Meeting report

Fungal biology reaps the benefit of genomics

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A report on the 23rd Fungal Genetics Conference, Pacific Grove, USA, 15-20 March 2005.

Earlier this year more than 700 fungal biologists from around the world, studying everything from yeast to saprophytes, pathogens, and endophytes, made their biennial spring pilgrimage to California for the 23rd Fungal Genetics Conference, where the breadth of fungal biology, evolution, pathogenesis, and reproduction was discussed. Research presented at this year's conference generated a level of energy and excitement not seen in recent memory, stemming from the explosion in the number of fungal genomes with full or partial sequence coverage since the previous meeting in 2003. This avalanche of genome sequence data has drastically changed the landscape of fungal research, and in many respects provides future investigations with a clearer path paved with rich datasets, extensive genetic resources, and robust technologies. A few of the scientific highlights of the meeting are described here, and abstracts for all presentations and posters can be found online at the Fungal Genetics Stock Center website [http://www.fgsc.net].

Understanding evolutionary relationships

Setting the stage, Rytas Vilgalys (Duke University, Durham, USA) gave the opening talk on the fungal tree of life. He described the Assembling the Fungal Tree of Life project [http://ocid.nacse.org/research/aftol], which will compare sequences from seven molecular regions (approximately 10,000 base-pairs, bp) from around 1,500 species of fungi with the aim of working out the evolutionary relationships within the kingdom Fungi. He highlighted the importance of understanding broad evolutionary relationships and the substantial gaps in the current state of knowledge, as organisms that have historically received the most attention and funding have been highly derived members of the tree; for example, sequenced fungal genomes almost exclusively represent recently evolved lineages. This work is timely and relevant because it presents the opportunity to create an evolutionary framework into which our ever-increasing knowledge of fungal diversity can be integrated. Current valid estimates suggest at least 2 million fungal species, of which only some 50,000 to 70,000 have been described.

The evolutionary theme continued with an overview by James Galagan (Massachusetts Institute of Technology-Broad Institute, Cambridge, USA) of comparative genomics within the ubiquitous mold genus *Aspergillus*, members of which are currently being sequenced. Noteworthy points that emerged from his overview include the existence of many upstream open reading frames (ORFs) in 5′ UTRs, suggesting they are more important for regulating eukaryotic gene expression than previously suspected. Comparison of the evolutionary rate of lineage-specific rearrangements provided a quantitative picture of the forces driving eukaryotic genome evolution. Kerry O'Donnell (US Department of Agriculture, Peoria, USA) detailed the evolutionary relationships and evolutionary dynamics among toxin-producing *Fusarium* species, noting the effects of selection and neutral polymorphism on genome structure and function. One of us (R.D.) showed the power of a completed genome sequence as a tool for dissecting biology, enumerating the insights into the pathogenesis of rice-blast disease made by the research community using the recently published completed sequence of the rice-blast pathogen *Magnaporthe grisea*. For example, analysis of the genome revealed a large and diverse set of secreted proteins as well as an expanded family of G-protein coupled receptors. Michael Snyder (Yale University, New Haven, USA) provided a glimpse of the direction in which genome-based research is heading, reviewing his group's

research on transcriptional and phosphorylation regulatory networks in *Saccharomyces cerevisiae* as they compare to those of other yeasts. The two discussions truly brought to light the exciting research that we are now able to consider.

Pathogenicity and pathogen-host interactions

Several impressive presentations discussed the link between fungal pathogenicity and other developmental processes. Joerg Kaemper (Max Planck Institute for Terrestrial Microbiology, Marburg, Germany) described the identification of novel DNA-binding proteins in the corn smut fungus *Ustilago maydis* through whole-genome transcriptional profiling. These proteins, such as Rbf1, are involved in tumor formation in the host plant and filamentous growth in the fungus. Christophe d'Enfert (Institute Pasteur, Paris, France) described work on the identification of novel genes that regulate biofilm formation - a transition from yeast-like to filamentous growth - in *Candida* species. His work revealed one of the frustrations of the 'candidate gene' approach. Although transcriptional profiling revealed many candidate genes, after functional analysis only a few appeared to play an obvious role in biofilm formation.

Gillian Turgeon (Cornell University, Ithaca, USA) also highlighted some trials and tribulations of the candidate-gene approach in her work on identifying toxin-coding genes in the northern corn leaf-blight fungus, the ascomycete *Cochliobolus heterostrophus*. Her functional analysis of 12 potential toxin-coding genes (for polyketide synthases (PKSs) or non-ribosomal peptide synthetases (NRPSs)) revealed that only one of them, *nsp*6, specified a virulence factor. Significantly, functional analysis in other toxin-producing plant pathogenic ascomycetes such as *Alternaria brassicicola* and *Fusarium graminearum* also revealed that *nsp*6 homologs act as potent virulence factors.

A poorly understood but key question in host-pathogen interactions is how avirulence gene products are delivered to the host cytoplasm. Sophien Kamoun (Ohio State University, Columbus, USA) described novel avirulence genes from the oomycete *Phytophthora infestans* that encode proteins with an unusual amino-terminal domain containing the core sequence RXLR. Intriguingly, a protozoan, the malaria pathogen *Plasmodium falciparum*, uses a similar motif to deliver proteins to red blood cells to avoid host detection. It remains to be determined whether similar motifs are found in true fungi (the oomycetes are classified in the kingdom Stramenopila). If this turns out to be the case, a combined bioinformatic and experimental approach may facilitate the identification of new avirulence genes in fungi.

Fungal cell biology

Fungi represent wonderful model systems for studying fundamental principles underlying cell growth and development. The septins are key regulators of budding growth in *S. cerevisiae*. Michelle Momany (University of Georgia, Athens, USA) presented an exciting new strategy for functional identification of septin genes that control the transition from budding to hyphal growth in *Aspergillus nidulans*. She demonstrated that *AspC* (a homolog of yeast *cdc12*, which encodes a protein involved in formation of the contractile ring in cytokinesis) induces *S. cerevisiae* to adopt a filamentous growth form, thus providing a convenient assay for such genes. Temperature and light have a profound impact on fungal development, and Reinhard Fischer (University of Karlsruhe, Germany) described the presence of a phytochrome, PhsA, in *A. nidulans* that acts as a red-light sensor and suppresses sexual development under red light conditions. Notably, PhsA is phylogeneticlly closer to sequences in bacteria than to plants, suggesting a bacterial origin.

Eukaryotic cells typically contain a single nucleus, although there are many exceptions, including fungal and cancer cells, which are multinucleate. Intriguingly, nuclear division in multinucleate fungal cells occurs asynchronously, even though the nuclei are bathed in a common cytoplasm. Amy Gladfelter (Dartmouth Medical School, Hanover, USA) presented her work unraveling the underlying mechanisms of this phenomenon in the *Ashbya gossypii*, a filamentous fungi related to yeast, and revealed a number of surprises. Notably, the levels of cyclins and other cell-cycle regulators do not fluctuate during the cell cycle in *Ashbya* as is common in other eukaryotes, including the uninucleate model yeasts *S. cerevisiae* and *Schizosaccharomyces pombe*. She suggested that the cell cycle in *Ashbya* might be controlled through a posttranslational mechanism affecting the activity of a particular cell-cycle component. This work clearly exemplifies the value of fungal systems in cell-biology research.

A fundamental feature of fungal cells is their ability to fuse (anastomose) with each other. In exciting work, Nick Read (University of Edinburgh, UK) presented micrographs and movies of fusion between conidial germ tubes of *Neurospora crassa*, for which he has coined the term conidial anastomosis tubes (CATs). To further understand the process of anastomosis, he and his colleagues have developed a spectacular microscopic manipulation tool - optical tweezers - with which they can physically move organelles within hyphae, a remarkable achievement.

Secondary metabolism, the production of compounds not essential for growth in culture, is thought to be integrally intertwined with development in fungi. Work with *Aspergillus* species has revealed a link between asexual reproduction and the production of toxic secondary metabolites. Interestingly, many genes involved in secondary metabolism and sporulation occur in separate clusters in the genome. Nancy Keller (University of Wisconsin, Madison, USA) presented work on the regulation of gene expression within such gene clusters. She has found that loss of *LeaA*, a

positive regulator of secondary metabolism, results in silencing of an *argB* marker gene introduced into the aflatoxin gene cluster. However, loss of *LeaA* did not appear to suppress the expression of genes in other clusters associated with sporulation. Deletion of any of the three histone deacetylase genes restored gene expression in the aflatoxin cluster, suggesting a role for chromatin modification in silencing, and Keller presented an elegant model for the involvement of *LeaA* in the epigenetic regulation of secondary metabolism.

As the meeting progressed, it became evident that fungal researchers are working towards the development of a conceptual systems-biology framework into which the massive amounts of theoretical and empirical data can be integrated. The session on evolutionary genomics exemplified the systems view of fungal biology. Jason Stajich (Duke University, Durham, USA) described his work on fungal intron evolution, which suggests an 'early' origin for introns, as intron distribution and density in Basidomycetes, Euascomycetes and Hemiascomycetes are best explained by recurrent rounds of intron loss. James Frasier (Duke University, Durham, USA) presented a masterful comparative study of the evolution of mating-type (*MAT*) loci in fungi - with an emphasis on *Cryptococcus neoformans* - and the sex-determining regions in animal and plant genomes, all of which show convergent evolution. His take-home message was that the *MAT* locus in *Cryptococcus* has many evolutionary microstrata, including the acquisition of transposable elements, gene conversion and chromosomal translocation, with four main steps yielding the present mating system. Ray St Leger (University of Maryland, College Park, USA) ended his talk on the role of molecular adaptation on host range with a call for the development of systems-biology concepts and experimental approaches.

The meeting also saw the Thomas Hunt Morgan Medal of the Genetics Society of America presented to Robert Metzenberg (University of California, Los Angeles, USA) for his life's work studying the biology of *N. crassa*, and the presentation of a new award, the Metzenberg Award, created by the *Neurospora* policy committee in recognition of Bob Metzenberg's contribution to science, to Jay Dunlap (Dartmouth Medical School, Hanover, USA) for his work on circadian rhythms in *N. crassa*.

In conclusion, the boom in fungal genome sequence data over the past few years came with high expectations for extraordinary insight into fungal biology, innovative products, and pathogen control strategies. Several talks touched on what types of strategies are now possible, such as computational approaches to deciphering genomes so as to derive biological meaning or evolutionary processes. When we meet again in two years time, we are sure to be able to learn more from fungal genomes and to search for ways to apply that knowledge towards solving animal and plant health issues as well as furthering our collective understanding of life and how it evolved.