

Meeting report

Evolution of developmental mechanisms

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A report on the joint Spring meeting of the British Society of Developmental Biology and the Genetics Society, York, UK, 20-23 March 2002.

The British Society of Developmental Biology and the Genetics Society decided to hold a joint Spring meeting this year, at York University in the UK. This joint endeavor helped to emphasize the interdisciplinary nature of evolutionary developmental biology ('evo-devo') and the increasing importance of comparative genomics to this field.

Gene and genome duplication

A recurrent theme of the meeting was the evidence for, and the role played by, gene and genome duplications in evolution. Virginia Walbot (Stanford University, USA) discussed gene duplications in maize and how the duplicates subsequently evolve. Maize is thought to have originated about 11 million years ago by an allotetraploidization event between an unknown (perhaps extinct) lineage and sorghum, in which the two species hybridized and a copy of both genomes was retained. Such an event resulted in all genes having duplicates in the 'new' genome, all of which would be initially redundant with each other and some of which might thus be expected to be rapidly lost, yet many are retained in modern maize. Why are so many duplicates retained, given this initial redundancy? The answer seems to be that the regulation of the duplicates has undergone rapid divergent evolution, so that distinctive functions have quickly arisen for each of the closely related genes. Such rapid evolution is facilitated by transposons acting as 'allele generators': these mobile elements can insert into promoters and alter the expression of the adjacent gene. Analysis of gene expression by microarrays in maize is problematic because there are so many closely related sequences; an 80% similarity over 100 base pairs leads to cross-hybridization. Walbot's technique for achieving

specificity is to construct microarrays of 45-mer oligonucleotides and to use multiple oligonucleotides for each gene cluster. This allows the different expression profiles of similar genes to be teased apart; her data suggest that changes in regulation leading to differential expression underlie the retention of many duplicate genes.

A major evolutionary transition that has been linked with genome expansion is the origin of the vertebrates, but whether this expansion involved duplications of ancestral genomes is debated. Peter Holland (University of Reading, UK) took a whole-genome approach to this question. In the original analysis of the human genome sequence (Lander *et al.*, *Nature* 2001, **409**:860-921), comparisons were made between the genomes of human, *Drosophila melanogaster* and the nematode *Caenorhabditis elegans*, examining 600 gene families that have a single copy in both fly and nematode genomes and at least one ortholog in the human genome (an arrangement that can be denoted 'fly 1: nematode 1: human x'). The resultant histogram revealed a preponderance of gene families for which there is also only a single member in human (as in fly and nematode), but also a significant number of genes for which humans have two, three or even more copies. Are the latter genes remnants of genome duplications? Holland has now done the reciprocal analysis, comparing the number of members of a gene family in nematodes that have single representatives in both fly and human (fly 1: nematode x: human 1), and the number of gene family members in flies with single representatives in nematode and human (fly x: nematode 1: human 1). These histograms show that virtually all the data points in each case are in the 'single' class, indicating that flies and nematodes do not have multiple versions of genes for which humans have only one and illustrating with dramatic clarity that the expansion is specific to the vertebrate lineage. Furthermore, the genes in the classes with multiple human genes are distributed throughout the genome, consistent with the ground-breaking hypothesis of Susumo Ohno

(*Evolution by Gene Duplication*. New York: Springer; 1970), that polyploidization (genome duplication) events occurred during the early evolution of chordates.

The rise of the sea squirt

Sea squirts or ascidians, such as *Ciona intestinalis*, are basal chordates, with a notochord and dorsal neural tube. As a group of animals, they are proving to be helpful for understanding the origin of the vertebrates, as they belong to a lineage that arose before the vertebrate genome expansion but are closer to vertebrates than are flies or nematodes. The rise of *C. intestinalis* as a new model system for genomics and molecular developmental biology is attributable in no small part to Nori Satoh (Kyoto University, Japan), who reported that the sequenced genome of *C. intestinalis* is scheduled to be released this year. Preliminary estimates suggest the 160 megabase genome contains about 15,000 genes. Data on the expression of thousands of these genes are also being gathered by Satoh and colleagues: 10,000–23,000 expressed sequence tags (ESTs) have been sequenced, from both the 5' and 3' ends, from each of five cDNA libraries (fertilized egg, 32–110-cell stage, tailbud stage, larva, and young adult). So far, analyses of about 1,000 genes for each of these stages by whole-mount *in situ* hybridization have been published by Satoh's group; this mountain of information is accessible at the website of Satoh's laboratory [<http://ghost.zool.kyoto-u.ac.jp>]. Sea squirts are amenable to manipulation by conventional embryology as well as by overexpression and underexpression of genes, the latter using morpholino oligonucleotides. Given their experimental potential coupled with the wealth of genomic data now available, we can expect to see a proliferation of sea-squirt science in future years.

Basal animals

When it comes to understanding where the genomes of the 'higher' animals (such as insects, nematodes and mammals) came from and how their developmental mechanisms arose, there are two very important stages that we need to know about: the last common ancestor of these higher animals and what came before it. Reconstructions of the identity of last common ancestors need outgroups for comparison, that is, groups that are not members of the group under consideration but are closely related to it. So, for the ancestor of flies, worms and humans we need to find and study a basal bilaterian (an animal or a lineage that arose just before all of the higher animals but that shares their characteristic three germ layers and bilateral symmetry). Jaume Baguña (Barcelona University, Spain) discussed whether the acoel flatworms are such a group. These animals have long been held to be basal bilaterians on morphological grounds. When they were suggested by Baguña and colleagues in 1999 to be basal bilaterians on the basis of 18S ribosomal DNA (rDNA) molecular phylogenetic studies, some researchers concurred. Many others expressed

doubts about the veracity of this molecular phylogeny, however, because of known artifacts produced by 18S rDNA phylogenies. At the meeting, Baguña described the gathering of additional gene sequences from a wider diversity of acoels and other animals, the analysis of which convincingly supported the original phylogeny. We may well have a basal bilaterian to hand.

Before the bilaterians evolved, there were diploblasts: animals with only two germ layers (ectoderm and endoderm), such as hydra, jellyfish, sea anemones, and comb jellies. Diploblasts are usually described as radially symmetrical, but on closer inspection they are better described as biradially symmetrical: superimposed on the radially symmetrical body is an additional plane of symmetry about which each side is reflected. How do these animals develop and how do their axes relate to those of the Bilateria? Mark Martindale (Hawaii University, Honolulu, USA) is investigating the embryology and the expression pattern of developmental genes in sea anemones (cnidarians) and comb jellies (ctenophores). The third germ layer in the Bilateria, the mesoderm, contains muscle cells. Diploblasts also have muscle cells, but they are not organized into a coherent layer. In ctenophores they come from endodermal precursors (as they also do, incidentally, in acoel flatworms, which fits with Baguña's hypothesis of their phylogenetic position), and in sea anemones there are muscle-like myo-epithelial cells. Martindale has examined genes in a sea anemone whose homologs are involved in muscle development in bilaterians, and he found that they are expressed in the gastrodermal layer, which is endodermal. So perhaps the muscle-producing mesoderm of bilaterians evolved from the endoderm of a diploblast.

No discussion of axial development is complete without mention of the Hox genes. Martindale has found a Hox cluster in the sea anemone, albeit with apparently fewer genes than the bilaterian Hox clusters. But the genes of the cluster do have restricted expression along one body axis, as they do in bilaterians. The sea-anemone Hox gene homologous to the bilaterian Hox genes that pattern the anterior end of higher animals is expressed in the end of the larva that will become the adult mouth, whereas the sea-anemone homolog of the bilaterian posterior Hox genes is expressed in the end of the anemone larva that will produce the adult foot. Axial expression of Hox genes is thus a basal condition in animals, and the oral-aboral axis of sea anemones could well be homologous to the anterior-posterior axis of bilaterians.

Linking genotype to phenotype

Any understanding of evolutionary developmental biology requires an understanding of the link between genotype and phenotype and of how the two evolve together. The powerful genetic techniques available for various plant species are providing routes into studying this issue. John Doebley

(Wisconsin University, Madison, USA) is investigating the morphology of maize by mapping quantitative trait loci (QTLs). An essential aid to his work is the fact that modern maize is known to have evolved from teosinte, about 7,500 years ago, and the two plant species are still inter-fertile. Morphologically, teosinte has long branches and small ears, whereas maize has short branches and long ears (selected for by humans, who want the corn in the ears). QTL mapping has uncovered *teosinte-branched 1 (TB1)* as the locus with the major effect on branch length. The gene encodes a basic helix-loop-helix transcription factor that can repress growth. The levels of expression of the gene in maize are higher than in teosinte, so the maize branches are shorter. Comparison of the promoter regions of teosinte and maize *TB1* reveals that levels of polymorphism in the maize promoter are much lower than in the teosinte promoter, presumably because of the action of humans selecting for maize plants with shorter branches and longer ears.

It is known that similar morphological architectures can evolve independently, but it is less clear whether the same genes are recruited independently for these 'convergent' structures or whether different genetic mechanisms are involved in each evolutionary event. Enrico Coen (John Innes Centre, Norwich, UK) is addressing this issue by looking at the dorsoventral asymmetry of flowers. The genetic pathway leading to dorsoventral asymmetry has been unraveled in the model system *Antirrhinum*, the snapdragon; asymmetric expression of the *cycloidea (cyc)* gene is one of the principal components of the developmental mechanism. Independent evolution of asymmetry occurred in *Senecio*, a member of the daisy family that has asymmetric ray florets (the individual flowers on the edge of the compound flower). Coen has established that it is the *cyc* genes that are again at work, but there is a twist to the *Senecio* story. In *Antirrhinum*, *cyc* works by being expressed asymmetrically in the floral bud. In *Senecio*, on the other hand, *cyc* seems to distinguish the asymmetrical ray florets from the symmetrical florets of the central disc of the compound flower, because it is expressed only in the ray florets, but it is expressed not asymmetrically in the buds but rather throughout each ray floret bud. The asymmetry within ray florets seems to arise from the asymmetric expression of another *cyc* gene (*cyc-like*) in all florets, which produces asymmetry only when in combination with *cyc*, as in the ray florets. So, similar morphological forms that have evolved independently do seem to recruit the same genes independently, but they can do so in slightly different ways.

It was eight years ago that the British Society for Developmental Biology last had a meeting concentrating on the evolution of developmental mechanisms. Between that meeting and this one, whole genomes have been sequenced, adding a whole new perspective to comparative biology - one that is settling down nicely among phylogenetics, embryology, paleontology and genetics.