=Locus>) /netrin⁴, (#B4) ⁵ (#B5). As a result, these mutants have severe defects in the axon outgrowth of the motor neurons and move poorly.

Brenner's screen was designed primarily to show that visible mutants could be obtained in the nematode. In addition to the uncoordinated class, Brenner identified mutants with small bodies, blistered cuticles, twitching muscles or rolling locomotion. He also identified mutants with long bodies, dumpy bodies, forked heads or bent heads. The variety of phenotypes that was observed by Brenner answered the criticism that it would be impossible to obtain enough useful genetic markers in an organism that was shaped like a pipe. One decade later, molecular tools were added to the geneticist's toolbox for the characterization of genes. Specifically, the genome was subcloned and sequenced, and straightforward transgenic techniques were developed ([Box 3](http://nrg/journal/v3/n5/box/nrg794_BX3.html) ([/nrg/journal/v3/n5/box/nrg794_BX3.html](http://nrg/journal/v3/n5/box/nrg794_BX3.html))).

[Box 3 | Cloning in *Caenorhabditis elegans*: moving from mutation to gene](http://nrg/journal/v3/n5/box/nrg794_BX3.html) ([/nrg/journal/v3/n5/box/nrg794_BX3.html](http://nrg/journal/v3/n5/box/nrg794_BX3.html))

[Full box](http://nrg/journal/v3/n5/box/nrg794_BX3.html) ([/nrg/journal/v3/n5/box/nrg794_BX3.html](http://nrg/journal/v3/n5/box/nrg794_BX3.html))

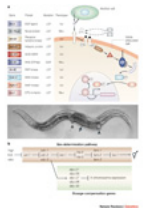
Identifying genetic pathways

A hunt for a mutant is, by nature, a random process. Although geneticists have preconceived ideas of what phenotypes are expected to be recovered in a screen, they are usually surprised at the actual phenotypic landscape of the organism. However, the presence of a particular mutant phenotype provides a geneticist with a point of entry into a biological process. Once the phenotype that is associated with a particular biological process is known, more genes that are involved in that process can be identified in two ways: using additional simple screens and using modifier screens.

Simple screens. The most straightforward method for identifying more genes that function in a given process is to screen for more mutants with the same phenotype.

For example, John Sulston and H. Robert Horvitz^{6 (#B6)} identified mutants with defects in the differentiation of the vulva from epidermal cells on the ventral surface of the animal. These mutants were identified as strains that either lacked a vulva ('vulvaless') or had ectopic vulvae (that is, showed the 'multivulva' phenotype; [Fig. 3b \(#f3\)](#)). Chip Ferguson, who was working with Horvitz, subsequently isolated 95 mutations that caused these phenotypes^{7 (#B7)}, comprising a total of 22 genes. Subsequent molecular studies revealed that mutants with vulvaless phenotypes defined two signalling pathways — the epidermal growth factor (EGF)/RAS pathway and the Notch signalling pathway^{8 (#B8)}.

Figure 3 | Signalling cascades. ([/nrg/journal/v3/n5/fig_tab/nrg794_F3.html](#))



([/nrg/journal/v3/n5/fig_tab/nrg794_F3.html](#))

a | The Ras signalling pathway is required for the formation of the vulva (the absence of the vulva is known as the vulvaless phenotype, Vul). The epidermal growth factor (EGF) ligand produced by the **ANCHOR CELL** ([/nrg/journal/v3/n5/glossary/nrg794.html#df5](#)) binds the receptor tyrosine kinase on one or a few of the five vulval precursor cells, and initiates a signal-transduction cascade that culminates in the inactivation of the LIN-1 transcriptional inhibitor. Constitutive formation of the vulva by all of the vulval precursor cells can be caused by a gain-of-function (GOF) mutation in Ras or by loss-of-function (LOF) mutations in, for example, both *lin-15a* and *lin-15b* (the two *lin-15* isoforms act redundantly). Constitutive activation of the Ras pathway causes the formation of pseudovulvae along the ventral surface (arrowheads; the arrow points to the true vulva). This multivulval (Muv) phenotype can be suppressed by lof mutations in downstream components of the pathway. **b** | The sex-determination pathway. The ratio of X chromosomes to autosomes (A) regulates the expression of the *xol-1* gene. In hermaphrodites, which have two X chromosomes, a high X/A ratio inhibits *xol-1* expression. In the absence of XOL-1 protein, the *sdc* genes are expressed. These genes inhibit the male-determining signal HER-1 and simultaneously activate the dosage-compensation genes. *dpy*, *dumpy*; ETS, E26 transformation defective; *fem*, *feminization*; GNRF, guanylyl-nucleotide-release factor; *her*, *hermaphrodization*; *let*, *lethal*; *lin*, *abnormal cell lineage*; *map*, *mitogen-activated protein*; *mek*, *MAPK/ERK kinase*; *mpk*, *MAP kinase*; *raf*, *Ras-*

associated factor; sdc, sex determination and dosage compensation; sem, sex muscle abnormal; SOS, son of sevenless; tra, transformer; trx, transcription; xol, XO lethal.

[High resolution image and legend \(97 KB\)](#)

[\(/nrg/journal/v3/n5/fig_tab/nrg794_F3.html\)](/nrg/journal/v3/n5/fig_tab/nrg794_F3.html)

[Figures and tables index](#)

[\(/nrg/journal/v3/n5/fig_tab/nrg794_ft.html\)](/nrg/journal/v3/n5/fig_tab/nrg794_ft.html)

Modifier screens. Another way to identify components that function in a genetic pathway is to use modifier screens — that is, enhancer or suppressor screens. The starting material in such a screen is a strain whose genetic composition causes a defined phenotypic defect. Second-site mutations that either enhance (worsen) or suppress (ameliorate) that phenotype can then be screened. These second-site mutations frequently identify proteins that are involved in the same process as that disrupted in the starting strain. Historically, suppressor screens are more important than enhancer screens in *C. elegans* research. However, enhancer screens are likely to become more important in the future (as discussed below) because they are more generally applicable and because they are inherently more powerful. Typically, many genes can enhance a mutant phenotype, whereas only mutations in a few key regulators can suppress a mutant phenotype.

In some cases, mutations in a protein constitutively activate a signalling cascade. For example, activating mutations in the RAS GTPase cause a multivulva phenotype⁹, [9](#), [10](#) ([#B10](#)). Second-site mutations that disrupt proteins in the signalling cascade that is initiated by activated RAS suppressed the formation of the ectopic vulvae and identified proteins in the MAP (mitogen-activated protein) kinase signalling pathway [11](#), ([#B11](#)) [12](#), ([#B12](#)) [13](#), ([#B13](#)) [14](#), ([#B14](#)) [15](#), ([#B15](#)) [16](#), ([#B16](#)) [17](#), ([#B17](#)) [18](#) ([#B18](#)). Suppressor screens for loss-of-function alleles have also been used to analyse a pathway. Mutations in the negative regulators of a pathway cause constitutive activation of the signalling cascade. For example, the [lin-15](#) (<http://www.wormbase.org/db/gene/locus?name=lin-15;class=Locus>) (*lineage 15*) **OPERON** (</nrg/journal/v3/n5/glossary/nrg794.html#df3>) negatively regulates the RAS pathway ([Fig. 3a](#) ([#f3](#))). Loss-of-function mutations of this operon result in a multivulval phenotype by allowing constitutive activation of EGF-receptor signalling. Screens for second-site mutations that suppressed the multivulval phenotype of *lin-15* mutations identified components upstream and downstream of RAS in this signalling cascade, including mutations in the EGF tyrosine-kinase receptor [LET-23](#) (<http://www.wormbase.org/db/gene/locus?name=let-23;class=Locus>) (lethal 23), the adaptor protein [SEM-5](#) ([<http://www.nature.com/nrg/journal/v3/n5/full/nrg794.html>](http://www.wormbase.org/db/gene/locus?name=sem-</p>
</div>
<div data-bbox=)

[5;class=Locus](#)) (sex muscle abnormal 5), the guanylyl-nucleotide-releasing factor LET-341 (also known as **SOS-1** (<http://www.wormbase.org/db/gene/locus?name=sos-1&class=Locus>)) and RAS itself **19** ([#B19](#)).

Negative regulatory hierarchies are particularly amenable to suppressor screens because simple loss-of-function mutations at several steps can activate the pathway, and mutations in alternating steps can suppress the activated pathway. Moreover, epistatic relationships — that is, the phenotypes of double mutants — can be used to order the genes in the pathway. The sex-determination pathway in *C. elegans* is an inhibitory cascade that results in the determination of either a hermaphrodite or a male (**Fig. 3b** ([#f3](#))). Mutations in genes in this pathway lead to the absence of males or the absence of hermaphrodites; for example, mutations in the **her-1** (<http://www.wormbase.org/db/gene/locus?name=sos-1&class=Locus>) (*hermaphrodization 1*) gene transform XO males into XO hermaphrodites. But how can we spot the rare, transformed hermaphrodite on a plate that is covered with hermaphrodites? Jonathan Hodgkin conducted a screen for genes that are required for male development in a **him-5** (<http://www.wormbase.org/db/gene/locus?name=sos-1&class=Locus>) (*high incidence of males 5*) **dpy-21** (<http://www.wormbase.org/db/gene/locus?name=sos-1&class=Locus>) (*dumpy 21*) background **20** ([#B20](#)). *him-5* causes a high frequency of XO males to be segregated due to non-disjunction of the X chromosome. *dpy-21* causes all XX, but not XO, animals to be dumpy (short and fat). Mutations in *her-1* will cause XO animals to appear as non-dumpy hermaphrodites and are easily spotted among the many dumpy hermaphrodites on the plate. The identification of mutations that transform one sex into the other can be used in subsequent screens to identify more components of the pathway. Specifically, second-site mutations can be observed that restore the presence of males or hermaphrodites. The **XOL-1** (<http://www.wormbase.org/db/gene/locus?name=xol-1;class=Locus>) protein (encoded by *xol-1*; *XO lethal 1*) specifies male development and enhances X-linked gene expression in males to compensate for their lower X-chromosomal dosage compared with hermaphrodites (**Fig. 3b** ([#f3](#))). *him-5 xol-1* strains produce numerous XO animals owing to the *him-5* mutation; however, these animals die because the *xol-1* mutation results in under-expression of X-linked genes. By screening for mutations that restored male viability in the *him-5 xol-1* strain — that is, for mutations that would allow the initiation of male development in XO animals and correct the levels of dosage compensation — Chad Nusbaum, Barbara Meyer and colleagues identified 21 alleles of **sdc-2** (<http://www.wormbase.org/db/gene/locus?name=sdc-2;class=Locus>) (*sex and dosage compensation 2*), which is directly downstream of, and repressed by, *xol-1* (Refs **21** ([#B21](#)), **22** ([#B22](#))) (**Fig. 3** ([#f3](#))).

Screens from heaven

There is a painting from Pieter Brueghel that portrays a magical land in which everything is edible — houses are made of pies, chickens cook themselves and throw themselves onto the plate, and pigs conveniently carry knives tucked into them so that a piece of bacon can be cut off. Geneticists dream of this land, a land in which mutants throw themselves onto Petri dishes and require minimal effort to isolate. Such a land exists in the form of selection screens. In contrast to the simple screens described above, which require every animal to be inspected carefully for the presence or absence of a particular phenotype, selection screens facilitate the identification of the desired mutant by eliminating individuals of irrelevant genotypes.

Selections. The easiest of such screens are drug selections. For example, Brenner screened for mutants that were resistant to inhibitors of acetylcholinesterase^{2 (#B2)}. Acetylcholine is normally removed from neuromuscular junctions by the enzyme acetylcholinesterase. Drugs such as the nerve gas Sarin or the pesticide Aldicarb kill an organism by blocking the degradative enzyme. In wild-type animals that are treated with Aldicarb, acetylcholine builds up in the synaptic cleft and eventually kills the animal by chronic excitation. Mutants that cannot release acetylcholine into the synaptic cleft cannot accumulate the neurotransmitter in the presence of the drug, and so these animals survive. Using this screen for Aldicarb-resistant mutants, Brenner identified mutations in a gene, *unc-17* (<http://www.wormbase.org/db/gene/locus?name=unc-17;class=Locus>), that is required to transport acetylcholine into the synaptic vesicle^{23 (#B23)}. Many other Aldicarb-resistant mutants have been isolated, including mutants for the kinesin that transports synaptic vesicles to the synapse^{24 (#B24)}, proteins that are involved in synaptic vesicle exocytosis^{25, (#B25) 26, (#B26) 27 (#B27)} and proteins that are involved in endocytosis^{28, (#B28) 29 (#B29)}.

Selections for suppressors. Screens that are suppressor screens as well as selections are particularly powerful. In some cases, the initial genotype can be engineered into the strain by expressing proteins that constitutively activate a pathway. For example, the trimeric G protein $G_{s\alpha}$ can be locked in the active form by mutating the GTPase domain. The expression of activated G_s under the control of a heat-shock promoter^{30 (#B30)} or a neuron-specific promoter^{31 (#B31)} causes neuronal degeneration, which induces death or paralysis in the animal. In theory, mutations that suppress this phenotype, by restoring viability or movement to these animals, could be found. Specifically, mutations in downstream components in the pathway — that is, in genes that encode proteins required for neuronal death — were identified as second-site mutations that restored cell viability. Suppressors of

neuronal degeneration showed that necrotic cell death acts through cyclic-AMP signals because adenylyl cyclase is required for normal levels of G_s-mediated cell death.

Benefits of large-scale screens. In the best cases, suppressor and selection screens in *C. elegans* can be designed to survey millions of animals. Screens of this magnitude are a powerful means to define genetic pathways for three reasons. First, saturation for genes that can be mutated to give a specific phenotype can identify many or all of the components in a particular pathway. The presence of many alleles in all complementation groups shows that the screen is saturated and suggests most of the components of a genetic pathway have been identified. Importantly, however, even saturation screens can miss some components. For example, a gene that functions in more than one pathway might be missed because it is associated with a different phenotype than the specific phenotype that is being selected. Alternatively, certain genes might be small targets for mutagenesis. [lin-4](#) (<http://www.wormbase.org/db/gene/locus?name=lin-4;class=Locus>) is a 22-nucleotide functional RNA that regulates the timing and order of larval stages during development³² (#B32). Only two alleles of *lin-4* have been isolated, despite extensive screening. Finally, the function of some proteins might be redundant with other proteins that are encoded elsewhere in the genome; null mutations in a single gene would therefore have a wild-type phenotype.

A second advantage of large-scale screens is that they can identify unusual mutations that arise less frequently than null mutations. For example, null mutations for most components of the RAS signalling pathway are lethal. However, partial loss-of-function alleles are associated with viable, vulvaless phenotypes that allowed researchers to define components of the RAS pathway⁷ (#B7). Large-scale screens can also identify gain-of-function alleles. Such alleles might be very rare as they might require changes in specific amino acids; for example, five gain-of-function alleles of RAS have been isolated that activate the protein, but all five cause an identical amino-acid change¹⁸ (#B18). Large-scale suppressor screens can also be carried out to obtain allele-specific suppressors. Such suppressors can identify proteins that interact physically with each other because altered conformations of a protein can be suppressed by compensating mutations in its partner. Normally, the size of screens that is necessary to identify such specific changes precludes their use in higher eukaryotes, unless the suppressor screen is designed as a selection. David Miller and co-workers³³ (#B33) identified a protein that interacts physically with the homeodomain protein **UNC-4** (<http://www.wormbase.org/db/gene/locus?name=unc-4;class=Locus>). *unc-4* mutants cannot crawl backwards because of defects in synaptic connectivity. By searching for mutants that could suppress a conditional

allele of *unc-4*, Miller identified gain-of-function mutations in [unc-37](http://www.wormbase.org/db/gene/locus?name=unc-37;class=Locus) (<http://www.wormbase.org/db/gene/locus?name=unc-37;class=Locus>). As expected, these unusual mutations in *unc-37* arose at a very low frequency: Miller found only four suppressor mutations after screening 10^6 haploid genomes, which is one thousandfold lower than the frequency of obtaining typical loss-of-function alleles. To make it feasible to survey such a large number of animals, Miller began with a strain carrying two mutations that together induced a 'stuck' phenotype — *unc-4* (cannot move backwards) and [unc-24](http://www.wormbase.org/db/gene/locus?name=unc-24;class=Locus) (<http://www.wormbase.org/db/gene/locus?name=unc-24;class=Locus>) (cannot move forwards) — and searched for worms that could move backwards towards a distant source of food. Importantly, the gain-of-function *unc-37* alleles that were isolated in this screen could not suppress a null allele of *unc-4*, which shows that suppression was not due to a bypass of *unc-4* activity. Moreover, the phenotype of loss-of-function mutations in *unc-37* resembled those associated with mutations in *unc-4*. Subsequent studies have shown that UNC-37 is a homologue of the *Drosophila melanogaster* gene known as [groucho](http://www.ncbi.nlm.nih.gov/LocusLink/LocRpt.cgi?l=43162) (<http://www.ncbi.nlm.nih.gov/LocusLink/LocRpt.cgi?l=43162>), and is a co-factor for UNC-4; together these two proteins regulate transcription in neuronal cells³⁴ ([#B34](#)).

Third, large-scale screens can be used for the structure–function analysis of a protein. For example, the analysis of the 16 mutations of [SDC-3](http://www.wormbase.org/db/gene/locus?name=sdC-3;class=Locus) (<http://www.wormbase.org/db/gene/locus?name=sdC-3;class=Locus>) revealed that this protein mediates dual functions³⁵ ([#B35](#)). The zinc-finger domain is required for downregulating the expression of genes on the two X chromosomes in hermaphrodites to match the gene dosage provided by the single X chromosome in males ([Fig. 3b](#) ([#f3](#))). A second domain in SDC-3 is similar to the ATP-binding domain of myosin and is required in hermaphrodites for sex determination. A second example of structure–function analysis comes from Andrew Chisholm's lab, which isolated and characterized many alleles of the ephrin receptor [vab-1](http://www.wormbase.org/db/gene/locus?name=vab-1;class=Locus) (<http://www.wormbase.org/db/gene/locus?name=vab-1;class=Locus>) (*variable 1*), and its ligand [vab-2](http://www.wormbase.org/db/gene/locus?name=vab-2;class=Locus) (<http://www.wormbase.org/db/gene/locus?name=vab-2;class=Locus>). This work indicated that VAB-1 might be both a receptor and a ligand³⁶, ([#B36](#)) ³⁷ ([#B37](#)). Eliminating the kinase domain of VAB-1 resulted in a weak phenotype compared with the null allele, which reveals that VAB-1 has functions that are independent of its kinase activity. Eliminating VAB-2 ephrin, the ligand for VAB-1, also produced a weak phenotype. Only by removing both VAB-1 kinase activity and VAB-2 ephrin were these researchers able to regenerate the VAB-1-null phenotype. Chisholm concluded that the VAB-1-null phenotype reflected a loss of intracellular signalling through the VAB-1 kinase domain and a loss of intercellular

signalling that uses the ephrin ligand as a receptor. Structure–function studies of mutations in endogenous genes have an added benefit of being expressed appropriately. By contrast, exogenous constructs are often expressed at a non-physiological level, time or place.

Screens from hell

Pieter Brueghel was also famous for his depiction of hell — a place where one toils forever with marginal progress. Such a place exists for geneticists as well. Not all biological processes are amenable to visible screens or selections. Some pathways have to be approached using brute force. A good example of this is the study of worms that are defective in mechanosensation. Lack of mechanosensation is not a visible phenotype. These screens, conducted by Marty Chalfie and colleagues³⁸ ([#B38](#)), required that every worm be touched by an eyebrow hair to determine whether it failed to respond to touch. These methods identified an ion channel that is likely to be activated by mechanical stress, as well as the associated proteins that are required for transduction of the mechanical signal.

Multigenerational screens. Some phenotypes cannot be observed in the first generation of homozygotes and can be evaluated only in subsequent generations. Germ lines are immortal: these cells do not senesce like somatic cells, as they are renewed every generation. So, germ-line cells have factors that prevent the ageing that occurs in somatic cells. To identify such factors, Shawn Ahmed and Jonathan Hodgkin screened for mutants with mortal germ lines by establishing clonal lines from 400 F₂s and then picking single worms for more than ten generations³⁹ ([#B39](#)). They then looked for strains that became sterile after the fourth generation. This screen identified *mrt-2* (<http://www.wormbase.org/db/gene/locus?name=mrt-2;class=Locus>) (*mortal germline 2*), which encodes a DNA-damage checkpoint protein that is homologous to the *Schizosaccharomyces pombe* protein *RAD1* (<http://www.genedb.org/genedb/Search?name=rad1&organism=pombe&desc=yes>). This protein is required to prevent telomere shortening. Because the phenotype of these mutants does not appear for many generations, the identification of these genes was laborious.

Microscope screens. Many phenotypes cannot be observed using a dissecting microscope but can be assayed only under high magnification. Visual screening using differential-interference contrast optics was pioneered by Ed Hedgecock. He examined living F₂ worms that were mounted *en masse* on a slide under a siliconized coverslip. The precise location of a mutant on the slide was recorded, and the animal recovered by sliding the coverslip off and transferring the worm back onto a culture dish. These screens were the first to identify mutants that are defective in the

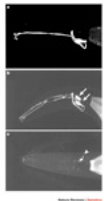
phagocytosis of dead cells, because the presence of persistent cell corpses was visible at high magnification⁴⁰ (#B40). An adaptation of this screen was used by Ronald Ellis and H. Robert Horvitz to identify mutants that are defective for the execution of apoptosis⁴¹, (#B41) ⁴² (#B42). The only phenotype of such mutants is the presence of extra cells in the animal. Ellis mounted mutagenized F₂ worms on slides and counted cells in the pharynx — worms with extra pharyngeal cells were recovered from the slides for propagation. This screen was arduous but fruitful; for example, it identified an allele of a **Bcl2** (<http://www.ncbi.nlm.nih.gov/LocusLink/LocRpt.cgi?l=12043>) (B-cell leukaemia 2) homologue, **ced-9** (<http://www.wormbase.org/db/gene/locus?name=ced-9;class=Locus>), which established the function of this oncogene in normal programmed cell death⁴³, (#B43) ⁴⁴ (#B44).

Green fluorescent protein screens. The screening of microscopic phenotypes has been greatly aided by the introduction into worms of green fluorescent protein (GFP) from the jellyfish *Aequoria victoria*⁴⁵ (#B45). These screens are particularly useful when the only phenotype of the mutant is the repositioning of a cell or protein in the mutant animal. GFP can be used to mark a protein, cell or subcellular compartment, and changes in GFP expression can be screened. For example, Mike Nonet⁴⁶ (#B46) tagged synaptic vesicles by fusing GFP to the synaptic-vesicle-protein synaptobrevin. Synaptic vesicles cluster at synapses, and synaptic number and position can then be assayed in transgenic animals using fluorescence microscopy. Three groups have used tagged synaptobrevin to screen for mutants that affect synaptic positioning and number⁴⁷, (#B47) ⁴⁸, (#B48) ⁴⁹ (#B49). Although they analysed synaptic distribution in different neurons, these screens identified similar sets of genes, including **rpm-1** (<http://www.wormbase.org/db/gene/locus?name=rpm-1;class=Locus>) (*regulator of presynaptic morphology 1*) and **sad-1** (<http://www.wormbase.org/db/gene/locus?name=sad-1;class=Locus>) (*synapses of the amphid defective 1*). RPM-1 and SAD-1 are required in sensory neurons and GABA motor neurons for the placement and distribution of synapses along axons. *rpm-1* and *sad-1* mutants move well and were therefore not recovered from screens for visibly uncoordinated animals. Other researchers have used GFP screens to identify mutants in various cellular processes, such as axonal pathfinding (for example, **sax-3/Robo** (<http://www.wormbase.org/db/gene/locus?name=sax-3;class=Locus>)⁵⁰ (#B50)), cell-fate specification (**ttx-1/otd** (<http://www.wormbase.org/db/gene/locus?name=ttx-1;class=Locus>)⁵¹ (#B51)), epigenetic silencing (**tam-1** (<http://www.wormbase.org/db/gene/locus?name=tam-1;class=Locus>) (Ref. ⁵² (#B52))), endocytosis⁵³, (#B53) ⁵⁴, (#B54) ⁵⁵ (#B55) and

developmental timing ([lin-58](http://www.wormbase.org/db/gene/locus?name=lin-58;class=Locus) (<http://www.wormbase.org/db/gene/locus?name=lin-58;class=Locus>)) (Ref. [56 \(#B56\)](#)). Emily Troemel and Cori Bargmann made particularly elegant use of GFP in a screen for defects in left–right asymmetry. They placed GFP under the control of a promoter that is expressed in either the left or the right olfactory neuron, but not both cells [57 \(#B57\)](#), then screened for mutants that either expressed the marker in both cells or in neither cell ([Fig. 4 \(#f4\)](#)). This screen revealed that signalling between the bilaterally symmetric neurons induces one of the neurons to adopt the 'ON' state from the basal 'OFF' state.

Figure 4 | Green fluorescent protein screen.

[\(/nrg/journal/v3/n5/fig_tab/nrg794_F4.html\)](/nrg/journal/v3/n5/fig_tab/nrg794_F4.html)



[\(/nrg/journal/v3/n5/fig_tab/nrg794_F4.html\)](/nrg/journal/v3/n5/fig_tab/nrg794_F4.html)

a | STR-2 (seven transmembrane receptor 2) is a candidate odorant receptor that is expressed in only one of the bilaterally symmetric AWC olfactory neurons in the wild type. Screens for mutants that are defective in left–right asymmetry identified mutants that expressed *str-2::GFP* in either **b** | both cells (arrows) or **c** | neither cell, although there is still faint staining in the cell body (arrowhead) [57 \(#B57\)](#). Photos reproduced with permission from Ref. [57 \(#B57\)](#) © (2001) the Genetics Society of America, courtesy of C. Bargmann. In all panels, dorsal is top and ventral is bottom. Anterior is to the left.

[High resolution image and legend \(58 KB\)](#)

[\(/nrg/journal/v3/n5/fig_tab/nrg794_F4.html\)](/nrg/journal/v3/n5/fig_tab/nrg794_F4.html)

[Figures and tables index](#)

[\(/nrg/journal/v3/n5/fig_tab/nrg794_ft.html\)](/nrg/journal/v3/n5/fig_tab/nrg794_ft.html)

Laser ablation screens. The grand prizewinner for difficult screens was conducted by Leon Avery, a geneticist who is known for clever and unusual screens. Avery was studying peristaltic pumping of the worm pharynx. If he ablated the **M4 MOTOR NEURON** (</nrg/journal/v3/n5/glossary/nrg794.html#df6>) with a laser microbeam, the pharynx lacked peristalsis owing to a lack of muscle contraction, and the animals that had been operated on arrested development [58. \(#B58\)](#) [59 \(#B59\)](#). Avery reasoned that mutations in genes that are responsible for muscle repolarization would restore contractions to the pharyngeal muscle. He mutagenized worms and then ablated the M4 motor neuron in hundreds of F₂ individuals and looked for mutants that continued to develop beyond the arrest caused by the surgery. In this screen, he identified an allele of a gene (*exp-2*) that encodes a sodium–potassium ATPase [60 \(#B60\)](#). Mutations in this gene cause the resting membrane potential of

the muscle to be close to threshold and thereby restore muscle contractions. Although this screen is technically a selection, the physical manipulations that were required to screen each F₂ worm place it firmly in hell.

Screens from purgatory

Lethal mutations. Unbiased screens for lethal mutations indicate that there might be 4,000 essential genes in the *C. elegans* genome^{61, (#B61) 62 (#B62)} (reviewed in Ref. ^{63 (#B63)}). Among these are genes that are involved in the developmental processes being examined in many laboratories; however, studying lethal mutations introduces two special problems, which makes this class of mutants a geneticist's purgatory. One difficulty is isolating and maintaining lethal mutations as heterozygotes. Second, because many genes can be mutated to a lethal phenotype, a researcher is faced with the daunting prospect of sorting through many lethal mutants to identify those that are defective for a particular biological process. We discuss each of these problems below.

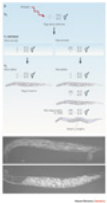
Standard F₂ screens are inadequate for the isolation of lethal mutations, because such screens rely on breeding a homozygous mutant animal (**Fig. 1 (#f1)**). However, lethal mutations can be recovered from their heterozygous siblings using a clonal F₁ screen^{2 (#B2)}. In this method, F₁ individuals from mutagenized P₀ animals are placed onto small Petri plates. If one-quarter of the F₂ progeny show the lethal phenotype of interest, the mutation is retrieved from heterozygous siblings. For this screen, a hermaphrodite is a tremendous advantage, because a single heterozygous mother is used to produce both homozygous-lethal mutants, which can be analysed, and heterozygous siblings, which are crucial to propagate the strain. Heterozygous strains can be maintained by inspecting the progeny from individual worms every generation: worms that no longer segregate arrested progeny are discarded. Lethal mutations are more conveniently maintained for long periods of time as heterozygotes by using a **BALANCER CHROMOSOME** ([/nrg/journal/v3/n5/glossary/nrg794.html#df7](http://nrg/journal/v3/n5/glossary/nrg794.html#df7))^{64, (#B64) 65 (#B65)}.

An adaptation of the clonal F₁ screen can be carried out on large plates by simply preventing the F₂ progeny from being laid by using egg-laying-defective mutant mothers^{66 (#B66)}. Such animals retain developing embryos in their uteruses; because the worm is transparent, individuals that segregate 25% arrested progeny can be identified and their phenotypes examined under the light microscope. The F₁ individual can then be transferred to a fresh plate. Although the F₁ mother is eventually consumed by her progeny to form 'a bag of worms' (**Fig. 5b (#f5)**), the mutation can be recovered from the heterozygous F₂ progeny. The advantage of this

approach is that it bypasses the need to clone individual F₁ animals onto plates.

Figure 5 | Maternal-effect screen.

[\(/nrg/journal/v3/n5/fig_tab/nrg794_F5.html\)](/nrg/journal/v3/n5/fig_tab/nrg794_F5.html)



[\(/nrg/journal/v3/n5/fig_tab/nrg794_F5.html\)](/nrg/journal/v3/n5/fig_tab/nrg794_F5.html)

a | Scheme for a maternal-effect screen. F₁ mothers (*mel*/+) that are derived from mutagenized parents are placed individually on plates and allowed to self-fertilize, producing +/+, *mel*/+ and *mel*/*mel* F₂ worms. *lin-2* animals are egg-laying defective so that self-progeny from the mother are not laid (*lin-2* animals are otherwise viable and fertile). The progeny eventually hatch and consume the mother to form a 'bag of worms'. So, at adulthood, the +/+ and *mel*/+ worms are lysed by their viable progeny. Animals that are homozygous for a maternal-effect mutation (*mel*/*mel*) will be viable adults filled with inviable progeny. The mutation cannot be recovered from these animals, but can be recovered from the *mel*/+ siblings on the plate. **b** | A *lin-2* homozygote is consumed by her progeny and the cuticle is filled with L1 larvae (top). The progeny from a double mutant of *lin-2* and an unidentified maternal-effect mutant (bottom) die as embryos and fill the mother with dead eggs. *lin*, abnormal cell lineage; *mel*, maternal-effect lethal.

High resolution image and legend (75 KB)

[\(/nrg/journal/v3/n5/fig_tab/nrg794_F5.html\)](/nrg/journal/v3/n5/fig_tab/nrg794_F5.html)

Figures and tables index

[\(/nrg/journal/v3/n5/fig_tab/nrg794_ft.html\)](/nrg/journal/v3/n5/fig_tab/nrg794_ft.html)

Maternal-effect lethal screens. The very earliest divisions of an embryo are directed by RNAs and proteins that are deposited by the mother. So, a homozygous embryo that lacks the gene for these components can still develop normally owing to normal RNAs and proteins that the heterozygous mother has deposited into the egg. However, F₃ individuals that are born from these homozygous progeny die because they lack this maternal contribution. Genes that are involved in these early developmental decisions can be identified in maternal-effect lethal (*mel*) screens⁶⁷, (#B67) ⁶⁸ (#B68). In such a screen, an egg-laying-defective mutant is used to retain the eggs in the F₂ mother.⁶⁹ (#B69) (**Fig. 5a** (#f5)). Most animals die as a bag of worms (**Fig. 5b** (#f5), top). The presence of viable adult worms that are filled with

inviable progeny (**Fig. 5b (#f5)**, bottom) is evidence of a maternal-effect mutation, which can then be recovered from the progeny of the lysed *mel/+* worms (siblings of the F₂ mothers). These screens have identified many components that are required to establish the early embryo, such as *skn-1* (<http://www.wormbase.org/db/gene/locus?name=skn-1;class=Locus>) (*skinhead 1*), which specifies blastomere fate, and the *par* (*embryonic partitioning abnormal*) genes, which are required for embryonic asymmetry^{70, (#B70) 71 (#B71)}. Alternatively, a screen can be carried out for maternal-effect-lethal mutations that are temperature sensitive, and the progeny from the homozygous mother can be recovered. Kevin O'Connell and John White also used egg-laying-defective animals to detect maternal-effect mutants^{72 (#B72)}; however, they carried out their screens at 25 °C so that temperature-sensitive mutations would be exposed to the non-permissive temperature. Animals that were filled with dead embryos were recovered and placed at the permissive temperature of 15 °C to allow development of live progeny and the recovery of the temperature-sensitive mutations. These screens yielded conditional lethal mutations in 19 genes that are required for early embryonic divisions in *C. elegans*.

Finding the right lethal mutant. Hundreds of lethal mutations have been identified. Many are involved in 'housekeeping' functions (for example, *dif-1* (<http://www.wormbase.org/db/gene/locus?name=dif-1;class=Locus>) (*differentiation defective 1*), a probable mitochondrial solute carrier^{73 (#B73)}), whereas others encode developmental regulators that are needed to pattern the embryo^{74, (#B74) 75 (#B75)}. One problem posed by lethal mutant screens is how to distinguish between these two classes of mutant. As lethality is not a specific phenotype, a secondary screen is essential to recognize interesting mutants. For example, Pierre Gönczy and colleagues screened chromosome III for all maternal-effect-lethal mutations, by using an inverted chromosome to balance and maintain the induced mutations. By re-screening these strains under high magnification for defects in cell division in the one-cell-stage embryo^{76 (#B76)}, these researchers identified 34 loci that are required for mitosis and cytokinesis in the first cell division.

Another successful strategy for identifying interesting lethal-mutant phenotypes has been to manipulate worms physically and thereby predict the relevant phenotype for which to screen. For example, because it has an invariant lineage, *C. elegans* was originally characterized as a simple developmental system that depended on the segregation of determinants into specific lineages — quite different from the development of higher organisms. However, Jim Priess removed a single cell in the four-cell-stage embryo and discovered that the development of a neighbouring cell,

called ABA, was disrupted^{77 (#B77)}. ABA made epidermis and neurons, as it did usually, but failed to produce pharyngeal muscles. By screening for mutants in which ABA failed to produce pharyngeal cells, Priess and colleagues identified three genes that are involved in the Notch signalling pathway^{69, (#B69) 78, (#B78) 79 (#B79)}. These studies and others revealed that the stereotypical lineage of *C. elegans* relies on invariant cell–cell interactions more than it does on the segregation of determinants into specific lineages.

The future of *Caenorhabditis elegans* genetics

Sensitized screens. A promising scheme for the future is the sensitized screen, in which recessive mutations that are involved in a specific process produce dominant phenotypes. Sensitized screens for dominant enhancers are routine in *Drosophila*. In flies, such screens often use a temperature-sensitive mutation; one strategy would be to maintain the F₁ progeny from mutagenized animals at a marginally permissive temperature so that the pathway of interest is compromised but not blocked completely. Mutations in a second locus disrupt the process so that a phenotype is visible even though this second locus is heterozygous. For example, a screen for dominant enhancers of temperature-sensitive mutations in the *sevenless* (<http://www.ncbi.nlm.nih.gov/LocusLink/LocRpt.cgi?l=32039>) tyrosine kinase identified loss-of-function mutations in the guanylyl-nucleotide-release factor for RAS^{80 (#B80)}. These screens are particularly powerful because they can be conducted in the F₁ generation. Because *C. elegans* hermaphrodites produce homozygous offspring, screens for recessive mutations are fairly easy to carry out, and so a search for dominant enhancers is usually unnecessary. However, in some circumstances, dominant F₁ screens can save a great deal of labour as every mutagenized genome can be scored once and only once (unlike in most F₂ screens, in which a mutagenized genome can be sampled several times). For example, in a screen for dominant enhancers, Chalfie and colleagues^{81 (#B81)} used a temperature-sensitive mutation in the gene that encodes the *MEC-4* (<http://www.wormbase.org/db/gene/locus?name=mec-4;class=Locus>) mechanosensory ion channel. They screened for dominant mutations that conferred a Mec mutant phenotype at the permissive temperature. Mutations in four genes enhanced the phenotype in a dominant manner. These protein products are believed to interact directly with the MEC-4 protein, which indicates that these types of screen might identify proteins that are members of protein complexes.

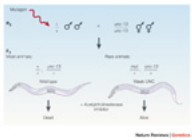
In another example, Brian Cali and Phil Anderson screened for alleles that were dominant when the *mRNA SURVEILLANCE PATHWAY* ([/nrg/journal/v3/n5/glossary/nrg794.html#df8](http://nrg/journal/v3/n5/glossary/nrg794.html#df8)) was inactivated^{82 (#B82)}. They

reasoned that, in the wild type, mRNAs produced from genes with nonsense mutations were rapidly degraded, precluding synthesis of mutant protein. However, if mRNA surveillance were inactivated, mutant alleles would produce stabilized mRNAs that could code for truncated proteins with dominant phenotypes. Their approach yielded dominant alleles in 15 genes, 7 of which depended, to some extent, on loss of mRNA surveillance [82 \(#B82\)](#). Many of these mutations caused uncoordinated movement as heterozygotes but were lethal as homozygotes. Presumably, these genes have a role in nervous-system function but are also required for viability. This pleiotropy would make such genes difficult to identify in conventional screens.

A special case of a sensitized screen is a non-allelic non-complementation screen (also called second-site non-complementation or extragenic non-complementation). This involves the isolation of recessive mutations that show a phenotype as a double heterozygote. Such mutations can be identified in a standard non-complementation screen, which is normally used to identify more alleles of a locus. In circumstances of non-allelic non-complementation, second-site mutations will seem to be dominant and can be observed in the F₁ progeny ([Fig. 6 \(#f6\)](#)). Even if these mutations are recessive lethal, they can be isolated and maintained as heterozygotes. In studies of genes that function at the synapse, this interaction required at least one partially functional protein [83 \(#B83\)](#). The strongest interactions were observed between proteins that formed a complex; presumably, the partially functional protein 'poisoned' the complex to some degree. However, interactions were also observed between distant components of the exocytosis pathway. So, non-allelic non-complementation screens can identify genes that act in a pathway that functions in adults even if the mutations are recessive lethals.

Figure 6 | Non-allelic non-complementation screen.

[\(/nrg/journal/v3/n5/fig_tab/nrg794_F6.html\)](http://nrg/journal/v3/n5/fig_tab/nrg794_F6.html)



[\(/nrg/journal/v3/n5/fig_tab/nrg794_F6.html\)](http://nrg/journal/v3/n5/fig_tab/nrg794_F6.html)

These screens involve the search for recessive mutations that show a phenotype as a double heterozygote with an initial mutation. The design of this screen resembles that of a non-complementation screen that is intended to find more alleles of a particular gene; however, it can also identify mutations at a second site. Mutagenized males are crossed to hermaphrodites that carry a homozygous mutation for one gene (*unc-13* in this example) to generate heterozygous animals that can be screened for the desired phenotype. In cases of non-allelic non-complementation, the observed phenotype reflects a new mutation in a second gene (*mut*). In the screen illustrated here, the double heterozygotes are selected using an

acetylcholinesterase inhibitor such as Aldicarb (see main text), because UNC-13 is required for the release of neurotransmitter. Even if this new mutation is homozygous lethal it can still be recovered from the heterozygous F₁ mutant animal. *mut*, *mutation*; *unc*, *uncoordinated*.

[High resolution image and legend \(37 KB\)](#)

[\(/nrg/journal/v3/n5/fig_tab/nrg794_F6.html\)](#)

[Figures and tables index](#)

[\(/nrg/journal/v3/n5/fig_tab/nrg794_ft.html\)](#)

Redundancy. It has been estimated that perhaps only 6,000 of the 20,000 genes in *C. elegans* can be mutated to a visible, lethal or sterile phenotype^{84, (#B84) 85, (#B85) 86, (#B86) 87, (#B87) 88 (#B88)}. How will we determine the functions of the other 14,000 genes? Numerous genes might show apparently wild-type null phenotypes because they are redundant under laboratory conditions, and only show a phenotype if mutations eliminate the activity of two or more loci^{89 (#B89)}. These estimates of redundant genes argue that devising strategies to reveal the function of 'silent' genes is crucial if we are to decipher the *C. elegans* genome.

In the simplest situation, functional redundancy arises because a gene has been duplicated and two or more closely related genes exist, any of which can carry out a particular task. This phenomenon is called homologous redundancy. For example, *end-1* (<http://www.wormbase.org/db/gene/locus?name=end-1;class=Locus>) (*endoderm 1*) and *end-3* (<http://www.wormbase.org/db/gene/locus?name=end-3;class=Locus>) encode tightly linked GATA-transcription-factor homologues^{90 (#B90)} (J. Rothman, personal communication). Loss of both genes leads to an absence of endoderm; however, mutants for either gene alone have no phenotype. The synergism between *end-1* and *end-3* was discovered because a deletion exists that removes both genes and produces arrested embryos that lack endoderm^{90 (#B90)}. Interestingly, the *C. elegans* genome contains many small duplications that carry pairs of potentially redundant genes^{85 (#B85)}. Mutagens that generate deletions might therefore be useful for the design of screens that circumvent redundancy.

In other cases, homologous genes might have diverged in function such that the genes are only partially redundant. Although the phenotype of each single mutant might be deceptive or uninformative, double mutants could direct researchers to new phenotypes that can be screened to isolate other components of a pathway. For example, a double mutant of the Notch-receptor homologues *glp-1*

(<http://www.wormbase.org/db/gene/locus?name=glp-1;class=Locus>) (*germline proliferation 1*) and [lin-12](http://www.wormbase.org/db/gene/locus?name=lin-12;class=Locus) (<http://www.wormbase.org/db/gene/locus?name=lin-12;class=Locus>) has a distinctive lethal phenotype that differs from either single mutant [91 \(#B91\)](#). Kimble and colleagues used an F₁ clonal screen to search for new mutations with the same phenotype as the *glp-1 lin-12* double mutant and identified two new genes, [lag-1](http://www.wormbase.org/db/gene/locus?name=lag-1;class=Locus) (<http://www.wormbase.org/db/gene/locus?name=lag-1;class=Locus>) (*lin-12* and *glp-1*) and [lag-2](http://www.wormbase.org/db/gene/locus?name=lag-2;class=Locus) (<http://www.wormbase.org/db/gene/locus?name=lag-2;class=Locus>). *lag-1* and *lag-2* encode a downstream effector and an upstream ligand in the Notch pathway, respectively. LAG-1 and LAG-2 presumably function with both GLP-1 and LIN-12 (Refs [92–94 \(#B92\)](#)).

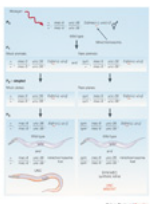
A more complex form of redundancy is non-homologous redundancy. In this case, proteins that do not resemble one another can nevertheless still provide the same cellular function. The most famous example of non-homologous redundancy is the synthetic multivulval, or SynMuv, pathways in vulval development. In this case, either of two separate molecular pathways can inhibit the unregulated formation of the vulva by the epidermal precursor cells. Only mutants that lack at least one component in both pathways result in a multivulval phenotype [95 \(#B95\)](#) ([Fig. 3 \(#f3\)](#)). The initial identification of the SynMuv pathways required a gambler's luck, as the simultaneous mutation in two unlinked genes, [lin-8](http://www.wormbase.org/db/gene/locus?name=lin-8;class=Locus) (<http://www.wormbase.org/db/gene/locus?name=lin-8;class=Locus>) and [lin-9](http://www.wormbase.org/db/gene/locus?name=lin-9;class=Locus) (<http://www.wormbase.org/db/gene/locus?name=lin-9;class=Locus>), in the genome occurs at a frequency of 10⁻⁷. However, once such a combination had been identified, Ferguson separated the loci and re-screened the genome for second-site mutations that generated the synthetic phenotype; this was in fact a sensitized screen designed for the purpose of revealing redundant genes. Because one pathway had already been inactivated, isolation of the second-site mutation occurred at a frequency typical for single loss-of-function mutations (10⁻³). For example, Ferguson used *lin-8* class A homozygotes to screen for second mutations in the class B pathway and found six loci that showed a synthetic interaction [95 \(#B95\)](#). Molecular analysis of this pathway showed that the B-pathway components are homologous to proteins in the retinoblastoma (Rb) pathway and regulate the NuRD (nucleosome remodelling and histone deacetylase) complex [96 \(#B96\)](#). Many other components of the SynMuv pathway are new proteins, and it will be exciting to learn whether homologues in other organisms also interface with chromatin-remodelling machinery.

The identification of non-homologous redundant pathways almost always depends on blind luck. Another example of this is to be found in the genetic interaction observed between [mec-8](http://www.wormbase.org/db/gene/locus?name=mec-8) ([http://www.wormbase.org/db/gene/locus?name=mec-](http://www.wormbase.org/db/gene/locus?name=mec-8)

[8;class=Locus](#)) and [unc-52](http://www.wormbase.org/db/gene/locus?name=unc-52;class=Locus) (<http://www.wormbase.org/db/gene/locus?name=unc-52;class=Locus>). Bob Herman discovered that mutations in these two genes were synthetically lethal when he found he could not construct a chromosome marked with both mutations. MEC-8 is a protein that is required for exon skipping in certain alternatively spliced mRNAs, whereas *unc-52* encodes perlecan, an essential component of the extracellular matrix. Transcripts from the *unc-52* locus are alternatively spliced, and the MEC-8 protein is required to skip exons 17 and 18. Nonsense mutations in exons 17 or 18 of *unc-52* are viable because MEC-8 can direct the synthesis of functional transcripts that lack these exons. However, double mutants between the viable alleles of *unc-52* and *mec-8* are lethal and resemble null alleles of *unc-52* (Ref. [97 \(#B97\)](#)). This synthetic interaction indicated a way to identify splicing factors that promote alternative splice forms or to identify other targets of MEC-8 splicing. Andrew Davies and Robert Herman carried out a screen that was similar to synthetic-lethal screens carried out in yeast to look for the presence of lethal sectors in a colony [98 \(#B98\)](#). They screened for mutants that were viable as simple homozygotes but were synthetically lethal with a *mec-8* mutation [99 \(#B99\)](#) ([Fig. 7 \(#f7\)](#)). They found mutations in five *sym* (*synthetically lethal with mec-8*) genes, which probably encode targets of MEC-8 or genes that are involved in alternatively splicing reactions with MEC-8. The design of the *mec-8* screen has been adapted to other contexts. For example, a similar approach was used to identify alleles of *fzr-1/fizzy related*, which show a genetic interaction with [lin-35](#) (<http://www.wormbase.org/db/gene/locus?name=lin-35;class=Locus>)/Rb [100 \(#B100\)](#). Mutations in each of these genes alone show a wild-type phenotype, but together they cause hyperproliferation of cells derived from all germ layers, which leads to double mutants that are very sick or are dead.

Figure 7 | Synthetic lethal screens.

([/nrg/journal/v3/n5/fig_tab/nrg794_F7.html](http://nrg/journal/v3/n5/fig_tab/nrg794_F7.html))



([/nrg/journal/v3/n5/fig_tab/nrg794_F7.html](http://nrg/journal/v3/n5/fig_tab/nrg794_F7.html))

Robert Herman and co-workers [99 \(#B99\)](#) screened for mutants that were viable as a single mutant but were synthetically lethal with a *mec-8* null allele. They generated a transgenic strain with homozygous-null mutations at the endogenous *mec-8* and *unc-36* loci and an exogenous copy of the *mec-8* and *unc-36* genes carried as an extrachromosomal array (*Ex[mec(+);unc(+)]*). A green fluorescent protein marker can be added as an extra marker for the presence of the array. Because extrachromosomal arrays are not transmitted to all progeny, this strain normally segregated some worms that had lost the exogenous DNA and were phenotypically Mec, which is

difficult to score, and *Unc*, which is easy to score. After mutagenesis, Herman and colleagues identified mutants that no longer segregated *Unc* progeny. Because the double mutant between *mec-8* and the new allele (*sym*; synthetically lethal with *mec-8*) were synthetically lethal, only animals that retained the *mec-8(+)* array were viable. See main text for details.

[High resolution image and legend \(99 KB\)](#)

[\(/nrg/journal/v3/n5/fig_tab/nrg794_F7.html\)](/nrg/journal/v3/n5/fig_tab/nrg794_F7.html)

[Figures and tables index](#)

[\(/nrg/journal/v3/n5/fig_tab/nrg794_ft.html\)](/nrg/journal/v3/n5/fig_tab/nrg794_ft.html)

The long perspective

The nematode *C. elegans* contains ~20,000 genes^{63 (#B63)}, fewer than 10% of which have been defined by mutation. Of these, 575 have been cloned and characterized at a molecular level. A goal for the future is to elucidate the role of the remaining genes. About one-third of these have a mammalian counterpart, and understanding their function in *C. elegans* will help us to determine their function in more complex animals. Many of the remainder could define genes that are specific to nematodes and will not be found in other phyla. Such genes are interesting from a macroevolutionary perspective in that they describe which proteins are required by an organism for the peculiarities of its lifestyle. However, the function of many of these proteins might not be clear in worms that are removed from their natural ecology and might be difficult to observe in the simple environment of the laboratory. So, studies of the ecology of natural populations of *C. elegans* will be essential for an in-depth understanding of the *C. elegans* genome. Microevolutionary processes can also be studied. Such processes define why populations of *C. elegans* differ from each other. For example, variations at the *npr-1* (<http://www.wormbase.org/db/gene/locus?name=npr-1;class=Locus>) (*neuropeptide receptor 1*) locus are responsible for differences in social behaviour between worm populations^{101 (#B101)}. Some of these behavioural differences might not be due to changes at single loci but rather are the result of concerted configurations of several genes. *C. elegans* is well suited for such studies, as the genome is well covered by single-nucleotide polymorphisms. Crosses between natural isolates can then be used to map multilocus or **QUANTITATIVE** (</nrg/journal/v3/n5/glossary/nrg794.html#df9>) contributions to differences between natural isolates.

It is clear that the genome of *C. elegans* is guarding secrets about the organization of life that will be pursued for many years to come. Forward genetic screens will continue

to be an important component of those studies, particularly when integrated with emerging technologies of whole-genome analysis, such as expression studies using microarray chips or gene reporters, protein-interaction maps and RNA-interference studies.

Links

DATABASES

LocusLink (<http://www.ncbi.nlm.nih.gov/LocusLink/>)

Bcl2 (<http://www.ncbi.nlm.nih.gov/LocusLink/LocRpt.cgi?l=12043>) ***groucho***

(<http://www.ncbi.nlm.nih.gov/LocusLink/LocRpt.cgi?l=43162>) ***sevenless***

(<http://www.ncbi.nlm.nih.gov/LocusLink/LocRpt.cgi?l=32039>)

<i>**Schizosaccharomyces pombe**</i> **GeneDB** ()

RAD1 (<http://www.genedb.org/genedb/Search?>

[name=rad1&organism=pombe&desc=yes](http://www.genedb.org/genedb/Search?name=rad1&organism=pombe&desc=yes))

Wormbase ()

ced-9 (<http://www.wormbase.org/db/gene/locus?name=ced-9;class=Locus>)

dif-1 (<http://www.wormbase.org/db/gene/locus?name=dif-1;class=Locus>)

dpy-21 (<http://www.wormbase.org/db/gene/locus?name=sos->

[1&class=Locus](http://www.wormbase.org/db/gene/locus?name=sos-1&class=Locus)) **end-1** (<http://www.wormbase.org/db/gene/locus?>

[name=end-1;class=Locus](http://www.wormbase.org/db/gene/locus?name=end-1;class=Locus)) **end-3**

(<http://www.wormbase.org/db/gene/locus?name=end-3;class=Locus>) ***glp-1***

(<http://www.wormbase.org/db/gene/locus?name=glp-1;class=Locus>) ***her-1***

(<http://www.wormbase.org/db/gene/locus?name=sos-1&class=Locus>) ***him-5***

(<http://www.wormbase.org/db/gene/locus?name=sos-1&class=Locus>) ***lag-1***

(<http://www.wormbase.org/db/gene/locus?name=lag-1;class=Locus>) ***lag-2***

(<http://www.wormbase.org/db/gene/locus?name=lag-2;class=Locus>) **LET-23**

(<http://www.wormbase.org/db/gene/locus?name=let-23;class=Locus>) ***lin-4***

(<http://www.wormbase.org/db/gene/locus?name=lin-4;class=Locus>) ***lin-8***

(<http://www.wormbase.org/db/gene/locus?name=lin-8;class=Locus>) ***lin-9***

(<http://www.wormbase.org/db/gene/locus?name=lin-9;class=Locus>) ***lin-12***

(<http://www.wormbase.org/db/gene/locus?name=lin-12;class=Locus>) ***lin-15***

(<http://www.wormbase.org/db/gene/locus?name=lin-15;class=Locus>) ***lin-35***

(<http://www.wormbase.org/db/gene/locus?name=lin-35;class=Locus>) ***lin-58***

(<http://www.wormbase.org/db/gene/locus?name=lin-58;class=Locus>) **MEC-4**

(<http://www.wormbase.org/db/gene/locus?name=mec-4;class=Locus>) ***mec-8***

(<http://www.wormbase.org/db/gene/locus?name=mec-8;class=Locus>) ***mrt-2***

(<http://www.wormbase.org/db/gene/locus?name=mrt-2;class=Locus>) ***npr-1***

(<http://www.wormbase.org/db/gene/locus?name=npr-1;class=Locus>) ***rpm-1***

(<http://www.wormbase.org/db/gene/locus?name=rpm-1;class=Locus>) ***sad-1***
 (<http://www.wormbase.org/db/gene/locus?name=sad-1;class=Locus>) ***SAX-3/Robo*** (<http://www.wormbase.org/db/gene/locus?name=sax-3;class=Locus>)
sdc-2 (<http://www.wormbase.org/db/gene/locus?name=sd-2;class=Locus>) ***SDC-3*** (<http://www.wormbase.org/db/gene/locus?name=sd-3;class=Locus>) ***SEM-5***
 (<http://www.wormbase.org/db/gene/locus?name=sem-5;class=Locus>) ***skn-1***
 (<http://www.wormbase.org/db/gene/locus?name=skn-1;class=Locus>) ***SOS-1***
 (<http://www.wormbase.org/db/gene/locus?name=sos-1&class=Locus>) ***tam-1***
 (<http://www.wormbase.org/db/gene/locus?name=tam-1;class=Locus>) ***TTX-1/OTD*** (<http://www.wormbase.org/db/gene/locus?name=ttx-1;class=Locus>)
UNC-4 (<http://www.wormbase.org/db/gene/locus?name=unc-4;class=Locus>) ***UNC-6*** (<http://www.wormbase.org/db/gene/locus?name=unc-6;class=Locus>) ***unc-17***
 (<http://www.wormbase.org/db/gene/locus?name=unc-17;class=Locus>) ***unc-24*** (<http://www.wormbase.org/db/gene/locus?name=unc-24;class=Locus>)
UNC-30 (<http://www.wormbase.org/db/gene/locus?name=unc-30;class=Locus>) ***unc-37*** (<http://www.wormbase.org/db/gene/locus?name=unc-37;class=Locus>) ***unc-52***
 (<http://www.wormbase.org/db/gene/locus?name=unc-52;class=Locus>) ***vab-1***
 (<http://www.wormbase.org/db/gene/locus?name=vab-1;class=Locus>) ***vab-2***
 (<http://www.wormbase.org/db/gene/locus?name=vab-2;class=Locus>) ***XOL-1***
 (<http://www.wormbase.org/db/gene/locus?name=xol-1;class=Locus>)

FURTHER INFORMATION

Encyclopedia of Life Sciences (<http://www.who.int>)

***Caenorhabditis elegans* as an experimental organism**

(<http://www.els.net/els/FDA/default.asp?id=2051999D-ACC5-485B-B1D3-71E4A5CF8281>)

- **AceDB** (<http://www.acedb.org>)
- ***C. elegans* WWW server** (<http://elegans.swmed.edu>)
- **Erik Jorgensen's lab** (<http://www.biology.utah.edu/jorgensen>)
- **Searchable *C. elegans* literature index** (<http://elegans.swmed.edu/wli>)
- **Susan Mango's lab** (<http://www.hci.utah.edu/labs/mango>)

top (#top)

Acknowledgements

We thank A. Chisholm, R. Herman and M. Labouesse for comments on the manuscript. J. Srinivasan, R. Sommer, E. Troemel, C. Bargmann and L. Kaltenbach provided photographs. P. Anderson, L. Avery, B. Bowerman, S. Clark, M. Han, T. Harris, M. Hengartner, J. Hodgkin, M. Nonet, R. Korswagen, D. Pilgrim, N. Pujol and

J. Priess made helpful contributions and suggestions.

[top \(#top\)](#)

References

- Ankeny, R. A. The natural history of *Caenorhabditis elegans* research. *Nature Rev. Genet.* **2**, 474–479 (2001).
- Brenner, S. The genetics of *Caenorhabditis elegans*. *Genetics* **77**, 71–94 (1974).
The paper that started it all; it remains a good introduction to *C. elegans* genetics.
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=4366476&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1974T582100007&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:STN:280:C5uB2s7hs1U%3D&pissn=1471-0056&pyear=2002&md5=ea624507db191doas2de5abeb9788957>)
- Jin, Y., Hoskins, R. & Horvitz, H. R. Control of type-D GABAergic neuron differentiation by *C. elegans* UNC-30 homeodomain protein. *Nature* **372**, 780–783 (1994).
Article ([/doi/10.1038/372780a0](http://dx.doi.org/10.1038/372780a0))
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=7997265&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1994PY21200053&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK2MXivVSjsro%3D&pissn=1471-0056&pyear=2002&md5=f39a822b21f20656eeb607ff0161dd91>)
- Hedgecock, E. M., Culotti, J. G. & Hall, D. H. The *unc-5*, *unc-6*, and *unc-40* genes guide circumferential migration of pioneer axons and mesodermal cells on the epidermis in *C. elegans*. *Neuron* **2**, 61–85 (1990).
Article ([http://dx.doi.org/10.1016/0896-6273\(90\)90444-K](http://dx.doi.org/10.1016/0896-6273(90)90444-K))
- Ishii, N., Wadsworth, W. G., Stern, B. D., Culotti, J. G. & Hedgecock, E. M. UNC-6, a laminin-related protein, guides cell and pioneer axon migrations in *C. elegans*. *Neuron* **9**, 873–881 (1992).
Article ([http://dx.doi.org/10.1016/0896-6273\(92\)90240-E](http://dx.doi.org/10.1016/0896-6273(92)90240-E))
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=1329863&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1992JY55200007&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK3sXkvV2ht7s%3D&pissn=1471-0056&pyear=2002&md5=68b25f1598ac5a02e156537fd54bc8d3>)
- Sulston, J. & Horvitz, H. R. Abnormal cell lineages in mutants of the nematode *Caenorhabditis elegans*. *Dev. Biol.* **82**, 41–55 (1981).
Article ([http://dx.doi.org/10.1016/0012-1606\(81\)90427-9](http://dx.doi.org/10.1016/0012-1606(81)90427-9))
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=7014288&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1981LE53800005&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:STN:280:Bi6C1cbkltw%3D&pissn=1471-0056&pyear=2002&md5=f9d4c5e0e0f4de677c3df28bed1fa9c1>)
- Ferguson, E. & Horvitz, H. R. Identification and characterization of 22 genes that affect the vulval cell lineages of *Caenorhabditis elegans*. *Genetics* **110**, 17–72 (1985).
A gigantic undertaking that clearly explains the various genetic tests that are used to categorize mutations.
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=3996896&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1985AFU9400002&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:STN:280:Bi6B3critVO%3D&pissn=1471->

- [10056&pyear=2002&md5=7c71c6d64e507b3b5e8445fd8d102c5c](http://dx.doi.org/10.1038/85505)
8. Wang, M. & Sternberg, P. W. Pattern formation during *C. elegans* vulval induction. *Curr. Top. Dev. Biol.* **51**, 189–220 (2001).
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=11236714&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=11236714&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000168037900006&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000168037900006&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3MXisFymsrw%3D&pissn=1471-0056&pyear=2002&md5=ffefc9b12d2fdb07408e8cf0505daf5) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3MXisFymsrw%3D&pissn=1471-0056&pyear=2002&md5=ffefc9b12d2fdb07408e8cf0505daf5>)
 9. Han, M. & Sternberg, P. W. *let-60*, a gene that specifies cell fates during *C. elegans* vulval induction, encodes a ras protein. *Cell* **63**, 921–931 (1990).
[Article](http://dx.doi.org/10.1016/0092-8674(90)90495-Z) ([http://dx.doi.org/10.1016/0092-8674\(90\)90495-Z](http://dx.doi.org/10.1016/0092-8674(90)90495-Z))
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=2257629&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=2257629&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1990EL75900007&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1990EL75900007&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK3MXhsFyhsbw%3D&pissn=1471-0056&pyear=2002&md5=b9a310d1ab52a9e644a632d0cd01766c) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK3MXhsFyhsbw%3D&pissn=1471-0056&pyear=2002&md5=b9a310d1ab52a9e644a632d0cd01766c>)
 10. Beitel, G. J., Clark, S. G. & Horvitz, H. R. *Caenorhabditis elegans* ras gene *let-60* acts as a switch in the pathway of vulval induction. *Nature* **348**, 503–509 (1990).
[Article](http://dx.doi.org/10.1038/348503a0) (<http://dx.doi.org/10.1038/348503a0>)
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=2123303&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=2123303&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1990EL76000052&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1990EL76000052&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK3MXls1Kktg%3D%3D&pissn=1471-0056&pyear=2002&md5=a7fa2b13c5d98bdcbd4c6d21e2ba22f7) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK3MXls1Kktg%3D%3D&pissn=1471-0056&pyear=2002&md5=a7fa2b13c5d98bdcbd4c6d21e2ba22f7>)
 11. Sternberg, P. W., Golden, A. & Han, M. Role of a raf proto-oncogene during *Caenorhabditis elegans* vulval development. *Phil. Trans. R. Soc. Lond. B Biol. Sci.* **340**, 259–265 (1993).
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1993LL72900001&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1993LL72900001&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK3sXltlGqu7w%3D&pissn=1471-0056&pyear=2002&md5=68819c2527b4b9212b71c36ea4b9cef8) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK3sXltlGqu7w%3D&pissn=1471-0056&pyear=2002&md5=68819c2527b4b9212b71c36ea4b9cef8>)
 12. Lackner, M. R., Kornfeld, K., Miller, L. M., Horvitz, H. R. & Kim, S. K. A MAP kinase homolog, *mpk-1*, is involved in ras-mediated induction of vulval cell fates in *Caenorhabditis elegans*. *Genes Dev.* **8**, 160–173 (1994).
[Article](http://dx.doi.org/10.1101/gad.8.2.160) (<http://dx.doi.org/10.1101/gad.8.2.160>)
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=8299936&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=8299936&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1994MU12700003&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1994MU12700003&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK2cXitlOnt78%3D&pissn=1471-0056&pyear=2002&md5=72043b5b510800fcae8268705e02759b) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK2cXitlOnt78%3D&pissn=1471-0056&pyear=2002&md5=72043b5b510800fcae8268705e02759b>)
 13. Wu, Y. & Han, M. Suppression of activated LET-60 ras protein defines a role of *Caenorhabditis elegans* sur-1 MAP kinase in vulval differentiation. *Genes Dev.* **8**, 147–159 (1994).
[Article](http://dx.doi.org/10.1101/gad.8.2.147) (<http://dx.doi.org/10.1101/gad.8.2.147>)
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=8299935&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=8299935&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1994MU12700002&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1994MU12700002&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK2cXitlOnt74%3D&pissn=1471-0056&pyear=2002&md5=8ed9876c73d25dd9e2f4252d68cb6c05) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK2cXitlOnt74%3D&pissn=1471-0056&pyear=2002&md5=8ed9876c73d25dd9e2f4252d68cb6c05>)
 14. Kornfeld, K., Hom, D. B. & Horvitz, H. R. The *ksr-1* gene encodes a novel protein kinase involved in ras-mediated signaling in *C. elegans*. *Cell* **83**, 903–913 (1995).
[Article](http://dx.doi.org/10.1016/0092-8674(95)90206-6) ([http://dx.doi.org/10.1016/0092-8674\(95\)90206-6](http://dx.doi.org/10.1016/0092-8674(95)90206-6))
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=8521514&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=8521514&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1995TK74500009&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1995TK74500009&DestApp=WOS_CPL)

- [ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1;CAS:528:DyaK2MXhtVSnu7bO&pissn=1471-0056&pyear=2002&md5=e7b92d1d68c94419a4151a7ed324568f) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1;CAS:528:DyaK2MXhtVSnu7bO&pissn=1471-0056&pyear=2002&md5=e7b92d1d68c94419a4151a7ed324568f>)
15. Kornfeld, K., Guan, K.-L. & Horvitz, H. R. The *Caenorhabditis elegans* gene *mek-2* is required for vulval induction and encodes a protein similar to the protein kinase MEK. *Genes Dev.* **9**, 756–768 (1995).
Article (<http://dx.doi.org/10.1101/gad.9.6.756>)
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=7729691&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1995QTo7800010&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1;CAS:528:DyaK2MXltVWqsLs%3D&pissn=1471-0056&pyear=2002&md5=2a28e06807ea256336230abfe366ff16>)
16. Singh, N. & Han, M. *sur-2*, a novel gene, functions late in the *let-60* ras-mediated signaling pathway during *Caenorhabditis elegans* vulval induction. *Genes Dev.* **9**, 2251–2265 (1995).
Article (<http://dx.doi.org/10.1101/gad.9.18.2251>)
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=7557379&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1995RW87700005&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1;CAS:528:DyaK2MXotlOjtrc%3D&pissn=1471-0056&pyear=2002&md5=c7ecdc4a299d863f2e038a19e87ac7c>)
17. Sundaram, M. & Han, M. The *C. elegans ksr-1* gene encodes a novel Raf-related kinase involved in Ras-mediated signal transduction. *Cell* **83**, 889–901 (1995).
Article ([http://dx.doi.org/10.1016/0092-8674\(95\)90205-8](http://dx.doi.org/10.1016/0092-8674(95)90205-8))
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=8521513&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1995TK74500008&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1;CAS:528:DyaK2MXhtVSnu7bN&pissn=1471-0056&pyear=2002&md5=eac966ad2b415efb94fbd928ff67978>)
18. Sternberg, P. W. & Han, M. Genetics of RAS signaling in *C. elegans*. *Trends Genet.* **14**, 466–472 (1998).
A more complete description of the RAS signalling pathway and the history of the genetic screens carried out to identify the genes in this pathway.
Article ([http://dx.doi.org/10.1016/S0168-9525\(98\)01592-3](http://dx.doi.org/10.1016/S0168-9525(98)01592-3))
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=9825675&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000076946100007&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1;CAS:528:DyaK1cXns1yqsLs%3D&pissn=1471-0056&pyear=2002&md5=adef8d134f0c0c94f3e113d6cce36e65>)
19. Clark, S. G., Stern, M. J. & Horvitz, H. R. Genes involved in two *Caenorhabditis elegans* cell-signaling pathways. *Cold Spring Harb. Symp. Quant. Biol.* **57**, 363–373 (1992).
By suppressing a loss-of-function mutation that constitutively activates the vulval pathway, mutations in the activators of the pathway were obtained.
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=1339671&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1992LV41600039&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1;CAS:528:DyaK3sXmt1ajtLY%3D&pissn=1471-0056&pyear=2002&md5=168221ec4cead859379545423030ccb4>)
20. Hodgkin, J. More sex-determination mutants of *Caenorhabditis elegans*. *Genetics* **96**, 649–664 (1980).
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=7262542&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1980LJ51300007&DestApp=WOS_CPL)

- [ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:STN:280:Bi6B287ovVY%3D&pissn=1471-0056&pyear=2002&md5=a4b21dca73a8080da62fcae588ebd4f2) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:STN:280:Bi6B287ovVY%3D&pissn=1471-0056&pyear=2002&md5=a4b21dca73a8080da62fcae588ebd4f2>)
21. Miller, L. M., Plenefisch, J. D., Casson, L. P. & Meyer, B. J. *xol-1*: a gene that controls the male modes of both sex determination and X chromosome dosage compensation in *C. elegans*. *Cell* **55**, 167–183 (1988).
[Article](http://dx.doi.org/10.1016/0092-8674(88)90019-0) ([http://dx.doi.org/10.1016/0092-8674\(88\)90019-0](http://dx.doi.org/10.1016/0092-8674(88)90019-0))
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=3167975&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=3167975&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1988Q510600018&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1988Q510600018&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaL1MXhs1OgtLk%3D&pissn=1471-0056&pyear=2002&md5=315eccf188815323e5d8a6279ceb69ce) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaL1MXhs1OgtLk%3D&pissn=1471-0056&pyear=2002&md5=315eccf188815323e5d8a6279ceb69ce>)
22. Nusbaum, C. & Meyer, B. J. The *Caenorhabditis elegans* gene *sdc-2* controls sex determination and dosage compensation in XX animals. *Genetics* **122**, 579–593 (1989).
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=2759421&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=2759421&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1989AE30400012&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1989AE30400012&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:STN:280:BiaA3sbhsVA%3D&pissn=1471-0056&pyear=2002&md5=9eoff2599cf172d7c99foccf62e841b) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:STN:280:BiaA3sbhsVA%3D&pissn=1471-0056&pyear=2002&md5=9eoff2599cf172d7c99foccf62e841b>)
23. Alfonso, A., Grundahl, K., Duerr, J. S., Han, H. P. & Rand, J. B. The *Caenorhabditis elegans unc-17* gene: a putative vesicular acetylcholine transporter. *Science* **261**, 617–619 (1993).
[Article](http://dx.doi.org/10.1126/science.8342028) (<http://dx.doi.org/10.1126/science.8342028>)
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=8342028&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=8342028&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1993LP72800042&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1993LP72800042&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK2cXht1Kgtb4%3D&pissn=1471-0056&pyear=2002&md5=5a2a5e90ed774af441a04bccc6926d37) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK2cXht1Kgtb4%3D&pissn=1471-0056&pyear=2002&md5=5a2a5e90ed774af441a04bccc6926d37>)
24. Otsuka, A. J. *et al.* The *C. elegans unc-104* gene encodes a putative kinesin heavy chain-like protein. *Neuron* **6**, 113–122 (1991).
[Article](http://dx.doi.org/10.1016/0896-6273(91)90126-K) ([http://dx.doi.org/10.1016/0896-6273\(91\)90126-K](http://dx.doi.org/10.1016/0896-6273(91)90126-K))
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=1846075&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=1846075&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1991EU27800011&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1991EU27800011&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK3MXlvF2qs7w%3D&pissn=1471-0056&pyear=2002&md5=a78533c14564dd4a9248c6d8c69741d9) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK3MXlvF2qs7w%3D&pissn=1471-0056&pyear=2002&md5=a78533c14564dd4a9248c6d8c69741d9>)
25. Hosono, R. *et al.* The *unc-18* gene encodes a novel protein affecting the kinetics of acetylcholine metabolism in the nematode *Caenorhabditis elegans*. *J. Neurochem.* **58**, 1517–1525 (1992).
[Article](http://dx.doi.org/10.1111/j.1471-4159.1992.tb11373.x) (<http://dx.doi.org/10.1111/j.1471-4159.1992.tb11373.x>)
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=1347782&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=1347782&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1992HK06100046&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1992HK06100046&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK3sXitVKgsr4%3D&pissn=1471-0056&pyear=2002&md5=a2b71fed8d470ec55b4daf33482992c6) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK3sXitVKgsr4%3D&pissn=1471-0056&pyear=2002&md5=a2b71fed8d470ec55b4daf33482992c6>)
26. Maruyama, I. N. & Brenner, S. A phorbol ester/diacylglycerol-binding protein encoded by the *unc-13* gene of *Caenorhabditis elegans*. *Proc. Natl Acad. Sci. USA* **88**, 5729–5733 (1991).
[Article](http://dx.doi.org/10.1073/pnas.88.13.5729) (<http://dx.doi.org/10.1073/pnas.88.13.5729>)
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=2062851&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=2062851&dopt=Abstract)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK38XhsVGisbg%3D&pissn=1471-0056&pyear=2002&md5=a6af180604e652d31743efdb0ac507a7) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK38XhsVGisbg%3D&pissn=1471-0056&pyear=2002&md5=a6af180604e652d31743efdb0ac507a7>)
27. Nonet, M. L., Grundahl, K., Meyer, B. J. & Rand, J. B. Synaptic function is impaired but not eliminated in *C. elegans* mutants lacking synaptotagmin. *Cell*

73, 1291–1305 (1993).

[Article](http://dx.doi.org/10.1016/0092-8674(93)90357-V) ([http://dx.doi.org/10.1016/0092-8674\(93\)90357-V](http://dx.doi.org/10.1016/0092-8674(93)90357-V))

[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=8391930&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=8391930&dopt=Abstract)

[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1993LL20900006&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1993LL20900006&DestApp=WOS_CPL)

[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK3sXlslOnsr0%3D&pissn=1471-0056&pyear=2002&md5=cc7f2e9141a060847ea5296b500d28ac) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK3sXlslOnsr0%3D&pissn=1471-0056&pyear=2002&md5=cc7f2e9141a060847ea5296b500d28ac>)

28. Nonet, M. L. *et al.* UNC-11, a *Caenorhabditis elegans* AP180 homologue, regulates the size and protein composition of synaptic vesicles. *Mol. Biol. Cell* **10**, 2343–2360 (1999).

[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=10397769&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=10397769&dopt=Abstract)

[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000081515400019&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000081515400019&DestApp=WOS_CPL)

[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK1MXks1KmsLg%3D&pissn=1471-0056&pyear=2002&md5=59c7e5e8cf674a0702cd75eb98d55e80) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK1MXks1KmsLg%3D&pissn=1471-0056&pyear=2002&md5=59c7e5e8cf674a0702cd75eb98d55e80>)

29. Harris, T. W., Hartweg, E., Horvitz, H. R. & Jorgensen, E. M. Mutations in synaptojanin disrupt synaptic vesicle recycling. *J. Cell Biol.* **150**, 589–600 (2000).

[Article](http://dx.doi.org/10.1083/JCB.150.3.589) (<http://dx.doi.org/10.1083/JCB.150.3.589>)

[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=10931870&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=10931870&dopt=Abstract)

[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000088727800017&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000088727800017&DestApp=WOS_CPL)

[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3cXlsFygsbc%3D&pissn=1471-0056&pyear=2002&md5=a62a2ff6b6b1e1c9509fc30cb451818c) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3cXlsFygsbc%3D&pissn=1471-0056&pyear=2002&md5=a62a2ff6b6b1e1c9509fc30cb451818c>)

30. Korswagen, H. C., Park, J. H., Ohshima, Y. & Plasterk, R. H. An activating mutation in a *Caenorhabditis elegans* G_s protein induces neural degeneration. *Genes Dev.* **11**, 1493–1503 (1997).

[Article](http://dx.doi.org/10.1101/gad.11.12.1493) (<http://dx.doi.org/10.1101/gad.11.12.1493>)

[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=9203577&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=9203577&dopt=Abstract)

[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1997XG85100001&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1997XG85100001&DestApp=WOS_CPL)

[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK2sXktFWqsro%3D&pissn=1471-0056&pyear=2002&md5=5f4dce3bcbb0599d430d9d5fcd79b626) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK2sXktFWqsro%3D&pissn=1471-0056&pyear=2002&md5=5f4dce3bcbb0599d430d9d5fcd79b626>)

31. Berger, A. J., Hart, A. C. & Kaplan, J. M. G_{αc}-induced neurodegeneration in *Caenorhabditis elegans*. *J. Neurosci.* **18**, 2871–2880 (1998).

[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=9526004&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=9526004&dopt=Abstract)

[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1997XG85100001&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1997XG85100001&DestApp=WOS_CPL)

[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK1cXis1ejtL4%3D&pissn=1471-0056&pyear=2002&md5=e45377f56cf99d2ad22470423a3f2503) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK1cXis1ejtL4%3D&pissn=1471-0056&pyear=2002&md5=e45377f56cf99d2ad22470423a3f2503>)

32. Ambros, V. in *C. elegans II* (eds Riddle, D. L., Blumenthal, T., Meyer, B. J. & Priess, J. R.) 501–518 (Cold Spring Harbor Laboratory Press, New York, 1997).

33. Miller, D. M., Niemeyer, C. J. & Chitkara, P. Dominant *unc-37* mutations suppress the movement defect of a homeodomain mutation in *unc-4*, a neural specificity gene in *C. elegans*. *Genetics* **135**, 741–753 (1993).

An elegant screen designed to survey numerous animals and find rare mutations. The screen identified two interacting proteins.

[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=7904971&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=7904971&dopt=Abstract)

[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1993MD63600012&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1993MD63600012&DestApp=WOS_CPL)

[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK2cXisVSkuyY%3D&pissn=1471-0056&pyear=2002&md5=fef64f51a2413c22831034a0ed2ee559) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK2cXisVSkuyY%3D&pissn=1471-0056&pyear=2002&md5=fef64f51a2413c22831034a0ed2ee559>)

34. Winnier, A. R. *et al.* UNC-4/UNC-37-dependent repression of motor neuron-specific genes controls synaptic choice in *Caenorhabditis elegans*. *Genes Dev.* **13**, 2774–2786 (1999).

- Article** (<http://dx.doi.org/10.1101/gad.13.21.2774>)
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=10557206&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000083685100003&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK1MXnsVGtL8%3D&pissn=1471-0056&pyear=2002&md5=e117e7d67992297e9e6f014815f140>)
35. Klein, R. D. & Meyer, B. J. Independent domains of the SDC-3 protein control sex determination and dosage compensation in *C. elegans*. *Cell* **72**, 349–364 (1993).
Article ([http://dx.doi.org/10.1016/0092-8674\(93\)90113-5](http://dx.doi.org/10.1016/0092-8674(93)90113-5))
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=8431944&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1993KM16200006&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK3sXhvVCrtbo%3D&pissn=1471-0056&pyear=2002&md5=0588cadoc0445733739e4e2fb172d5c>)
36. George, S. E., Simokat, K., Hardin, J. & Chisholm, A. D. The VAB-1 Eph receptor tyrosine kinase functions in neural and epithelial morphogenesis in *C. elegans*. *Cell* **92**, 633–643 (1998).
Article ([http://dx.doi.org/10.1016/S0092-8674\(00\)81131-9](http://dx.doi.org/10.1016/S0092-8674(00)81131-9))
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=9506518&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000072406000009&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK1cXhvVWqt7k%3D&pissn=1471-0056&pyear=2002&md5=09fec9c8e07500878d0e52a1aa572bb7>)
37. Chin-Sang, I. D. *et al.* The ephrin VAB-2/EFN-1 functions in neuronal signaling to regulate epidermal morphogenesis in *C. elegans*. *Cell* **99**, 781–790 (1999).
Article ([http://dx.doi.org/10.1016/S0092-8674\(00\)81675-X](http://dx.doi.org/10.1016/S0092-8674(00)81675-X))
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=10619431&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000084488200011&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3cXislStA%3D%3D&pissn=1471-0056&pyear=2002&md5=3d4d2d91a1d6a06e9c0f07a91c984e7>)
38. Goodman, M. B. *et al.* MEC-2 regulates *C. elegans* DEG/ENaC channels needed for mechanosensation. *Nature* **415**, 1039–1042 (2002).
Article (<http://dx.doi.org/10.1038/4151039a>)
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=11875573&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000174075000049&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD38XhvVWjtr0%3D&pissn=1471-0056&pyear=2002&md5=a2beee9ff7efb09f97e7389b45dc2bbe>)
39. Ahmed, S. & Hodgkin, J. MRT-2 checkpoint protein is required for germline immortality and telomere replication in *C. elegans*. *Nature* **403**, 159–164 (2000).
Article (<http://dx.doi.org/10.1038/35003120>)
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=10646593&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000084835300044&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3cXms1WqsQ%3D%3D&pissn=1471-0056&pyear=2002&md5=e24fef9f751d9aa93e743d61ffe7df94>)
40. Hedgecock, E. M., Sulston, J. E. & Thomson, J. N. Mutations affecting programmed cell deaths in the nematode *Caenorhabditis elegans*. *Science* **220**, 1277–1279 (1983).
Article (<http://dx.doi.org/10.1126/science.6857247>)
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=6857247&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1983QT60800031&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?>)

- [APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:STN:280:ByvB38zls1E%3D&pissn=1471-0056&pyear=2002&md5=717d726c5ebb342e8d7d72e179a1bbb9\)](http://dx.doi.org/10.1016/S0165-0270(99)00031-X)
41. Ellis, H. M. & Horvitz, H. R. Genetic control of programmed cell death in the nematode *C. elegans*. *Cell* **44**, 817–829 (1986).
Article ([http://dx.doi.org/10.1016/0092-8674\(86\)90004-8](http://dx.doi.org/10.1016/0092-8674(86)90004-8))
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=3955651&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1986A741800002&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaL28XhvVelsLw%3D&pissn=1471-0056&pyear=2002&md5=35da47912073b185dbadb9c875ff900c>)
42. Liu, Q. A. & Hengartner, M. O. The molecular mechanism of programmed cell death in *C. elegans*. *Ann. NY Acad. Sci.* **887**, 92–104 (1999).
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=10668467&dopt=Abstract)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3cXnt1SgsA%3D%3D&pissn=1471-0056&pyear=2002&md5=55c69ef07ed5e638ccdf5b786abff554>)
43. Hengartner, M. O., Ellis, R. E. & Horvitz, H. R. *Caenorhabditis elegans* gene *ced-9* protects cells from programmed cell death. *Nature* **356**, 494–499 (1992).
Article ([/doi/10.1038/356494a0](http://dx.doi.org/10.1038/356494a0))
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=1560823&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1992HN23100048&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK38XisV2rtLs%3D&pissn=1471-0056&pyear=2002&md5=70d14b4e3c8f766601778a7a03dca11>)
44. Hengartner, M. O. & Horvitz, H. R. *C. elegans* cell survival gene *ced-9* encodes a functional homolog of the mammalian proto-oncogene *bcl-2*. *Cell* **76**, 665–676 (1994).
Article ([http://dx.doi.org/10.1016/0092-8674\(94\)90506-1](http://dx.doi.org/10.1016/0092-8674(94)90506-1))
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=7907274&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1994MZ28500009&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK2cXis1altbs%3D&pissn=1471-0056&pyear=2002&md5=d1ef23df3abba50d42aded1de4922728>)
45. Chalfie, M., Tu, Y., Euskirchen, G., Ward, W. W. & Prasher, D. C. Green fluorescent protein as a marker for gene expression. *Science* **263**, 802–805 (1994).
Article (<http://dx.doi.org/10.1126/science.8303295>)
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=8303295&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1994MV86600033&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK2cXitFWkurc%3D&pissn=1471-0056&pyear=2002&md5=7c58309d4425c6b980beb516a87c13f2>)
46. Nonet, M. L. Visualization of synaptic specializations in live *C. elegans* with synaptic vesicle protein–GFP fusions. *J. Neurosci. Methods* **89**, 33–40 (1999).
Article ([http://dx.doi.org/10.1016/S0165-0270\(99\)00031-X](http://dx.doi.org/10.1016/S0165-0270(99)00031-X))
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=10476681&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000082007000005&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK1MXlvVOMtr8%3D&pissn=1471-0056&pyear=2002&md5=5b8310831e0ea79572e45d8db733d553>)
47. Schaefer, A. M., Hadwiger, G. D. & Nonet, M. L. *rpm-1*, a conserved neuronal gene that regulates targeting and synaptogenesis in *C. elegans*. *Neuron* **26**, 345–356 (2000).
Article ([http://dx.doi.org/10.1016/S0896-6273\(00\)81168-X](http://dx.doi.org/10.1016/S0896-6273(00)81168-X))
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=10839354&dopt=Abstract)

- [ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000087296500012&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000087296500012&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3cXjvFensrc%3D&pissn=1471-0056&pyear=2002&md5=1d18af6cb6661567dfb65cdbca562e52) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3cXjvFensrc%3D&pissn=1471-0056&pyear=2002&md5=1d18af6cb6661567dfb65cdbca562e52>)
48. Zhen, M., Huang, X., Bamber, B. & Jin, Y. Regulation of presynaptic terminal organization by *C. elegans* RPM-1, a putative guanine nucleotide exchanger with a RING-H2 finger domain. *Neuron* **26**, 331–343 (2000).
[Article](http://dx.doi.org/10.1016/S0896-6273(00)81167-8) ([http://dx.doi.org/10.1016/S0896-6273\(00\)81167-8](http://dx.doi.org/10.1016/S0896-6273(00)81167-8))
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=10839353&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=10839353&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000087296500011&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000087296500011&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3cXjvFensrY%3D&pissn=1471-0056&pyear=2002&md5=56fef923ed7bf2916doefc4ad9bb62) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3cXjvFensrY%3D&pissn=1471-0056&pyear=2002&md5=56fef923ed7bf2916doefc4ad9bb62>)
49. Crump, J. G., Zhen, M., Jin, Y. & Bargmann, C. I. The SAD-1 kinase regulates presynaptic vesicle clustering and axon termination. *Neuron* **29**, 115–129 (2001).
[Article](http://dx.doi.org/10.1016/S0896-6273(01)00184-2) ([http://dx.doi.org/10.1016/S0896-6273\(01\)00184-2](http://dx.doi.org/10.1016/S0896-6273(01)00184-2))
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=11182085&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=11182085&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000166702700013&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000166702700013&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3MXisleisLo%3D&pissn=1471-0056&pyear=2002&md5=c19306a08fd2407e3cf9889043c05163) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3MXisleisLo%3D&pissn=1471-0056&pyear=2002&md5=c19306a08fd2407e3cf9889043c05163>)
50. Zallen, J. A., Yi, B. A. & Bargmann, C. I. The conserved immunoglobulin superfamily member SAX-3/Robo directs multiple aspects of axon guidance in *C. elegans*. *Cell* **92**, 217–227 (1998).
[Article](http://dx.doi.org/10.1016/S0092-8674(00)80916-2) ([http://dx.doi.org/10.1016/S0092-8674\(00\)80916-2](http://dx.doi.org/10.1016/S0092-8674(00)80916-2))
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=9458046&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=9458046&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000071672600011&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000071672600011&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK1cXnslaktw%3D%3D&pissn=1471-0056&pyear=2002&md5=bd7277151045b9b7620f53c5ade19942) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK1cXnslaktw%3D%3D&pissn=1471-0056&pyear=2002&md5=bd7277151045b9b7620f53c5ade19942>)
51. Satterlee, J. S. *et al.* Specification of thermosensory neuron fate in *C. elegans* requires *ttx-1*, a homolog of *otd/Otx*. *Neuron* **31**, 943–956 (2001).
[Article](http://dx.doi.org/10.1016/S0896-6273(01)00431-7) ([http://dx.doi.org/10.1016/S0896-6273\(01\)00431-7](http://dx.doi.org/10.1016/S0896-6273(01)00431-7))
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=11580895&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=11580895&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000171281300010&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000171281300010&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3MXns1Cgsrs%3D&pissn=1471-0056&pyear=2002&md5=fa2c9f73694bd1acd730d0cco462e83e) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3MXns1Cgsrs%3D&pissn=1471-0056&pyear=2002&md5=fa2c9f73694bd1acd730d0cco462e83e>)
52. Hsieh, J. *et al.* The RING finger/B-box factor TAM-1 and a retinoblastoma-like protein LIN-35 modulate context-dependent gene silencing in *Caenorhabditis elegans*. *Genes Dev.* **13**, 2958–2970 (1999).
[Article](http://dx.doi.org/10.1101/gad.13.22.2958) (<http://dx.doi.org/10.1101/gad.13.22.2958>)
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=10580003&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=10580003&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000084048600006&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000084048600006&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK1MXnvVClLc%3D&pissn=1471-0056&pyear=2002&md5=de07204c21eco804df96b45e8be7dde5) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK1MXnvVClLc%3D&pissn=1471-0056&pyear=2002&md5=de07204c21eco804df96b45e8be7dde5>)
53. Grant, B. & Hirsh, D. Receptor-mediated endocytosis in the *Caenorhabditis elegans* oocyte. *Mol. Biol. Cell* **10**, 4311–4326 (1999).
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=10588660&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=10588660&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000084146900023&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000084146900023&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK1MXnvFKqsby%3D&pissn=1471-0056&pyear=2002&md5=378259a021a307b838cba301584b4a6a) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK1MXnvFKqsby%3D&pissn=1471-0056&pyear=2002&md5=378259a021a307b838cba301584b4a6a>)

54. Fares, H. & Greenwald, I. Regulation of endocytosis by CUP-5, the *Caenorhabditis elegans* mucopolipin-1 homolog. *Nature Genet.* **28**, 64–68 (2001).
[Article](#) ([/doifinder/10.1038/ng0501-64](http://dx.doi.org/10.1038/ng0501-64))
55. Fares, H. & Greenwald, I. Genetic analysis of endocytosis in *Caenorhabditis elegans*: coelomocyte uptake defective mutants. *Genetics* **159**, 133–145 (2001).
[PubMed](#) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=11560892&dopt=Abstract)
[ISI](#) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000171252500011&DestApp=WOS_CPL)
[ChemPort](#) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3MXns12js7s%3D&pissn=1471-0056&pyear=2002&md5=c1244555ef43c11847c3c4edfd0234f1>)
56. Abrahante, J. E., Miller, E. A. & Rougvie, A. E. Identification of heterochronic mutants in *Caenorhabditis elegans*. Temporal misexpression of a collagen::green fluorescent protein fusion gene. *Genetics* **149**, 1335–1351 (1998).
[PubMed](#) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=9649524&dopt=Abstract)
[ISI](#) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000074708200014&DestApp=WOS_CPL)
[ChemPort](#) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK1cXkslOnur4%3D&pissn=1471-0056&pyear=2002&md5=9c44b93f91beeefa34c5ddb344670bc0>)
57. Troemel, E. R., Sagasti, A. & Bargmann, C. I. Lateral signaling mediated by axon contact and calcium entry regulates asymmetric odorant receptor expression in *C. elegans*. *Cell* **99**, 387–398 (1999).
[Article](#) ([http://dx.doi.org/10.1016/S0092-8674\(00\)81525-1](http://dx.doi.org/10.1016/S0092-8674(00)81525-1))
[PubMed](#) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=10571181&dopt=Abstract)
[ISI](#) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000083709300006&DestApp=WOS_CPL)
[ChemPort](#) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK1MXns1egsLs%3D&pissn=1471-0056&pyear=2002&md5=756b10538008a3b1bb803bb501f065dc>)
58. Avery, L. & Horvitz, H. R. A cell that dies during wild-type *C. elegans* development can function as a neuron in a *ced-3* mutant. *Cell* **51**, 1071–1078 (1987).
[Article](#) ([http://dx.doi.org/10.1016/0092-8674\(87\)90593-9](http://dx.doi.org/10.1016/0092-8674(87)90593-9))
[PubMed](#) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=3690660&dopt=Abstract)
[ISI](#) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1987L491900021&DestApp=WOS_CPL)
[ChemPort](#) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:STN:280:BieD1c%2Fks1E%3D&pissn=1471-0056&pyear=2002&md5=64f48cc80fb5aff8e35cbef097d1446b>)
59. Avery, L. The genetics of feeding in *Caenorhabditis elegans*. *Genetics* **133**, 897–917 (1993).
[PubMed](#) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=8462849&dopt=Abstract)
[ISI](#) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1993KT99900013&DestApp=WOS_CPL)
[ChemPort](#) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:STN:280:ByyB3MngvVw%3D&pissn=1471-0056&pyear=2002&md5=3aa6fa67d7e7a1506cc9747bda2700f6>)
60. Davis, M. W., Fleischhauer, R., Dent, J. A., Joho, R. H. & Avery, L. A mutation in the *C. elegans* EXP-2 potassium channel that alters feeding behavior. *Science* **286**, 2501–2504 (1999).
[Article](#) (<http://dx.doi.org/10.1126/science.286.5449.2501>)
[PubMed](#) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=10617464&dopt=Abstract)
[ISI](#) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000084429700047&DestApp=WOS_CPL)
[ChemPort](#) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3cXmvVKk&pissn=1471-0056&pyear=2002&md5=995d72d9f6ad13c6d068ce3de99dbbce>)
61. Clark, D. V., Rogalski, R. M., Donati, L. M. & Baillie, D. L. The *unc-22(IV)* region of *Caenorhabditis elegans*: genetic analysis of lethal mutations. *Genetics* **119**,

345–353 (1988).

PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=3396868&dopt=Abstract)

ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1988N663300012&DestApp=WOS_CPL)

ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:STN:280:BieB1cvjt1E%3D&pissn=1471-0056&pyear=2002&md5=f6018b8f617bf44859e3273ad67c6fc2>)

62. Johnsen, R. C. & Baillie, D. L. Genetic analysis of a major segment [LGV(left)] of the genome of *Caenorhabditis elegans*. *Genetics* **129**, 735–752 (1991).

PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=1752418&dopt=Abstract)

ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1991GL9600015&DestApp=WOS_CPL)

ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:STN:280:DyaK38XhsVGhsrs%3D&pissn=1471-0056&pyear=2002&md5=b523a13b0117a03659dfcd4aba75e503>)

63. Hodgkin, J. What does a worm want with 20,000 genes? *Genome Biol.* **2**, 2008.1–2008.4 (2001).

64. Herman, R. K. Crossover suppressors and balanced recessive lethals in *Caenorhabditis elegans*. *Genetics* **88**, 49–65 (1978).

PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=631558&dopt=Abstract)

ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1978ER32000004&DestApp=WOS_CPL)

ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:STN:280:CSeC38fgtII%3D&pissn=1471-0056&pyear=2002&md5=c9fb4a28ab26c10aa7d8e9c50bc0146e>)

65. Rosenbluth, R. E. & Baillie, D. L. The genetic analysis of a reciprocal translocation, *eT1(III; V)*, in *Caenorhabditis elegans*. *Genetics* **99**, 415–428 (1981).

PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=6953041&dopt=Abstract)

ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1981NK71200004&DestApp=WOS_CPL)

ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:STN:280:Bi2B3M7nsVI%3D&pissn=1471-0056&pyear=2002&md5=15cce71772a400760e80e1baaffaf157>)

66. Page, B. D., Zhang, W., Steward, K., Blumenthal, T. & Priess, J. R. ELT-1, a GATA-like transcription factor, is required for epidermal cell fates in *Caenorhabditis elegans* embryos. *Genes Dev.* **11**, 1651–1661 (1997).

Article (<http://dx.doi.org/10.1101/gad.11.13.1651>)

PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=9224715&dopt=Abstract)

ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1997XK99500003&DestApp=WOS_CPL)

ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:STN:280:DyaK2sXks1ymt78%3D&pissn=1471-0056&pyear=2002&md5=96038b47f25d349116cff9bdbd135223>)

67. Schnabel, R. & Priess, J. in *C. elegans II* (eds Riddle, D. L., Blumenthal, T., Meyer, B. J. & Priess, J. R.) 361–382 (Cold Spring Harbor Laboratory Press, New York, 1997).

68. Kemphues, K. J. & Strome, S. in *C. elegans II* (eds Riddle, D. L., Blumenthal, T., Meyer, B. J. & Priess, J. R.) 335–359 (Cold Spring Harbor Laboratory Press, New York, 1997).

69. Priess, J. R., Schnabel, H. & Schnabel, R. The *glp-1* locus and cellular interactions in early *C. elegans* embryos. *Cell* **51**, 601–611 (1987).

A successful maternal-effect screen that identified and characterized the first regulator of embryonic cell fate in *C. elegans*.

Article ([http://dx.doi.org/10.1016/0092-8674\(87\)90129-2](http://dx.doi.org/10.1016/0092-8674(87)90129-2))

PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=3677169&dopt=Abstract)

ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1987K982000013&DestApp=WOS_CPL)

ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:STN:280:DvaL1cXhslWlug%3D%3D&pissn=1471-0056&pyear=2002&md5=96038b47f25d349116cff9bdbd135223>)

- [0056&pyear=2002&md5=f68007f2fdcf1d7376a51a8cc74556f0](http://dx.doi.org/10.1016/S0092-8674(88)80024-2)
70. Kemphues, K. J., Priess, J. R., Morton, D. G. & Cheng, N. Identification of genes required for cytoplasmic localization of early *C. elegans* embryos. *Cell* **52**, 311–320 (1988).
Article ([http://dx.doi.org/10.1016/S0092-8674\(88\)80024-2](http://dx.doi.org/10.1016/S0092-8674(88)80024-2))
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=3345562&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1988M255200003&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaL1cXhvVeqtro%3D&pissn=1471-0056&pyear=2002&md5=1270893914a1be99d95e96ecfba92ad0>)
71. Bowerman, B., Eaton, B. A. & Priess, J. R. *skn-1*, a maternally expressed gene required to specify the fate of ventral blastomeres in the early *C. elegans* embryo. *Cell* **68**, 1061–1075 (1992).
Article ([http://dx.doi.org/10.1016/0092-8674\(92\)90078-0](http://dx.doi.org/10.1016/0092-8674(92)90078-0))
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=1547503&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1992HK67400010&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK3sXks1Churk%3D&pissn=1471-0056&pyear=2002&md5=d0d2d9a178c3af961a6f28edcf0d2fdb>)
72. O'Connell, K. F., Leys, C. M. & White, J. G. A genetic screen for temperature-sensitive cell-division mutants of *Caenorhabditis elegans*. *Genetics* **149**, 1303–1321 (1998).
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=9649522&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000074708200012&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK1cXkslOntbY%3D&pissn=1471-0056&pyear=2002&md5=a8bdd0d9657154c1d885d27b797a2afc>)
73. Ahringer, J. Embryonic tissue differentiation in *Caenorhabditis elegans* requires *dif-1*, a gene homologous to mitochondrial solute carriers. *EMBO J.* **14**, 2307–2316 (1995).
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=7774589&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1995QZ86200019&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK2MXlvFyntr4%3D&pissn=1471-0056&pyear=2002&md5=b9c6f50dfo436cd4fd1c32c4e8doaf7>)
74. Labouesse, M. & Mango, S. E. Patterning the *C. elegans* embryo: moving beyond the cell lineage. *Trends Genet.* **15**, 307–313 (1999).
Article ([http://dx.doi.org/10.1016/S0168-9525\(99\)01750-3](http://dx.doi.org/10.1016/S0168-9525(99)01750-3))
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=10431192&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000081822600006&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK1MXltVemtLk%3D&pissn=1471-0056&pyear=2002&md5=2fce5c5159a63b95d637ed238644bea>)
75. Bowerman, B. Embryonic polarity: protein stability in asymmetric cell division. *Curr. Biol.* **10**, R637–R641 (2000).
Article ([http://dx.doi.org/10.1016/S0960-9822\(00\)00660-6](http://dx.doi.org/10.1016/S0960-9822(00)00660-6))
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=10996090&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000089303900010&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3cXmt1aisbc%3D&pissn=1471-0056&pyear=2002&md5=74576977ab86f1590b61d0ac1a681a07>)
76. Gonczy, P. *et al.* Dissection of cell division processes in the one cell stage *Caenorhabditis elegans* embryo by mutational analysis. *J. Cell Biol.* **144**, 927–946 (1999).

Article (<http://dx.doi.org/10.1083/jcb.144.5.927>)

PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=10085292&dopt=Abstract)

ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000079377100012&DestApp=WOS_CPL)

ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK1MXhs1yqur8%3D&pissn=1471-0056&pyear=2002&md5=b7a266c9e6473ee30f9dce71f2fc5cc>)

77. Priess, J. R. & Thomson, J. N. Cellular interactions in early *C. elegans* embryos. *Cell* **48**, 241–250 (1987).

Article ([http://dx.doi.org/10.1016/0092-8674\(87\)90427-2](http://dx.doi.org/10.1016/0092-8674(87)90427-2))

PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=3802194&dopt=Abstract)

ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1987F975900009&DestApp=WOS_CPL)

ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:STN:280:BiiC3c3oslU%3D&pissn=1471-0056&pyear=2002&md5=1d6e9e7e2e54b50ffcc7cdd9e395714a>)

78. Goutte, C., Hepler, W., Mickey, K. M. & Priess, J. R. *aph-2* encodes a novel extracellular protein required for GLP-1-mediated signaling. *Development* **127**, 2481–2492 (2000).

PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=10804188&dopt=Abstract)

ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000087881900022&DestApp=WOS_CPL)

ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3cXksVKmsL4%3D&pissn=1471-0056&pyear=2002&md5=85df300092097bdb6e18e6e61e223a64>)

79. Goutte, C., Tsunozaki, M., Hale, V. A. & Priess, J. R. APH-1 is a multipass membrane protein essential for the Notch signaling pathway in *Caenorhabditis elegans* embryos. *Proc. Natl Acad. Sci. USA* **99**, 775–779 (2002).

Article (<http://dx.doi.org/10.1073/PNAS.022523499>)

PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=11792846&dopt=Abstract)

ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000087881900022&DestApp=WOS_CPL)

ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD38Xht1Wisrs%3D&pissn=1471-0056&pyear=2002&md5=77e6a89bcc3cod98436979187329c575>)

80. Simon, M. A., Bowtell, D. D., Dodson, G. S., Laverty, T. R. & Rubin, G. M. Ras1 and a putative guanine nucleotide exchange factor perform crucial steps in signaling by the sevenless protein tyrosine kinase. *Cell* **67**, 701–716 (1991).

Article ([http://dx.doi.org/10.1016/0092-8674\(91\)90065-7](http://dx.doi.org/10.1016/0092-8674(91)90065-7))

PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=1934068&dopt=Abstract)

ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1991GQ40700007&DestApp=WOS_CPL)

ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK3sXhsVektbc%3D&pissn=1471-0056&pyear=2002&md5=63e2ea7151dc451d3a9a9dca157ae4e7>)

81. Gu, G., Caldwell, G. A. & Chalfie, M. Genetic interactions affecting touch sensitivity in *Caenorhabditis elegans*. *Proc. Natl Acad. Sci. USA* **93**, 6577–6582 (1996).

Article (<http://dx.doi.org/10.1073/pnas.93.13.6577>)

PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=8692859&dopt=Abstract)

ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000077435400005&DestApp=WOS_CPL)

ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK28XjvFeisrY%3D&pissn=1471-0056&pyear=2002&md5=f35674dcfb8199a5c46e82969db603ac>)

82. Cali, B. M. & Anderson, P. mRNA surveillance mitigates genetic dominance in *Caenorhabditis elegans*. *Mol. Gen. Genet.* **260**, 176–184 (1998).

Article (<http://dx.doi.org/10.1007/s004380050883>)

PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=9862469&dopt=Abstract)

ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000077435400005&DestApp=WOS_CPL)

ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:STN:280:DyaK1M%2Fnsartw%3D%3D&pissn=1471-0056&pyear=2002&md5=e2a4994044f7c857330789608f946002>)

83. Yook, K. J., Proulx, S. R. & Jorgensen, E. M. Rules of nonallelic noncomplementation at the synapse in *Caenorhabditis elegans*. *Genetics* **158**, 209–220 (2001).
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=11333231&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=11333231&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000168637000019&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000168637000019&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3MXkt1OjsL0%3D&pissn=1471-0056&pyear=2002&md5=4d88ddc3c1e1ba437f33105310d913co) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3MXkt1OjsL0%3D&pissn=1471-0056&pyear=2002&md5=4d88ddc3c1e1ba437f33105310d913co>)
84. Waterston, R. H., Sulston, J. E. & Couson, A. R. in *C. elegans II* Vol. **33** (eds Riddle, D. L., Blumenthal, T., Meyer, B. J. & Priess, J. R.) 23–45 (Cold Spring Harbor Laboratory Press, New York, 1997).
85. The *C. elegans* Sequencing Consortium. Genome sequence of the nematode *C. elegans*: a platform for investigating biology. *Science* **282**, 2012–2018 (1998).
[Article](http://dx.doi.org/10.1126/science.282.5386.53) (<http://dx.doi.org/10.1126/science.282.5386.53>)
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=9851916&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=9851916&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000077467100034&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000077467100034&DestApp=WOS_CPL)
86. Hodgkin, J. & Herman, R. K. Changing styles in *C. elegans* genetics. *Trends Genet.* **14**, 352–357 (1998).
[Article](http://dx.doi.org/10.1016/S0168-9525(98)01543-1) ([http://dx.doi.org/10.1016/S0168-9525\(98\)01543-1](http://dx.doi.org/10.1016/S0168-9525(98)01543-1))
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=9769730&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=9769730&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000075663300005&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000075663300005&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK1cXlvV2qur4%3D&pissn=1471-0056&pyear=2002&md5=934950e29425d433de23166741d8aaf8) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK1cXlvV2qur4%3D&pissn=1471-0056&pyear=2002&md5=934950e29425d433de23166741d8aaf8>)
87. Fraser, A. G. *et al.* Functional genomic analysis of *C. elegans* chromosome I by systematic RNA interference. *Nature* **408**, 325–330 (2000).
[Article](http://dx.doi.org/10.1038/35042517) (<http://dx.doi.org/10.1038/35042517>)
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=11099033&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=11099033&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000165296000036&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000165296000036&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3cXosVelsrc%3D&pissn=1471-0056&pyear=2002&md5=e5b8f496ed335b692ac24aa211be43d) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3cXosVelsrc%3D&pissn=1471-0056&pyear=2002&md5=e5b8f496ed335b692ac24aa211be43d>)
88. Gonczy, P. *et al.* Functional genomic analysis of cell division in *C. elegans* using RNAi of genes on chromosome III. *Nature* **408**, 331–336 (2000).
[Article](http://dx.doi.org/10.1038/35042526) (<http://dx.doi.org/10.1038/35042526>)
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=11099034&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=11099034&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=ERROR&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=ERROR&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3cXosVelur8%3D&pissn=1471-0056&pyear=2002&md5=3d287c9a32651e9dcf622f5f84eb506b) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3cXosVelur8%3D&pissn=1471-0056&pyear=2002&md5=3d287c9a32651e9dcf622f5f84eb506b>)
89. Thomas, J. H. Thinking about genetic redundancy. *Trends Genet.* **9**, 395–399 (1993).
[Article](http://dx.doi.org/10.1016/0168-9525(93)90140-D) ([http://dx.doi.org/10.1016/0168-9525\(93\)90140-D](http://dx.doi.org/10.1016/0168-9525(93)90140-D))
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=8310537&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=8310537&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1993MD91100009&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1993MD91100009&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:STN:280:ByuC2cvgtVc%3D&pissn=1471-0056&pyear=2002&md5=b877aa235252c7f44e886e2b5ad31bf7) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:STN:280:ByuC2cvgtVc%3D&pissn=1471-0056&pyear=2002&md5=b877aa235252c7f44e886e2b5ad31bf7>)
90. Zhu, J. *et al.* *end-1* encodes an apparent GATA factor that specifies the endoderm precursor in *Caenorhabditis elegans* embryos. *Genes Dev.* **11**, 2883–2896 (1997).
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=9353257&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=9353257&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1997YF58300012&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1997YF58300012&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?) (<http://chemport.cas.org/cgi-bin/sdcgi?>)

- [APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1;CAS:528:DyaK2sXntlOisbc%3D&pissn=1471-0056&pyear=2002&md5=6f124ce2ed5b64e272826072957dd56b](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=1769331&dopt=Abstract)
91. Lambie, E. J. & Kimble, J. Two homologous regulatory genes, *lin-12* and *glp-1*, have overlapping functions. *Development* **112**, 231–240 (1991).
A description of two genes with unique and redundant functions, and how that information was used as the basis for a genetic screen.
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=1769331&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1991FN47500021&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1;CAS:528:DyaK3MXmjlajs7c%3D&pissn=1471-0056&pyear=2002&md5=56c5d3c5b5a505a4c47b05e3037badof>)
92. Christensen, S., Kodoyianni, V., Bosenberg, M., Friedman, L. & Kimble, J. *lag-1*, a gene required for *lin-12* and *glp-1* signaling in *Caenorhabditis elegans*, is homologous to human *CBF1* and *Drosophila Su(H)*. *Development* **122**, 1373–1383 (1996).
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=8625826&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1996UM55800004&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1;CAS:528:DyaK28Xjt1Gju7c%3D&pissn=1471-0056&pyear=2002&md5=cf2945052df750a4a20ca1f7cd14bbff>)
93. Henderson, S. T., Gao, D., Lambie, E. J. & Kimble, J. *lag-2* may encode a signaling ligand for the GLP-1 and LIN-12 receptors of *C. elegans*. *Development* **120**, 2913–2924 (1994).
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=7607081&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1994PN07600016&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1;CAS:528:DyaK2MXhtl2gtrg%3D&pissn=1471-0056&pyear=2002&md5=4f50ac3562e661040352ac09b203037d>)
94. Tax, F. E., Yeagers, J. J. & Thomas, J. H. Sequence of *C. elegans lag-2* reveals a cell-signalling domain shared with *Delta* and *Serrate* of *Drosophila*. *Nature* **368**, 150–154 (1994).
Article ([/doi/10.1038/368150a0](http://dx.doi.org/10.1038/368150a0))
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=8139658&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1994NA03000067&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1;CAS:528:DyaK2cXjtFOqtr8%3D&pissn=1471-0056&pyear=2002&md5=ce7f7eafa1bcd703b6f6bdd481001352>)
95. Ferguson, E. & Horvitz, H. R. The multivulva phenotype of certain *C. elegans* mutants results from defects in two functionally-redundant pathways. *Genetics* **123**, 109–121 (1989).
A genetic analysis of an intriguing example of non-homologous redundancy.
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=2806880&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1989AN07000010&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1;STN:280:By%2BD3svhtVI%3D&pissn=1471-0056&pyear=2002&md5=96119d9c4d34150f60c7062393c10a96>)
96. Fay, D. S. & Han, M. The synthetic multivulval genes of *C. elegans*: functional redundancy, Ras-antagonism, and cell fate determination. *Genesis* **26**, 279–284 (2000).
Article ([http://dx.doi.org/10.1002/\(SICI\)1526-968X\(200004\)26:4<279::AID-GENE100>3.0.CO;2-C](http://dx.doi.org/10.1002/(SICI)1526-968X(200004)26:4<279::AID-GENE100>3.0.CO;2-C))
PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=10748467&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000089556800010&DestApp=WOS_CPL)

- [ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1;CAS:528:DC%2BD3cXjSlSkL0%3D&pissn=1471-0056&pyear=2002&md5=72858122f4e5931b5b3374467eca24fc) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1;CAS:528:DC%2BD3cXjSlSkL0%3D&pissn=1471-0056&pyear=2002&md5=72858122f4e5931b5b3374467eca24fc>)
97. Lundquist, E. A. *et al.* The *mec-8* gene of *C. elegans* encodes a protein with two RNA recognition motifs and regulates alternative splicing of *unc-52* transcripts. *Development* **122**, 1601–1610 (1996).
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=8625846&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=8625846&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1996UM55800024&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1996UM55800024&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1;CAS:528:DyaK28Xjt1Gis7c%3D&pissn=1471-0056&pyear=2002&md5=02f639c6c48e6a6cc60ca427ff1cd431) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1;CAS:528:DyaK28Xjt1Gis7c%3D&pissn=1471-0056&pyear=2002&md5=02f639c6c48e6a6cc60ca427ff1cd431>)
98. Bender, A. & Pringle, J. R. Use of a screen for synthetic lethal and multicopy suppressor mutants to identify two new genes involved in morphogenesis in *Saccharomyces cerevisiae*. *Mol. Cell. Biol.* **11**, 1295–1305 (1991).
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=1996092&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=1996092&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1991EZ33100012&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1991EZ33100012&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1;CAS:528:DyaK3MXltVONsb4%3D&pissn=1471-0056&pyear=2002&md5=fd470e360f9067ba180be380cfd8dcb) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1;CAS:528:DyaK3MXltVONsb4%3D&pissn=1471-0056&pyear=2002&md5=fd470e360f9067ba180be380cfd8dcb>)
99. Davies, A. G., Spike, C. A., Shaw, J. E. & Herman, R. K. Functional overlap between the *mec-8* gene and five *sym* genes in *Caenorhabditis elegans*. *Genetics* **153**, 117–134 (1999).
This paper describes an approach that is broadly applicable for isolating mutations in redundant genes.
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=10471705&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=10471705&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000082421600012&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000082421600012&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1;CAS:528:DyaK1MXmsVWqtLo%3D&pissn=1471-0056&pyear=2002&md5=adb2f755c7913eed7a85e6371ae35242) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1;CAS:528:DyaK1MXmsVWqtLo%3D&pissn=1471-0056&pyear=2002&md5=adb2f755c7913eed7a85e6371ae35242>)
100. Fay, D. S., Keenan, S. & Han, M. *fzr-1* and *lin-35*/Rb function redundantly to control cell proliferation in *C. elegans* as revealed by a nonbiased synthetic screen. *Genes Dev.* **16**, 503–517 (2002).
[Article](http://dx.doi.org/10.1101/gad.952302) (<http://dx.doi.org/10.1101/gad.952302>)
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=11850412&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=11850412&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000174044600010&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000174044600010&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1;CAS:528:DC%2BD38XhvFKgs7c%3D&pissn=1471-0056&pyear=2002&md5=d89a8b7054cdea0d02cea8c54821e629) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1;CAS:528:DC%2BD38XhvFKgs7c%3D&pissn=1471-0056&pyear=2002&md5=d89a8b7054cdea0d02cea8c54821e629>)
101. De Bono, M. & Bargmann, C. I. Natural variation in a neuropeptide Y receptor homolog modifies social behavior and food response in *C. elegans*. *Cell* **94**, 679–689 (1998).
[Article](http://dx.doi.org/10.1016/S0092-8674(00)81609-8) ([http://dx.doi.org/10.1016/S0092-8674\(00\)81609-8](http://dx.doi.org/10.1016/S0092-8674(00)81609-8))
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=9741632&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=9741632&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000075851900015&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000075851900015&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1;CAS:528:DyaK1cXmtVWksrY%3D&pissn=1471-0056&pyear=2002&md5=b98e0809236fbf36299b027790235305) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1;CAS:528:DyaK1cXmtVWksrY%3D&pissn=1471-0056&pyear=2002&md5=b98e0809236fbf36299b027790235305>)
102. Sulston, J. E. & Horvitz, H. R. Post-embryonic cell lineages of the nematode *Caenorhabditis elegans*. *Dev. Biol.* **56**, 110–156 (1977).
[Article](http://dx.doi.org/10.1016/0012-1606(77)90158-0) ([http://dx.doi.org/10.1016/0012-1606\(77\)90158-0](http://dx.doi.org/10.1016/0012-1606(77)90158-0))
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=838129&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=838129&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1977CY53300009&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1977CY53300009&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1;STN:280:CSiC3Mnls1E%3D&pissn=1471-0056&pyear=2002&md5=746b60163dde2c7bbb70cob3f81c18ca) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1;STN:280:CSiC3Mnls1E%3D&pissn=1471-0056&pyear=2002&md5=746b60163dde2c7bbb70cob3f81c18ca>)

103. Sulston, J. E., Schierenberg, E., White, J. G. & Thomson, J. N. The embryonic cell lineage of the nematode *Caenorhabditis elegans*. *Dev. Biol.* **100**, 64–119 (1983).
[Article](http://dx.doi.org/10.1016/0012-1606(83)90201-4) ([http://dx.doi.org/10.1016/0012-1606\(83\)90201-4](http://dx.doi.org/10.1016/0012-1606(83)90201-4))
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=6684600&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=6684600&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1983RN28500007&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1983RN28500007&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:STN:280:BiuD3crks1M%3D&pissn=1471-0056&pyear=2002&md5=6e5ed7d75bfe37cbbbea01b3010fdbec) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:STN:280:BiuD3crks1M%3D&pissn=1471-0056&pyear=2002&md5=6e5ed7d75bfe37cbbbea01b3010fdbec>)
104. Riddle, D. & Albert, P. S. in *C. elegans II* Vol. **1** (eds Riddle, D. L., Blumenthal, T., Meyer, B. J. & Priess, J. R.) 739–768 (Cold Spring Harbor Laboratory Press, New York, 1997).
105. Anderson, P. in *Caenorhabditis elegans: modern biological analysis of an organism* Vol. **48** (eds Epstein, H. F. & Shakes, D. C.) 31–58 (Academic, San Diego, California, 1995).
A comprehensive and quantitative discussion of mutagenesis approaches in *C. elegans*.
106. Coulson, A., Sulston, J., Brenner, S. & Karn, J. Toward a physical map of the genome of the nematode *C. elegans*. *Proc. Natl Acad. Sci. USA* **83**, 7821–7825 (1986).
[Article](http://dx.doi.org/10.1073/pnas.83.20.7821) (<http://dx.doi.org/10.1073/pnas.83.20.7821>)
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=16593771&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=16593771&dopt=Abstract)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaL28XmtVCisLo%3D&pissn=1471-0056&pyear=2002&md5=a18d735a057a3d5b100c42725e2b4686) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaL28XmtVCisLo%3D&pissn=1471-0056&pyear=2002&md5=a18d735a057a3d5b100c42725e2b4686>)
107. Fire, A. Integrative transformation of *Caenorhabditis elegans*. *EMBO J.* **5**, 2673–2680 (1986).
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=16453714&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=16453714&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1986E419000035&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=A1986E419000035&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaL2sXhtlSn&pissn=1471-0056&pyear=2002&md5=0d2448580dce79ec1e754dc76babf6d7) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaL2sXhtlSn&pissn=1471-0056&pyear=2002&md5=0d2448580dce79ec1e754dc76babf6d7>)
108. Koch, R., Van Luenen, H. G., Van der Horst, M., Thijssen, K. L. & Plasterk, R. H. Single nucleotide polymorphisms in wild isolates of *Caenorhabditis elegans*. *Genome Res.* **10**, 1690–1696 (2000).
[Article](http://dx.doi.org/10.1101/gr.GR-1471R) (<http://dx.doi.org/10.1101/gr.GR-1471R>)
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=11076854&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=11076854&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000165364700007&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000165364700007&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3cXosVWjt7c%3D&pissn=1471-0056&pyear=2002&md5=32f98f30fc30e102835b860f52bb09c5) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3cXosVWjt7c%3D&pissn=1471-0056&pyear=2002&md5=32f98f30fc30e102835b860f52bb09c5>)
109. Plasterk, R. H. A. & Van Luenen, H. G. A. M. in *C. elegans II* Vol. **1** (eds Riddle, D. L., Blumenthal, T., Meyer, B. J. & Priess, J. R.) 97–116 (Cold Spring Harbor Laboratory Press, New York, 1997).
110. Bessereau, J. L. *et al.* Mobilization of a *Drosophila* transposon in the *Caenorhabditis elegans* germ line. *Nature* **413**, 70–74 (2001).
[Article](http://dx.doi.org/10.1038/35092567) (<http://dx.doi.org/10.1038/35092567>)
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=11544527&dopt=Abstract) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=11544527&dopt=Abstract)
[ISI](http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000170801200040&DestApp=WOS_CPL) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000170801200040&DestApp=WOS_CPL)
[ChemPort](http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3MXmvFSktbY%3D&pissn=1471-0056&pyear=2002&md5=75f1ac7936e7dba5c541a0e2c60f2271) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3MXmvFSktbY%3D&pissn=1471-0056&pyear=2002&md5=75f1ac7936e7dba5c541a0e2c60f2271>)
111. Fire, A. *et al.* Potent and specific genetic interference by double-stranded RNA in *Caenorhabditis elegans*. *Nature* **391**, 806–811 (1998).
[Article](http://dx.doi.org/10.1038/35888) (<http://dx.doi.org/10.1038/35888>)
[PubMed](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?) (<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?>)

- [holding=npg&cmd=Retrieve&db=PubMed&list_uids=9486653&dopt=Abstract](#)
[ISI](#) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000072089500057&DestApp=WOS_CPL)
[ChemPort](#) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK1cXhtlCju74%3D&pissn=1471-0056&pyear=2002&md5=fe59f9fc07e13d234f6df66632440c09>)
112. Bernstein, E., Denli, A. M. & Hannon, G. J. The rest is silence. *RNA* **7**, 1509–1521 (2001).
[PubMed](#) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=11720281&dopt=Abstract)
[ISI](#) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000172225800001&DestApp=WOS_CPL)
[ChemPort](#) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3MXos1Khtbc%3D&pissn=1471-0056&pyear=2002&md5=2f638343cee2bd834f8dfffbc1052ade>)
113. Mango, S. E. Stop making nonsense: the *C. elegans smg* genes. *Trends Genet.* **17**, 646–653 (2001).
[Article](#) ([http://dx.doi.org/10.1016/S0168-9525\(01\)02479-9](http://dx.doi.org/10.1016/S0168-9525(01)02479-9))
[PubMed](#) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=11672865&dopt=Abstract)
[ISI](#) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000171791200014&DestApp=WOS_CPL)
[ChemPort](#) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3MXnslemur8%3D&pissn=1471-0056&pyear=2002&md5=a22438d8c794b3fa896f33c306dc1b1d>)
114. Maine, E. M. RNAi as a tool for understanding germline development in *Caenorhabditis elegans*: uses and cautions. *Dev. Biol.* **239**, 177–189 (2001).
[Article](#) (<http://dx.doi.org/10.1006/dbio.2001.0394>)
[PubMed](#) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=11784027&dopt=Abstract)
[ISI](#) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000172453300001&DestApp=WOS_CPL)
[ChemPort](#) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3MXnvFGitbo%3D&pissn=1471-0056&pyear=2002&md5=0b150d96872f9b547b638ae00982114a>)
115. Zwaal, R. R., Broeks, A., Van Meurs, J., Groenen, J. T. & Plasterk, R. H. Target-selected gene inactivation in *Caenorhabditis elegans* by using a frozen transposon insertion mutant bank. *Proc. Natl Acad. Sci. USA* **90**, 7431–7435 (1993).
[Article](#) (<http://dx.doi.org/10.1073/pnas.90.16.7431>)
[PubMed](#) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=8395047&dopt=Abstract)
[ChemPort](#) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK3sXlvFKktbk%3D&pissn=1471-0056&pyear=2002&md5=95a9865a4c7d4d75aa8aa593d746e553>)
116. Jansen, G., Hazendonk, E., Thijssen, K. L. & Plasterk, R. H. Reverse genetics by chemical mutagenesis in *Caenorhabditis elegans*. *Nature Genet.* **17**, 119–121 (1997).
[Article](#) (<http://dx.doi.org/10.1038/ng0997-119>)
117. Liu, L. X. *et al.* High-throughput isolation of *Caenorhabditis elegans* deletion mutants. *Genome Res.* **9**, 859–867 (1999).
[Article](#) (<http://dx.doi.org/10.1101/gr.9.9.859>)
[PubMed](#) (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=10508845&dopt=Abstract)
[ISI](#) (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000082946400009&DestApp=WOS_CPL)
[ChemPort](#) (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DyaK1MXmslKgs7k%3D&pissn=1471-0056&pyear=2002&md5=6ebf26edf322664fc1f293d7d446094e>)
118. Jansen, G., Hazendonk, E., Thijssen, K. L. & Plasterk, R. H. Reverse genetics by chemical mutagenesis in *Caenorhabditis elegans*. *Nature Genet.* **17**, 119–121 (1997).
[Article](#) (<http://dx.doi.org/10.1038/ng0997-119>)
119. Pujol, N., Bonnerot, C., Ewbank, J. J., Kohara, Y. & Thierry-Mieg, D. The *Caenorhabditis elegans unc-32* gene encodes alternative forms of a vacuolar ATPase a subunit. *J. Biol. Chem.* **276**, 11913–11921 (2001).
[Article](#) (<http://dx.doi.org/10.1074/jbc.M009451200>)

PubMed (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=11110798&dopt=Abstract)
ISI (http://links.isiglobalnet2.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=Nature&SrcApp=Nature&DestLinkType=FullRecord&KeyUT=000168081800065&DestApp=WOS_CPL)
ChemPort (<http://chemport.cas.org/cgi-bin/sdcgi?APP=ftslink&action=reflink&origin=npg&version=1.0&coi=1:CAS:528:DC%2BD3MXjtFylsbo%3D&pissn=1471-0056&pyear=2002&md5=9163cbf4de672f87b821e78fbf7c4850>)

top (#top)

Author affiliations

1. Department of Biology, University of Utah, Salt Lake City, Utah 84112, USA.
Email: jorgensen@biology.utah.edu (<mailto:jorgensen@biology.utah.edu>)
2. Huntsman Cancer Institute, Department of Oncological Sciences, University of Utah, Salt Lake City, Utah 84112, USA.
Email: susan.mango@hci.utah.edu (<mailto:susan.mango@hci.utah.edu>)

top (#top)

MORE ARTICLES LIKE THIS

These links to content published by NPG are automatically generated

REFERENCE

[Caenorhabditis elegans Neural Development](http://dx.doi.org/10.1038/npg.els.0000792) (<http://dx.doi.org/10.1038/npg.els.0000792>)

Nature Encyclopaedia of Life Sciences

[Caenorhabditis elegans Nervous System](http://dx.doi.org/10.1038/npg.els.0000110) (<http://dx.doi.org/10.1038/npg.els.0000110>)

Nature Encyclopaedia of Life Sciences

▶ **[See all 3 matches for Reference](http://sherman.nature.com/arls/Query?src_jrnl=Nature%20Reviews%20Genetics&src_vol=3&query=http://www.nature.com/doifinder/10.1038/nrg794&type=RV&src_pp=356-369&prod=NRG&src_date=2002&src_title=THE%20ART%20AND%20DESIGN%20OF%20GENETIC%20SCREENS:<i>CAENORHABDITIS%20ELEGANS</i>&showall=reference)** ([http://sherman.nature.com/arls/Query?src_jrnl=Nature Reviews Genetics&src_vol=3&query=http://www.nature.com/doifinder/10.1038/nrg794&type=RV&src_pp=356-369&prod=NRG&src_date=2002&src_title=THE ART AND DESIGN OF GENETIC SCREENS:<i>CAENORHABDITIS ELEGANS</i>&showall=reference](http://sherman.nature.com/arls/Query?src_jrnl=Nature%20Reviews%20Genetics&src_vol=3&query=http://www.nature.com/doifinder/10.1038/nrg794&type=RV&src_pp=356-369&prod=NRG&src_date=2002&src_title=THE%20ART%20AND%20DESIGN%20OF%20GENETIC%20SCREENS:<i>CAENORHABDITIS%20ELEGANS</i>&showall=reference))

NEWS AND VIEWS

[Genome sequencing: The worm revealed](http://www.nature.com/doifinder/10.1038/25228) (<http://www.nature.com/doifinder/10.1038/25228>)

Nature News and Views (17 Dec 1998)

[Taking sides in the nervous system with miRNA](http://www.nature.com/doifinder/10.1038/nn0204-100)

(<http://www.nature.com/doifinder/10.1038/nn0204-100>)

Nature Neuroscience News and Views (01 Feb 2004)

▶ **[See all 3 matches for News And Views](http://sherman.nature.com/arls/Query?src_jrnl=Nature%20Reviews%20Genetics&src_vol=3&query=http://www.nature.com/doifinder/10.1038/nrg794&type=RV&src_pp=356-369&prod=NRG&src_date=2002&src_title=THE%20ART%20AND%20DESIGN%20OF%20GENETIC%20SCREENS:<i>CAENORHABDITIS%20ELEGANS</i>&showall=news)** ([http://sherman.nature.com/arls/Query?src_jrnl=Nature Reviews Genetics&src_vol=3&query=http://www.nature.com/doifinder/10.1038/nrg794&type=RV&src_pp=356-369&prod=NRG&src_date=2002&src_title=THE ART AND DESIGN OF GENETIC SCREENS:<i>CAENORHABDITIS ELEGANS</i>&showall=news](http://sherman.nature.com/arls/Query?src_jrnl=Nature%20Reviews%20Genetics&src_vol=3&query=http://www.nature.com/doifinder/10.1038/nrg794&type=RV&src_pp=356-369&prod=NRG&src_date=2002&src_title=THE%20ART%20AND%20DESIGN%20OF%20GENETIC%20SCREENS:<i>CAENORHABDITIS%20ELEGANS</i>&showall=news))

RESEARCH

[The nuclear hormone receptor SEX-1 is an X-chromosome signal that determines nematode sex](http://www.nature.com/doifinder/10.1038/24164) (<http://www.nature.com/doifinder/10.1038/24164>)

Nature Letters to Editor (12 Nov 1998)

▶ [See all 20 matches for Research](http://sherman.nature.com/args/Query?src_jrnl=Nature) (http://sherman.nature.com/args/Query?src_jrnl=Nature

[Reviews](#)

[Genetics&src_vol=3&query=http://www.nature.com/doi/10.1038/nrg794&type=RV&src_pp=356-369&prod=NRG&src_date=2002&src_title=THE ART AND DESIGN OF GENETIC SCREENS: <i>CAENORHABDITIS ELEGANS</i>&showall=research](http://www.nature.com/doi/10.1038/nrg794&type=RV&src_pp=356-369&prod=NRG&src_date=2002&src_title=THE ART AND DESIGN OF GENETIC SCREENS: <i>CAENORHABDITIS ELEGANS</i>&showall=research)

[Previous article](#)

[\(/nrg/journal/v3/n5/full/nrg799.html\)](/nrg/journal/v3/n5/full/nrg799.html)

[Next article](#)

[\(/nrg/journal/v3/n5/full/nrg798.html\)](/nrg/journal/v3/n5/full/nrg798.html)