Structure, Function and Evolution of The Nematode Genome

Advanced article

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In the past few years, an increasing number of draft genome sequences of multiple free-living and parasitic nematodes have been published. Although nematode genomes vary in size within an order of magnitude, compared with mammalian genomes, they are all very small. Nevertheless, nematodes possess only marginally fewer genes than mammals do. Nematode genomes are very compact and therefore form a highly attractive system for comparative studies of genome structure and evolution. Strikingly, approximately one-third of the genes in every sequenced nematode genome has no recognisable homologues outside their genus. One observes high rates of gene losses and gains, among them numerous examples of gene acquisition by horizontal gene transfer. Not only does the 'gene for parasitism' not exist, but also there appear to be no common genomic characteristics of parasitic nematode genomes which would distinguish them from genomes of free-living nematodes.

Introduction

Nematodes are the largest animal phylum. But, out of the estimated number of 1–10 million species, only approximately 25 000 are formally described (Lambshead, 1993). Next to their species richness, their ecological omnipresence in virtually all terrestrial and aquatic habitats and also their high number of individuals contribute to the importance of nematodes (Floyd *et al*., 2002; Lambshead, 1993). **See also**: Nematoda (Roundworms)

Generally, nematodes develop through an embryonic stage followed by four developmental stages interchangeably called larval (L1–L4) or juvenile (J1–J4), which are separated by molts (Lee, 2002). This life cycle exists in numerous variations. In some instances, multiple alternative forms for particular developmental stages exist, most notably dauer juveniles, an alternative third juvenile stage capable of surviving long periods of starvation and other adverse conditions. Some or all stages can be parasitic (Anderson, 2000; Community; Eckert *et al*., 2005; Riddle *et al*., 1997). The minimal generation times and the life expectancies vary greatly among nematodes and range from a few days to several years.

Among the nematodes, numerous parasites of plants and animals, including man are of great medical and economic importance (Lee, 2002). From phylogenetic analyses, it can be concluded that parasitic life styles evolved at least seven times independently within the nematodes (four times with animals and three times with plants as hosts) (Blaxter *et al*., 1998). This raises the question whether the different transitions to a parasitic life style were paralleled by similar changes in the genomes. Should this be the case, it would be indicative for strong genomic constraints for the switch of life styles. Alternatively, if there are many ways to parasitism, one would expect that there are no unifying genomic features among independent cases of parasitism. A switch from a fully free-living to a parasitic life style in one step appears highly unlikely. It is, therefore, generally accepted that prior to the transition to parasitism, so-called 'pre-adaptations' must have existed. These features evolved for entirely different reasons but later on facilitated the step to parasitism (Dieterich and Sommer, 2009; Osche, 1962; Poulin, 2007). Indeed, many nematodes spend at least a part of their lives in association with other organisms without being parasitic (Lee, 2002). These associations range from short-term, rather unspecific, so-called phoretic interactions to highly species-specific long-term associations (Dieterich and Sommer, 2009; Poulin, 2007). Frequently, the dauer juveniles are the developmental stage, which engages in the interaction. In the example of the genus *Pristionchus*, they associate in a species-specific manner with scarab beetles and only resume development after the death of the beetle (necromenic association) (Sommer and Ogawa, 2011). The hypothesis that at least for some parasitic nematodes the infective stages are homologous to the dauer juveniles in free-living nematodes is supported by empirical evidence (Ogawa *et al*., 2009; Wang *et al*., 2009). Therefore, the ability to form dauer

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juveniles and phoretic and necromenic interactions might have served as preadaptations for the evolution of parasitism because they allowed a stepwise formation of tight and specific interactions (Dieterich and Sommer, 2009) prior to the transition to a truly parasitic life style.

One of the best studied model organisms, the free-living worm *Caenorhabditis elegans* belongs to the nematodes (Community). With the extensive knowledge about *C. elegans* as an excellent base line, nematodes are becoming increasingly popular for evolutionary studies (Sommer, 2009). *C. elegans* was the first multicellular organism that had its genome sequenced in 1998 (*C. elegans* Sequencing Consortium, 1998). It is important to note that until today, *C. elegans* is the only metazoan with a fully sequenced genome in the sense that there are no sequence gaps left. Recently, draft genome sequences of multiple other free-living and parasitic nematodes were published and their number is increasing rapidly (http://www.nematodes.org/nematodegenomes/index.php/959_Nematode_Genomes).

See also: *Caenorhabditis elegans* as an Experimental Organism; *Caenorhabditis elegans* Genome Project

In combination with the excellent understanding of the phylogenetic relationship of the species in question (Blaxter *et al*., 1998; Holterman *et al*., 2006; **Figure 1**), these genome sequences are a yielding source for the investigation of the structure and evolution of genomes. Among nematodes, examples of phylogenetically very closely related species that have completely different ecologies and species with very similar ecologies that are, however, only very distantly related are found. This makes nematodes an attractive system to study how genomes are shaped by the environment and evolutionary descent.

Below are briefly introduced those nematode species for which whole genome draft sequences were published at the time when this article was written (August, 2012). For this review the authors limit themselves to the discussion of these published genome sequences. Additionally, almost complete genomes are in the process of being analysed and annotated and are available from various institutions (see http://www.nematodes.org/nematodegenomes/index.php/959_Nematode_Genomes). The life cycles and the basic biology of the different nematodes are described in numerous textbooks. (For space restriction, the information presented below is without references; the reader is advised to refer the literature used to compile it (Anderson, 2000; Castagnone-Sereno, 2006; Community; Eckert *et al*., 2005; Lee, 2002; Riddle *et al*., 1997; Wenk and Renz, 2003; Zhao *et al*., 2008 and the respective genome publications, **Table 1**).) To illustrate the differences between nematodes, for each species numbers for the size of the adult, minimal generation time and adult reproductive life span are provided. These numbers are to be taken as ballpark figures only because the published numbers often vary considerably between different sources. The phylogenetic clade listed is according to Blaxter *et al*. (1998).

Free-living nematodes

C. elegans, Caenorhabditis briggsae, Caenorhabditis angaria and *Pristionchus pacificus* (all clade V)

Adult length: 1 mm long (hermaphrodite/female, males slightly smaller)
Minimal generation time: 3–4 days

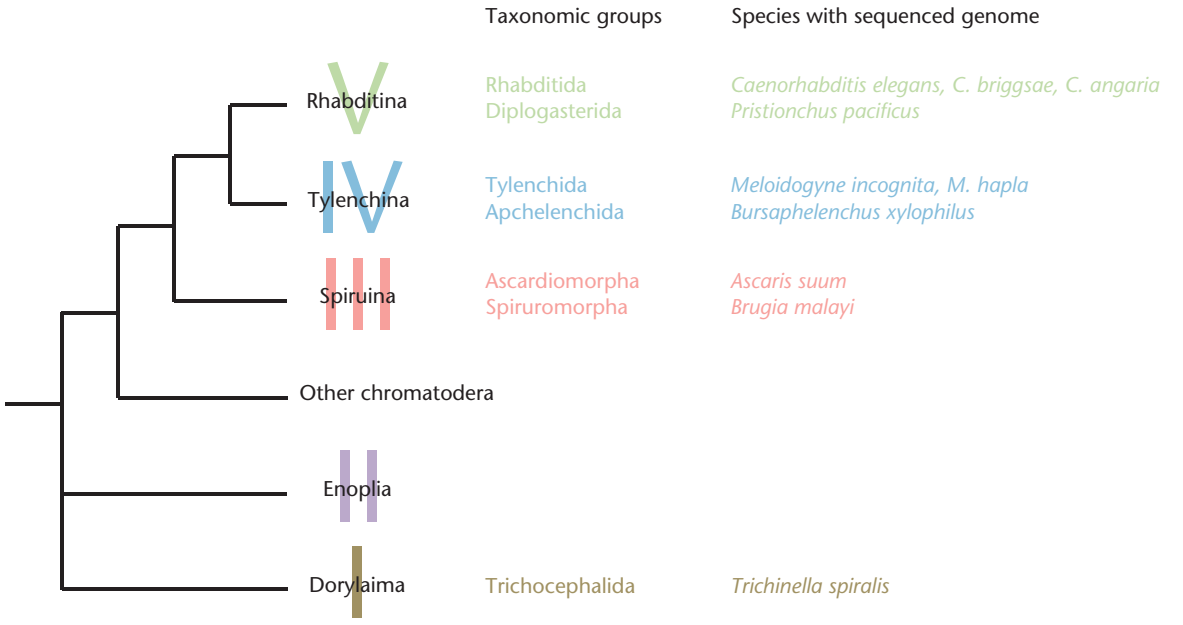

Figure 1 Phylogenetic relationship of the nematodes with published genome sequences. The phylogeny follows Blaxter *et al*. (1998). Roman numerals denote the clade.

Table 1 Summary statistics of nematode genomes. Overview of genomic features for 10 nematode genome assemblies. Numbers differ from the original publications as they were recomputed from genome assemblies and gene annotations from wormbase (www.wormbase.org) release WS230. The program mreps 2.5 was used for repeat annotation

Species	*C. elegans*	*C. briggsae*	*C. angaria*	*P. pacificus*	*B. malayi*	*M. hapla*	*M. incognita*	*B. xylophilus*	*A. suum*	*T. spiralis*
Assembly size (Mb)	100.3	105.4	79.7	153.2	89.3	53.0	82.1	73.1	265.3	58.5
Number of scaffolds	7	12	33 559	18 083	27 210	3452	9538	5527	29 831	6863
N50 scaffold size (Mb)	17.5	17.5	0.01	1.2	0.04	0.3	0.1	1.0	0.4	6.4
GC content (%)	35.4	37.3	36.3	42.8	30.1	27.4	31.4	40.3	37.9	33.9
Number of genes	20 517	21 961	26 265	24 217	21 332	13 072	20 332	18 074	18 449	16 380
Median protein length (aa)	340	310	270	241	193	250	249	263	234	192
Median number of exons per gene	5	5	3	8	3	4	5	4	5	4
Size of coding sequences (Mb)	30.0	27.1	23.2	23.6	16.1	18.9	20.5	18.6	18.1	15.6
Size of repeats (Mb)	4.4	4.4	4.0	6.8	9.9	11.7	12.4	2.2	8.6	3.7
References	(*C. elegans* Sequencing Consortium, 1998)	(Stein *et al.*, 2003)	(Mortazavi *et al.*, 2010)	(Dieterich *et al.*, 2008)	(Ghedin *et al.*, 2007)	(Opperman *et al.*, 2008)	(Abad *et al.*, 2008)	(Kikuchi *et al.*, 2011)	(Jex *et al.*, 2011)	(Mitreva *et al.*, 2011)

Adult reproductive life span: a few days
Reproductive mode: sexual, androdioecious (*C. elegans*, *C. briggsae* and *P. pacificus*) or gonochoristic (*C. angaria*).

These four species are representatives of the families Rhabditidae (*Caenorhabditis* spp.) and Diplogastridae (*P. pacificus*). In *C. elegans*, *C. briggsae* and *P. pacificus* hermaphrodites replace females in the populations. They can self-fertilize a portion of their eggs, in addition to mating with males. In both genera, such androdioecious mating systems have evolved multiple times independently and closely related gonochoristic species exist. Although representatives of the genus *Caenorhabditis* can be found on rotting plant material, *Pristionchus* sp. forms rather species-specific necromenic interactions with mostly scarab beetles.

Animal including human parasitic nematodes

Ascaris suum (clade III)

Adult length: up to 30 cm (females), up to 25 cm (males)
Minimal generation time: 2–3 months
Adult reproductive life span: months
Reproductive mode: sexual, gonochoristic.

This parasite of swine is a very close relative of *Ascaris lumbricoides*, the most prevalent nematode parasite of man. Parasitic adults live in the small intestine and the eggs are passed with the faeces. The development to the infective third-stage juvenile occurs within the eggshell. After being taken up orally by a new host, the infective larvae hatch, invade the intestinal veins and undergo a multistep migration through the liver (where they molt to J4s), lungs, mouth cavity and digestive tract back to the small intestine, where they mature to adults. In *A. suum* and its close relatives, the somatic tissues contain less genetic material than that of the germ line due to chromatin diminution, which occurs in early somatic blastomeres (Müller and Tobler, 2000). **See also**: Chromatin Diminution

Trichinella spiralis (clade I)

Adult size: 3 mm (females), 1.5 mm (males)
Minimal generation time: 3 weeks
Adult reproductive life span: one month
Reproductive mode: sexual, gonochoristic.

This nematode is an intracellular parasite and in contrast to most other gastrointestinal nematodes, it does not form any nonparasitic developmental stages. The adult worms live in syncytia in the small intestine of the host. The viviparous females release first-stage juveniles, which migrate to the striated musculature, where they invade muscle fibres. They induce the formation of so-called nurse cells in which they can remain dormant for years and wait for a predator or scavenger to take them up. In the new host's small intestine, they invade epithelial cells and complete their development to adulthood.

Brugia malayi (clade III)

Adult size: 5–8 cm (females), 2–3 cm (males)
Minimal generation time: months
Adult reproductive life span: years
Reproductive mode: sexual, gonochoristic.

The adults inhabit the lymphatic system of their hosts including humans and cause the South East Asian form of elephantiasis. First-stage juveniles (microfilariae) hatch within the uterus of their mother. They translocate to the blood of the host and wait to be taken up by a mosquito, which serves as intermediate host. In the vector, the larvae develop to J3s, which are capable of infecting a new host during a subsequent blood meal of the mosquito.

Plant parasitic nematodes

Meloidogyne hapla and *Meloidogyne incognita* (clade IV)

Adult size: 0.2 mm (female, pyriform), 0.8 mm (male, vermiform)
Minimal generation time: 40 days
Adult reproductive life span: a few months
Reproductive mode: meiotic parthenogenetic with occasional outcrossing (*M. hapla*), mitotic parthenogenetic (*M. incognita*).

Members of the genus *Meloidogyne* are among the most important agricultural pests. Although males do exist, *M. incognita* reproduces exclusively parthenogenetically. In *M. hapla*, occasional outcrossing is possible. Second-stage juveniles invade the roots of plants at the growing tip. They migrate between the cells and establish a permanent feeding site close to the developing vascular cylinder. There, they molt three times to become adults, without feeding between molts. At the feeding site, they induce the formation of multinucleated 'giant cells' off which they feed. Eggs are pushed to the surface of the root. The first molt takes place within the eggshell, and the J2s hatch and disperse in the soil to search for a host.

Bursaphelenchus xylophilus (clade IV)

Adult size: 0.8 mm (female), 0.7 mm (male)
Minimal generation time: 5 days
Adult reproductive life span: a few days
Reproductive mode: sexual, gonochoristic.

Individuals of this important parasite of pine trees live and reproduce rapidly in the xylem of their host. If

conditions deteriorate, they also form dauer larvae, which, when stimulated by the presence of suitable beetle larvae, molt into fourth-stage larvae specialised for dispersal. These larvae enter a phoretic association with the emerging adult beetle in order to reach a new host.

Main Text

Some key statistical numbers of the published genome assemblies are listed in **Table 1**. When comparing the genomes, it is important to note that the various genome projects differ in sequencing platforms, the amount of sequencing data and computational methodology for genome assembly and gene prediction. Therefore, some of the obtained differences might be due to methodology and not reflect real differences. However, even with these caveats, several important features in nematode genomes emerge: (1) nematode genomes tend to be compact; (2) nematode genomes contain a substantial fraction of genes with no recognisable homologues outside their genus, indicating high rates of gene gain and loss; (3) a portion of the genes in nematode genomes are organised in gene clusters called operons; and (4) no unifying genomic features were identified in parasitic nematodes that would distinguish them from free-living nematodes. These four points are elaborated below in more detail.

Nematode genomes are compact

In comparison with genomes of many other metazoans, in particular vertebrates which have genome sizes between 300 Mb and 3.3 Gb (Rödelsperger and Dieterich, 2010), all published nematode genomes are very small and compact (**Table 1**). The assemblies of published nematode genomes, which in all cases are estimated to cover more than 90% of the actual genome sizes, range from 53 Mb to 265 Mb. However, nematode genomes are predicted to contain only marginally fewer genes than that of humans. Given the small genome size and the high number of genes, the average gene density is much higher in nematodes. The size of an average nematode exon is very comparable to that of a human exon, but the introns and the intergenic regions as well as the average number of exons per gene tend to be considerably smaller. Little is known about why nematodes show reduced genome size in comparison with vertebrates. It may be speculated that the regulation of gene expression as encoded in promoters, introns and intergenic regions might be more complex in vertebrates and as a consequence needs to be encoded in a greater portion of the genome; but it could also mean that nematodes are simply more efficient to control transposon activity, which is one major contributor to the larger genome sizes observed in vertebrates. For example, the human genome contains more than 1.3 Gb of sequence that is derived from transposable elements. These transposon-derived human sequences are larger than the entire genome of all sequenced nematode genomes. **See also**: Transposons

Nematode genomes contain a substantial fraction of genes with no recognisable homologues indicating a high rate of gene acquisition and loss

Strikingly, approximately one-third of genes in all sequenced nematode genomes have no recognisable homologues in other nematodes outside the same genus (**Figure 2a**). Such genes are often referred to as orphan or pioneer genes. It is also noteworthy that the number of orphan genes appears not to decrease with the increasing number of sequences genomes, which is supported by large-scale sequencing of expressed sequence tags (ESTs) from several nematode species. EST sequencing from two dozens nematode species shows that the number of ESTs without homologues in any other nematode species increased linearly with the number of species (**Figure 2b**), suggesting that the sampling of the nematode protein space is far from being complete (Wasmuth *et al*., 2008 and http://www.nematodes.org/nembase4/). This observation indicates that nematode genomes form an inexhaustible resource to study novel proteins and their associated functions because frequent loss and gain of genes is a recurrent motif in nematode evolution.

The apparent gain of genes can be explained by different evolutionary scenarios that are: (1) rapid evolution beyond the level of recognition as homologues; (2) *de novo* formation from previously noncoding sequences; or (3) horizontal gene transfer (HGT) from other organisms.

Rapid evolution, in particular after gene duplication events, seems to be a plausible explanation for the apparent lack of homologues of some genes. Duplications have been proposed to allow for the generation of novel protein functions in one of the two copies, whereas the original function is still retained by the other duplicate (Katju and Lynch, 2006). Indeed, many orphan genes belong to larger gene families of which other members do have homologues in other nematode species. This suggests that evolution within gene families is highly dynamic and some members might have diverged to the extent that they are classified as orphan genes, whereas other members have recognisable homologues in other species.

Evidence for *de novo* formation of genes from noncoding sequences has only been reported in yeast (Li *et al*., 2010), mouse (Heinen *et al*., 2009) and human (Knowles and McLysaght, 2009). Therefore, although concrete examples await discovery, this is also a likely mechanism for the generation of some of the novel genes in nematodes.

In contrast to the two mechanisms mentioned above, horizontally acquired genes are relatively easily identifiable because they mostly form phylogenetic patterns that are inconsistent with the evolutionary relationship of the species they are found in. Indeed, one of the most surprising findings that emerged from nematode genome

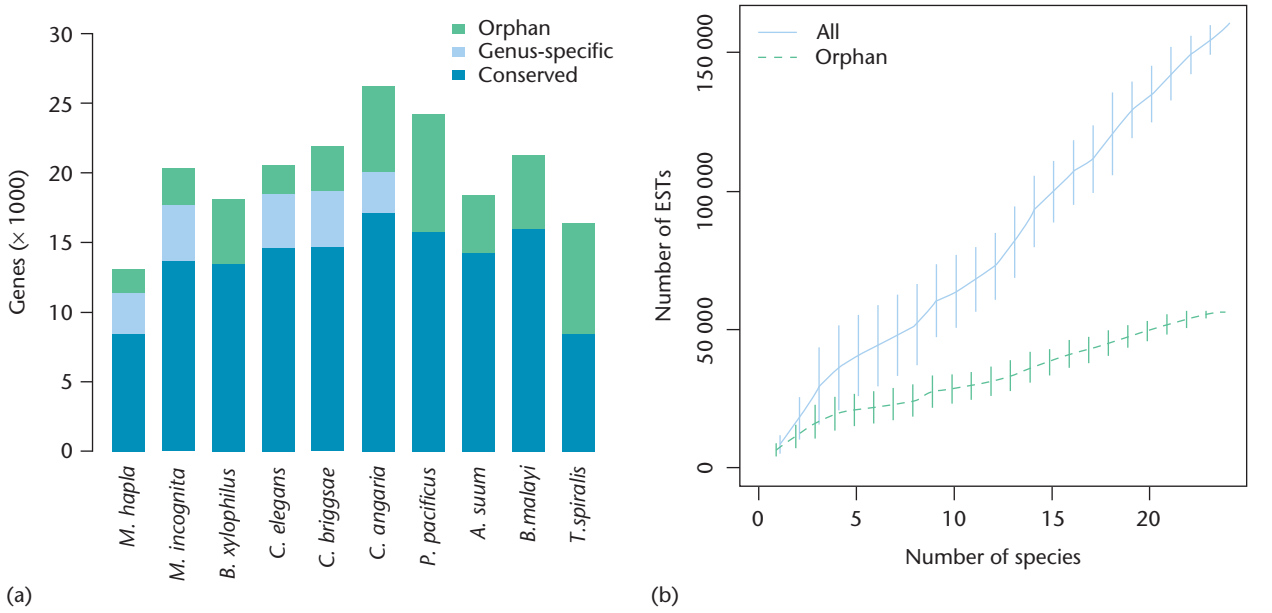

Figure 2 Evolution of orphan genes. (a) Number of genes per nematode for seven nematode genomes. Genes that lack homologues in any other nematode species are denoted 'orphan' genes, otherwise as genus specific or as conserved across other nematode genera. Approximately one-third of genes in each genome are classified as orphan or genus specific. (b) Saturation analysis of translated EST data from 25 nematode species (from nematode.net). For any number of species, the mean total number of ESTs and the mean number of 'orphan' ESTs without homologues in any other species is shown. The number of orphan ESTs increases linearly with the number of species suggesting that the nematode protein space is still undersampled. Error bars indicate standard deviations for different species permutations.

sequencing projects is the relatively high frequency of genes acquired by HGT. Although HGT was known to be frequent in prokaryotes, it was considered to be rare in sexually reproducing eukaryotes (Andersson, 2005). However, the recently determined genome sequences discussed here, as well as EST sequencing project (Wasmuth *et al*., 2008), provided strong evidence for the acquisition of numerous genes through HGT by various nematodes. There are examples of genes originating from bacteria, fungi, amoebozoa, endosymbionts and arthropods. The best characterised examples of HGT occurred in plant parasites of the *Meloidogyne*, *Heterodera, Globodera* and *Pratylenchus* groups and the fungivorous/plant parasitic genus *Bursaphelenchus* as well as the necromenic genus *Pristionchus* and the filarial parasite *B. malayi* (Dieterich and Sommer, 2009; Dunning Hotopp *et al*., 2007). A highly interesting set of questions around these HGT events concerns the roles the transmitted genes play in the receiver organism. Many of the genes acquired by HGT encode cell wall-degrading enzymes (Mitreva *et al*., 2009). The role of HGT in the evolution of plant parasitism has been discussed in several reviews in the past (McCarter, 2008; Mitreva *et al*., 2009). **See also**: Horizontal Gene Transfer in Evolution

To illustrate the process, the example of cellulases, which were acquired independently by several nematode lineages, is discussed below. Phylogenetic reconstruction of nematode cellulase genes strongly indicates their independent acquisition from distinct microbial donors (Danchin *et al*., 2010; Dieterich and Sommer, 2009). For example, the cellulases found in plant-parasitic Tylenchida (among them *Meloidogyne* sp.) belong to the glycoside hydrolase family 5 (GHF5) and presumably are derived from an intronless ancestral gene acquired from bacterial donors (Kyndt *et al*., 2008). The pinewood nematode *B. xylophilus* has independently acquired cellulases of a different family (GHF45) from fungi (Kikuchi *et al*., 2004).

These studies also suggest that genes after being acquired by HGT tend to undergo extensive gene duplications. Indicators for the successful integration of HGT-acquired genes into the biology of the recipient are gene activity and longevity, and such genes would also be expected to be under positive selection (Blaxter, 2007). Testing these predictions for individual cases of HGT requires a detailed analysis of the evolutionary history of the genes in question. This can only be done in the context of well-established phylogenetic framework of the organisms carrying the products of the HGT event. One test case that fulfills these requirements is cellulase genes of the genus *Pristionchus*. A recent study by Mayer *et al*. (2011) showed that among seven *Pristionchus* and three additional diplogastrid species, cellulase activity was strictly correlated with the presence of genes in the genome/transcriptome of the corresponding species. The cellulase genes showed high turnover with significant birth and death rates and the cellulase genes within one species were phylogenetically more closely related than they were between species. Comparison of cellulase genes in 24 different natural isolates of *P. pacificus* indicated copy number

variations and signs of positive selection (Mayer *et al*., 2011). Thus, HGT-acquired genes show extreme turnover in the receiver organism.

A portion of nematode genes are organised in polycistronic transcription units called operons

In *C. elegans*, in a process called trans-splicing, a 22-nucleotide-long ribonucleic acid (RNA) fragment (spliced leader, SL) is added post-transcriptionally to the 5′ ends of the messenger RNAs (mRNAs) of approximately 70% of all genes (Blumenthal, 2005). Trans-splicing, along with polyadenylation, is also used to break up polycistronic pre-mRNAs into multiple mRNAs coding for a single protein each. In *C. elegans*, approximately 25% of all genes are organised in such polycistronic transcription units called operons. Although the same term is used, operons in nematodes are neither evolutionarily related nor functionally equivalent to bacterial operons, which combine multiple functionally related genes and give rise to a single polycistronic mRNA. **See also**: *Escherichia coli* Lactose Operon; Gene Clustering in Eukaryotes; Trans Splicing

Trans-splicing and operons were shown to exist in all nematode species with a sequenced genome, and the process appears widespread among nematodes of Clades III–V (Guiliano and Blaxter, 2006). In *T. spiralis* (Clade I) only approximately 1% of the mRNAs are trans-spliced and the 19 known SLs are highly variable and appear unrelated to the rather conserved SLs of other nematodes (Mitreva *et al*., 2011; Pettitt *et al*., 2008). However, this is not typical for all representatives of Clade I (Harrison *et al*., 2010).

It is still an open question, why operons evolved in nematodes. Unlike in bacteria, genes within an operon are frequently not functionally related (Blumenthal, 2005). However, a recent study supported by extensive gene expression studies proposed that operons are an evolutionary innovation to optimise the usage of limited transcriptional resources during the recovery from growth-arrested states (Zaslaver *et al*., 2011).

No gene for parasitism found

When the sequencing projects mentioned above were initiated, one of the hopes was that they would reveal interesting insights into the essence of certain ecological niches, in particular parasitic life styles. So far, these hopes were not fulfilled. Some examples of genomic features that made sense in the context of the ecology of the particular species were identified, for example, the acquisition of cell wall-degrading enzymes in plant-parasitic nematodes or an expansion in detoxification genes in the beetle-associated *P. pacificus*. Also, as expected, the similarity of sequences of homologous proteins frequently parallels the phylogenetic relationship of the nematodes they are found in. However, so far, no genomic features were identified that would unify species with similar ecology but large phylogenetic difference. Although the ten available nematode genomes are not yet a sufficient basis to claim that no such features exist, additional EST sequencing projects in many more parasitic and free-living nematodes (Wasmuth *et al*., 2008 and http://www.nematodes.org/nembase4/) do not change this picture. It seems that each parasitic lineage has found its own way of adapting to the new life style and there are no strong constraints that would enforce one particular solution.

Taken together, nematode genomes emerge as an excellent test case for the study of the evolutionary dynamics of genomes. Although the ten genomes currently available are only able to detect the most obvious features of nematode genomes, the small size and low abundance of repetitive sequences will facilitate the sequencing of many more species and different isolates of the same species with manageable effort. In the future, within- and cross-species comparisons over the full range of evolutionary distances will facilitate dating the formation of novel genes and detecting signatures of selective constraints or rapid evolution.

References

Abad P, Gouzy J, Aury JM *et al*. (2008) Genome sequence of the metazoan plant-parasitic nematode *Meloidogyne incognita*. *Nature Biotechnology* **26**: 909–915.

Anderson RC (2000) *Nematode Parasites of Vertebrates. Their Development and Transmission*, 2nd edn. Oxon: CAB International.

Andersson JO (2005) Lateral gene transfer in eukaryotes. *Cellular and Molecular Life Sciences* **62**: 1182–1197.

Blaxter M (2007) Symbiont genes in host genomes: fragments with a future? *Cell Host and Microbe* **2**: 211–213.

Blaxter ML, De Ley P, Garey JR *et al*. (1998) A molecular evolutionary framework for the phylum Nematoda. *Nature* **392**: 71–75.

Blumenthal T (2005) Trans-splicing and operons (25 June 2005). In WormBook T*Ce*R Community, ed (WormBook, doi: 10.1895/wormbook.1.5.1, http://www.wormbook.org).

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

Castagnone-Sereno P (2006) Genetic variability and adaptive evolution in parthenogenetic root-knot nematodes. *Heredity* **96**: 282–289.

Community, TCeR WormBook (WormBook, doi: 10.1895/wormbook.1.141.1, http://www.wormbook.org).

Danchin EG, Rosso MN, Vieira P *et al*. (2010) Multiple lateral gene transfers and duplications have promoted plant parasitism ability in nematodes. *Proceedings of the National Academy of Sciences of the USA* **107**: 17651–17656.

Dieterich C, Clifton SW, Schuster LN *et al*. (2008) The *Pristionchus pacificus* genome provides a unique perspective on nematode lifestyle and parasitism. *Nature Genetics* **40**: 1193–1198.

Dieterich C and Sommer RJ (2009) How to become a parasite – lessons from the genomes of nematodes. *Trends in Genetics* **25**: 203–209.

Dunning Hotopp JC, Clark ME, Oliveira DC *et al*. (2007) Widespread lateral gene transfer from intracellular bacteria to multicellular eukaryotes. *Science* **317**: 1753–1756.

Eckert J, Friedhoff KT, Zahner H and Deplazes P (2005) *Lehrbuch der Parasitologie für die Tiermedizin*. Stuttgart: Enke Verlag.

Floyd R, Abebe E, Papert A and Blaxter M (2002) Molecular barcodes for soil nematode identification. *Molecular Ecology* **11**: 839–850.

Ghedin E, Wang S, Spiro D *et al*. (2007) Draft genome of the filarial nematode parasite *Brugia malayi*. *Science* **317**: 1756–1760.

Guiliano DB and Blaxter ML (2006) Operon conservation and the evolution of trans-splicing in the phylum Nematoda. *PLoS Genetics* **2**: e198.

Harrison N, Kalbfleisch A, Connolly B, Pettitt J and Muller B (2010) SL2-like spliced leader RNAs in the basal nematode *Prionchulus punctatus*: new insight into the evolution of nematode SL2 RNAs. *RNA* **16**: 1–8.

Heinen TJ, Staubach F, Haming D and Tautz D (2009) Emergence of a new gene from an intergenic region. *Current biology* **19**: 1527–1531.

Holterman M, van der Wurff A, van den Elsen S *et al*. (2006) Phylum-wide analysis of SSU rDNA reveals deep phylogenetic relationships among nematodes and accelerated evolution toward crown Clades. *Molecular Biology and Evolution* **23**: 1792–1800.

Jex AR, Liu S, Li B *et al*. (2011) *Ascaris suum* draft genome. *Nature* **479**: 529–533.

Katju V and Lynch M (2006) On the formation of novel genes by duplication in the *Caenorhabditis elegans* genome. *Molecular Biology and Evolution* **23**: 1056–1067.

Kikuchi T, Cotton JA, Dalzell JJ *et al*. (2011) Genomic insights into the origin of parasitism in the emerging plant pathogen *Bursaphelenchus xylophilus*. *PLoS pathogens* **7**: e1002219.

Kikuchi T, Jones JT, Aikawa T, Kosaka H and Ogura N (2004) A family of glycosyl hydrolase family 45 cellulases from the pine wood nematode *Bursaphelenchus xylophilus*. *FEBS Letters* **572**: 201–205.

Knowles DG and McLysaght A (2009) Recent *de novo* origin of human protein-coding genes. *Genome Research* **19**: 1752–1759.

Kyndt T, Haegeman A and Gheysen G (2008) Evolution of GHF5 endoglucanase gene structure in plant-parasitic nematodes: no evidence for an early domain shuffling event. *BMC Evolutionary Biology* **8**: 305.

Lambshead PJ (1993) Recent developments in marine benthic biodiversity research. *Oceanis* **19**: 5–24.

Lee DL (2002) *The Biology of Nematodes*. London: Taylor & Francis.

Li D, Dong Y, Jiang Y *et al*. (2010) A de novo originated gene depresses budding yeast mating pathway and is repressed by the protein encoded by its antisense strand. *Cell Research* **20**: 408–420.

Mayer WE, Schuster LN, Bartelmes G, Dieterich C and Sommer RJ (2011) Horizontal gene transfer of microbial cellulases into nematode genomes is associated with functional assimilation and gene turnover. *BMC Evolutionary Biology* **11**: 13.

McCarter JP (2008) Nematology: terra incognita no more. *Nature Biotechnology* **26**: 882–884.

Mitreva M, Jasmer DP, Zarlenga DS *et al*. (2011) The draft genome of the parasitic nematode *Trichinella spiralis*. *Nature Genetics* **43**: 228–235.

Mitreva M, Smant G and Helder J (2009) Role of horizontal gene transfer in the evolution of plant parasitism among nematodes. *Methods in Molecular Biology* **532**: 517–535.

Mortazavi A, Schwarz EM, Williams B *et al*. (2010) Scaffolding a *Caenorhabditis* nematode genome with RNA-seq. *Genome Research* **20**: 1740–1747.

Müller F and Tobler H (2000) Chromatin diminution in the parasitic nematodes *Ascaris suum* and *Parascaris univalens*. *International Journal for Parasitology* **30**: 391–399.

Ogawa A, Streit A, Antebi A and Sommer RJ (2009) A conserved endocrine mechanism controls the formation of dauer and infective larvae in nematodes. *Current Biology* **19**: 67–71.

Opperman CH, Bird DM, Williamson VM *et al*. (2008) Sequence and genetic map of *Meloidogyne hapla*: a compact nematode genome for plant parasitism. *Proceedings of the National Academy of Sciences of the USA* **105**: 14802–14807.

Osche G (1962) Das Praeadaptationsphänomen und seine Bedeutung für die evolution. *Zoologischer Anzeiger* **169**: 14–49.

Pettitt J, Muller B, Stansfield I and Connolly B (2008) Spliced leader trans-splicing in the nematode *Trichinella spiralis* uses highly polymorphic, noncanonical spliced leaders. *RNA* **14**: 760–770.

Poulin R (2007) *Evolutionary Ecology of Parasites*, 2nd edn. Princeton: Princeton University Press.

Riddle DL, Blumenthal T, Meyer BJ and Priess JR (1997) *C. elegans II*. New York: Cold Spring Harbor Laboratory Press.

Rödelsperger C and Dieterich C (2010) CYNTENATOR: progressive gene order alignment of 17 vertebrate genomes. *PloS One* **5**: e8861.

Sommer RJ (2009) The future of evo-devo: model systems and evolutionary theory. *Nature Reviews Genetics* **10**: 416–422.

Sommer RJ and Ogawa A (2011) Hormone signaling and phenotypic plasticity in nematode development and evolution. *Current Biology* **21**: R758–R766.

Stein LD, Bao Z, Blasiar D *et al*. (2003) The genome sequence of *Caenorhabditis briggsae*: a platform for comparative genomics. *PLoS Biology* **1**: E45.

Wang Z, Zhou XE, Motola DL *et al*. (2009) Identification of the nuclear receptor DAF-12 as a therapeutic target in parasitic nematodes. *Proceedings of the National Academy of Sciences of the USA* **106**: 9138–9143.

Wasmuth J, Schmid R, Hedley A and Blaxter M (2008) On the extent and origins of genic novelty in the phylum Nematoda. *PLoS Neglected Tropical Diseases* **2**: e258.

Wenk P and Renz A (2003) *Parasitologie*. Stuttgart: Georg Thieme Verlag.

Zaslaver A, Baugh LR and Sternberg PW (2011) Metazoan operons accelerate recovery from growth-arrested states. *Cell* **145**: 981–992.

Zhao BG, Futai K, Sutherland JR and Takeuchi Y (2008) *Pine Wilt Disease*. Tokyo: Springer.

Further Reading

Blaxter M, Kumar S, Kaur G, Koutsovoulos G and Elsworth B (2012) Genomics and transcriptomics across the diversity of the Nematoda. *Parasite Immunology* **34**: 108–120.

Carvunis AR, Rolland T, Wapinski I *et al*. (2012) Proto-genes and *de novo* gene birth. *Nature* **487**: 370–374.

Cutter AD (2009) Evolution of the *C. elegans* Genome. *Molecular Biology and Evolution* **26**: 1199–1234.

Danchin EG (2011) What Nematode genomes tell us about the importance of horizontal gene transfers in the evolutionary history of animals. *Mobile Genetic Elements* **1**: 269–273.

Lynch M (2007) *The Origins of Genome Architecture*. Sunderland: Sinauer Associates Inc.

Markov GV and Sommer RJ (2012) The evolution of novelty in conserved gene families. *International Journal of Evolutionary Biology* **2012**: 8. doi:10.1155/2012/490894.

Sommer RJ and Streit A (2011) Comparative genetics and genomics of nematodes: genome structure, development, and lifestyle. *Annual Review of Genetics* **45**: 1–20.

Tauz D and Domazet-Lošo T (2011) The evolutionary origin of orphan genes. *Nature Reviews Genetics* **12**: 692–702.