Perspectives on Basidiomycete Genomes for Biotechnology and Pharmacy

Ursula Kües*
Division of Molecular Wood Biotechnology and Technical Mycology, Büsgen-Institute, University of Göttingen, Göttingen, Germany
*For Correspondence - ukuees@gwdg.de

Dr. Igor Grigoriev from the American Department of Energy Joint Genome Institute (JGI) organised at March 22nd - 23rd 2010 in Walnut Creek (CA) a Jamboree on Basidiomycete genomes. The progress and current status on understanding genomes of distinct basidiomycetes were summarized by the principal investigators of genome consortia and future perspectives in basidiomycete genome research were discussed.

At this point of time, complete genomes from 16 species are publically available for basidiomycetes (http://genome.jgi-psf.org/pages/fungi/home.jsf), representing saprotrophs growing on organic waste materials in composts and soils (Agaricus bisporus, Coprinopsis cinerea, Sporobolomyces roseus), white-rotting species living preferentially on dead and decaying wood (Pleurotus ostreatus, Phanerochaete chrysosporium, Schizophyllum commune, Tremella mesenterica) and brown-rotting wood decay fungi (Postia placenta, Serpula lacrymans), plant symbionts (Laccaria bicolor), biotrophic (Melampsora laricis-populina, Puccinia graminis, Ustilago maydis) and necrotrophic plant pathogens (Heterobasidion annosum), as well as human pathogens infecting lungs (Cryptococcus neoformans) and skins (Malassezia globosa). Currently, summarising views on the completed genome sequences are published for six of these fungi (1-6) and reports for others are in the pipeline. Following first computational genome analysis, gene predictions and annotations, consortia of scientists are actively continuing annotating genes in the genomes and sorting them into new large groups and families. Most of the sequenced species have around 10,000 to 12,000 predicted genes, however with S. roseus (http://genome.jgi-psf.org/Sporo1/Sporo1.home.html) and U. maydis (2) with around 5,500 and 6,900 genes, respectively, being at a lower scale and L. bicolor with about 20,000 genes (5) at an upper scale of gene content.

Why is it so interesting to focus on these specific fungal genomes? Pathogenic species attacking our crops or valuable tree species destroy valuable food and renewable energy resources which results in huge economical losses with also apparent socio-political and environmental consequences. For example, alone in Europe wood losses by the conifer pathogen H. annosum are estimated 800 million Euro annually (7). The maize pathogen U. maydis is of less economic importance but a range of close relatives of this experimentally easy-to-access smut model-organism causes significant losses to crops worldwide, including to wheat, barley and sugarcane (8). Wheat stem rust caused by P. graminis has been in control for 50 years by using resistant wheat cultivars but, in fact, new highly virulent races appeared recently in Africa that rapidly spread into other continents as existent
thread of food security (9,10). Studying the genomes of plant pathogenic fungi and encoded protein functions is done in order to find new efficient ways in pathogen management and in the constant fight against dreadful plant diseases.

Wanting to understand the mode of infection of the human opportunistic pathogen *C. neoformans* in both immuno-compromised and immuno-competent individuals for human health protection is evident (11) – genome studies can help to identify efficient targets for drugs and methods of defeat. The biochemical pathway of melanization for example has been recognized has a concept to target disease (12). The US detergent and cosmetics company Proctor & Gamble financed the sequencing of the dandruff fungus *M. globosa* in order to improve their shampoos for better dandruff beat and prevention (4). Whole genome analysis aims at defining new treatments by changing the level or activities of *Malassezia* genes that act for example in skin colonization (13).

The mission of JGI relates to clean energy generation and environmental characterization and cleanup in systems-based scientific approaches, addressed by integrated high-throughput sequencing and computational analysis (http://www.jgi.doe.gov/whoweare/index.html). Particularly the basidiomycetes are in the focus of the JGI bioenergy program along the line biomass production – protection – conversion.

Symbionts such as *L. bicolor* stand at the beginning of a production chain of biomass as renewable energy. The symbiotic species helps in tree growth and thus ultimately in the fixation of CO$_2$ in the form of wood (5) - a reason for JGI to initiate studies on the genomes of such organisms. In combination with the genomes of their tree hosts and studies on genome-wide resistance and defence responses host genes, (14,15), a logic choice in the progression of wood production and protection is to establish genomes of pathogenic fungi like *M. laricis-populina* and *H. annosum* harassing the health and biomass output of trees by infecting either their leaves or their roots and stems.

Once harvested, wood made of energy-rich lignocellulose might be transferred by into sugars through the action of wood-decay fungi or, at least, through fungal lignin degradation the celluloses and hemicelluloses in the wood might become more accessible to microbial hydrolases. Freed cellulose and hemicellulose and released sugars might serve as substrates for environmentally friendly bioethanol production, for example with the help of natural or engineered yeasts (16). Lignocellulose is the most abundant carbohydrate source in nature and represents an ideal renewable energy source to which we will have to turn for replacing the expiring fossil energy by bioethanol and biofuels that are produced without stressing any foodstuff. However, due to lignin incorporation lignocellulose is extremely recalcitrant to depolymerisation into its simple chemical units. Plant waste degrading saprotrophic and particularly wood-decay basidiomycetes are especially rich in genes for enzymes expected to act at degrading plant cell wall components including the difficult lignin. Quite often, large families of genes for such enzymes have been generated in the individual species by repeated gene duplications (1,6,17).

Surprisingly, the cannon of genes potentially functioning in degradation of lignocellulose very much differs from basidiomycete to basidiomycete, not only between species of different life style but also between species of seemingly a same life style (1,5,6,18 and reports on basidiomycete genomes expected to come up in the nearer future). Whilst in one fungus a gene family can be fully missing, in other species genes of the same family are multiple duplicated. For
example, *P. chrysosporium* is lacking any laccase genes (1), whereas the brown-rot *P. placenta* surprisingly has two (6), the saprotrophic *C. cinerea* in total seventeen (17) and the symbiont *L. bicolor* 9 different laccase genes (18). On the contrary, *C. cinerea* has only one gene for a basal lineage class II fungal peroxidase (i.e. the well known Cip; 19), similarly as *P. placenta* and *L. bicolor* (5,6). In contrast, *P. chrysosporium* has 10 gene copies for lignin peroxidases (LiPs), five for manganese-dependent peroxidases (MnP) as well as a gene for a basal peroxidase (Nop) (20,21). Only a minority of the encoded redox-enzymes have so far been biochemically characterized (22-27) as a step forward for their usage in biotechnological applications. Recombinant expression and production of the enzymes can be a requisite to both, biochemical enzyme characterization and biotechnological application (23-25,28,29).

The wealth of the multiple gene families in the genomes of basidiomycetes offers plentiful new opportunities in biotechnology. Only a few other very interesting families with enlarged numbers of genes were so far analyzed with genes for enzymes such as for P450 oxygenases in *P. chrysosporium* (30) and genes for metallopeptidases of the fungalysin family (31), for glycoside hydrolases (32-34), and for P450 oxygenases and sesquiterpene synthases in *C. cinerea* (35). Particularly the currently known largest fungal P450ome found in *P. chrysosporium* accelerated numerous innovative studies on biochemical conversion of a diversity of organic compounds with often a harmful character for the environment (36-39). Many of the P450 oxygenases have thus potential in detoxification of hazardous and toxic organic substances and may be applied in remediation or bioremediation of polluted water and soils and other substrates but there might be also enzymes useful in biotechnological production of desperately wanted chemicals such as drugs for medical purposes and other fine chemicals (40).

For all of the above mentioned species being now fully in the post-genomics-era – at this point applying on them the versatile fast developing and newly emerging methods of transcriptomics, proteomics, metabolomics and other omics and the computational options of networking of data obtained from an omics study and between omics studies (41-43) – we likely will be provided with many more yet unseen discoveries with high value in practical applications. As clearly seen from the so far available genomes, various different ways in degradation of lignocellulose in general and in attack of lignin by different sets enzymes in special have been verified by the basidiomycetes. The JGI launched new calls in their bioenergy program for sequencing genomes of further fungi, with good potential in biomass production and/or degradation, global carbon cycling and biogeochemistry. In addition, there are ongoing projects and calls to sequence metagenomes of microbial communities e.g. in soils (http://www.jgi.doe.gov/CSP/user_guide/index.html). Of these, we can also expect to obtain more exciting data on basidiomycetes. Since amongst the so far sequenced basidiomycetes no enzyme fitting for decay of plant cell wall material has been found twice, we anticipate to discover new cocktails of interesting enzymes from sequencing more species. The rapid advances in basidiomycete genomics promise that more impact on biotechnology and pharmacy has to be expected by this work in the near future.

References


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