Meeting report

Comparative biology and genomics join forces to decipher the diversity of life

Nicole King

Address: Howard Hughes Medical Institute and University of Wisconsin, Madison, 1525 Linden Drive, Madison, WI 53706, USA.
E-mail: nicoleking@facstaff.wisc.edu

Published: 15 July 2002

Genome ***Biology*** 2002, **3(8)**:reports4023.1–4023.3

The electronic version of this article is the complete one and can be found online at http://genomebiology.com/2002/3/8/reports/4023

© BioMed Central Ltd (Print ISSN 1465-6906; Online ISSN 1465-6914)

A report on the Cold Spring Harbor Laboratory meeting on the Evolution of Developmental Diversity, Cold Spring Harbor, NY, USA, 17-21 April 2002.

The bridge between evolution and development, once a rickety tightrope and now a solid fixture in the biology landscape, continues to provide unexpected insights into the two fields it connects. A major lesson from the meeting on the Evolution of Developmental Diversity was that important inputs into the regulation of development can be revealed by comparative biology, be it between distantly related species or between variants within a natural population.

The idea that the genome contains the 'blueprint of life' stems in part from our understanding of the strict relationship between the coding sequences of genes and the amino-acid compositions of their protein products. But we are only beginning to decipher the more elaborate language of non-coding, regulatory DNA. Developmental biologists are particularly interested in understanding how *cis*-regulatory elements in the DNA, which recruit specific combinations of transcription factors, control the timing and level of gene expression. If there is a *cis*-regulatory 'code' or set of rules for gene regulation, the prediction is that sets of genes expressed in the same place and time may be regulated by enhancers that share combinations of binding sites for transcription factors.

The new code-breakers, such as Michele Markstein in the laboratory of Mike Levine (University of California, Berkeley, USA), have employed a variety of approaches to tackle the enigma of gene regulation on a genomic scale. A bioinformatic approach that searches the *Drosophila melanogaster* genome for clusters of a consensus sequence known to recruit the transcription factor Dorsal led the Levine lab to 16 potential target genes. At least six are probably directly activated by Dorsal. In a complementary approach, analyses of the global expression patterns of embryos producing different levels of Dorsal protein revealed 30 potential Dorsal targets. Levine predicted that comparison of the intergenic and intronic DNA associated with the newly discovered Dorsal-regulated genes may reveal additional shared elements and help define the *cis*-regulatory code of the Dorsal-regulated gene set in the fly genome.

Code-breaker Simona Santini (University of Konstanz, Germany) described a comparative genomic approach that may prove important for predicting the architecture of the *cis*-regulatory regions of conserved genes. By aligning the intergenic regions of a conserved cluster of *Hox* genes from diverse vertebrates, she identified a surprising number of conserved sequences, maintained presumably in response to functional constraints. That some of these sequences have been previously shown to act as regulatory elements and binding sites for transcription factors attests to the strength of her strategy. The remaining newly discovered motifs await future study to determine their potential role in the regulation of *Hox* gene expression and to further the effort to decode the *cis*-regulatory language.

The broadest-reaching contribution of the 'evo-devo' (evolutionary developmental biology) community has been the discovery that much of development in diverse species is regulated by a conserved set of genes and *cis*-regulatory elements. Against a backdrop of sequence similarity, it has been a conceptual and technical challenge to map the genetic differences underlying the origin of morphologically distinct species. By turning to the principles of quantitative genetics, Detlef Weigel (Salk Institute, La Jolla, USA) and others are attempting to determine the genetic variation within populations or species upon which natural selection can act to yield morphological diversity. Natural variants of *Arabidopsis thaliana* produce different embryonic stem lengths in response to the same light cues. Weigel described efforts to

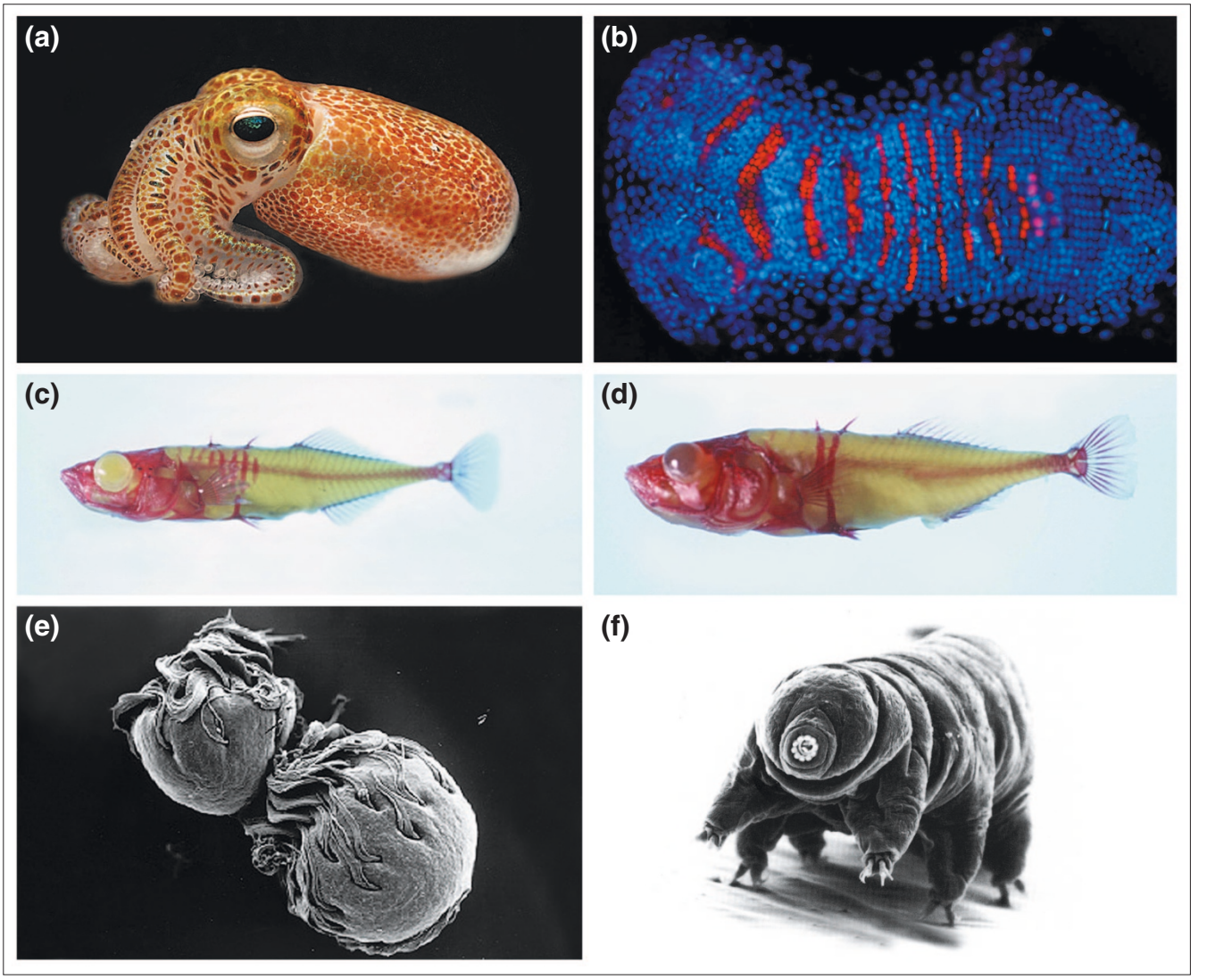

Figure 1
To understand the evolution of morphological diversity, researchers are turning to lesser known organisms. **(a)** The offspring of *Euprymna scolopes*, a sepiolid squid studied by Heinz de Couet (University of Hawaii, Honolulu, USA), display nested expression of *Hox* genes during development of the cephalopod arm crown. **(b)** Matthias Gerberding of Nipam Patel's lab (University of Chicago, USA) described studies of the crustacean *Parhyale hawiensis*, whose embryos (stained for Engrailed protein, in red, and DNA, in blue) develop a distinct grid of cell rows not observed in embryos of model arthropods. By comparing allele frequencies in **(c)** limnetic and **(d)** benthic species of the three-spine stickleback, Katie Peichel (Stanford University, USA) seeks to identify genetic changes underlying morphological evolution. **(e)** Laura Katz (Smith College, Northampton, USA) discussed the diversity of ciliates, such as *Halteria grandinella* (shown here immediately after division), and the developmentally regulated genome rearrangements that mark their somatic and germline nuclei. **(f)** Tardigrades, an intermediate group between nematodes and arthropods, have a small number of cells whose lineages are being mapped by Bob Goldstein (University of North Carolina, Chapel Hill, USA) in an effort to develop a new system for experimental embryology. Images courtesy of (a) Patricia Lee; (b) William Browne and Nipam Patel; (c) and (d) Katie Peichel; (e) Lasek-Nesselquist, Salcedo, Briggs and Katz; (f) Diane Nelson.

use natural variation to discover genes required for the regulation of seedling development and flowering. For 144 natural variants raised under a battery of different light conditions (such as white, blue, red, and far red), Julin Maloof and coworkers in the labs of Weigel and Joanne Chory (The Salk Institute) collected a dataset correlating seedling stem length with light treatment for each variant. Then, in a nod to the bioinformatics crowd, they used hierarchical clustering to link the light-response patterns of natural variants to those of characterized mutants. On the basis of this analysis, Weigel and his group linked an amino acid substitution that reduces the light responsiveness of the phytochrome A protein to lengthening of the embryonic stem in one natural variant. A similar study of flowering time variants revealed a natural genetic variant with a deletion in a 'MADS box' transcription factor gene known to regulate flowering in *Arabidopsis*.

In keeping with its title, the meeting also served to introduce the larger community to a developmentally diverse set of organisms, ranging from ciliates to squid to hemichordates, each of which has benefited from the molecular genetic and bioinformatic revolution (see Figure 1). Understanding the meaningful genetic differences between species, and between variants within species, may eventually lead us to the molecular determinants of morphological evolution.