

## MEETING REPORT

# The yeast factory

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### Abstract

A report on the 13th International Congress on Yeasts (ICY), held at Madison, Wisconsin, USA, 26-30 August 2012.

Almost 400 scientists attended the 13th International Congress on Yeasts (ICY), where advances in yeast physiology, genomics, biotechnology, ecology and taxonomy were reported. In addition, the meeting celebrated the achievements accomplished with yeast in the past two decades, with the keynote speaker, Steve Oliver (University of Cambridge, UK), giving an overview of the scientific findings in yeast genomics, starting from the pioneering sequencing of *Saccharomyces cerevisiae* chromosome III in 1992 to the recent translational studies using yeast as a model to predict copy number variation phenotypes in human cancer cell lines. The plenary speaker Bernard Dujon (Institut Pasteur, France) also superbly summarized the history of comparative genomics with yeasts, the achievements of the Génolevures consortium (<http://www.genolevures.org/>) and the evolutionary insights gained in the hemiascomycetes lineage.

Here, I highlight some contributions from three key themes of the meeting, including genomic diversity, comparative studies and evolution; biogeography; and taxonomy.

### Genomic diversity, comparative analysis and evolution

*S. cerevisiae* yeasts form diversified groups, usually defined by the source from which they were isolated. Justin Fay (Washington University, USA) analyzed a highly differentiated group of *S. cerevisiae* isolated from grapes to assess whether the level of phenotypic variation between natural and domesticated strains could be a consequence of limited gene flow between sympatric

wild and vineyard strains. Chardonnay must (pressed grapes) was fermented with both oak tree isolates and wine strains of yeast, and differences in the aroma and flavor of the resulting wine were assessed by 51 human volunteers. Not only was the oak tree wine the least palatable, but genome comparative analysis also showed that the wild isolates were exchanging genes with vineyard strains, potentially contaminating wine production with off-flavors. Fay concluded there is no clear link between the genetic diversification of vineyard yeasts and domestication.

Understanding the molecular basis of phenotypic differences among yeast strains may lead to the engineering of new strains of biotechnological relevance. Amparo Querol (IATA-CSIC, Valencia, Spain) presented her studies on differential expression profiles during wine fermentation of 29 yeast strains (14 fermentative yeasts and 15 wild isolates). The detection of differences in transcript levels between homologous genes from natural and wine strains can help the selection of properties that are desirable in enology (fermentation at low temperature, high production of glycerol and lower ethanol yield).

Comparative genomics studies have also explored the evolution and reconstruction of yeast carbon metabolism. Jure Piskur (Lund University, Sweden) investigated the origin of the Crabtree effect, which enables some species of yeast to produce ethanol, rather than biomass, at high sugar concentrations, by analyzing 40 different yeasts in the Saccharomycetes class, covering 200 million years of history. Interestingly, he found that species that originated before the whole genome duplication, such as *Lachancea* species, were 'Crabtree positive', producing as much ethanol as biomass. He concluded that the ability to produce ethanol from sugar is independent from the whole genome duplication, and originated about 120 million years ago, when the first modern flowering plants and fruits appeared on our planet.

Dawn Thompson (Broad Institute, USA) compared transcriptome data for 15 fungal species grown in a variety of conditions in order to study how regulation evolves and how network rewiring can lead to phenotypic adaptation. Growth rate, expression profiles, metabolites and nucleosome organization profiles were analyzed and compared to reconstruct molecular networks of ancestral and extant species.

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Interspecies hybridization is a source of phenotypic diversity for the colonization of new environments. Eladio Barrio (University of Valencia, Spain) analyzed the genomes of hybrids between *S. cerevisiae* and *Saccharomyces kudriavzevii*, focusing on mitochondrial inheritance. There was a tendency for the hybrids to lose the portion of the genome derived from *S. kudriavzevii*, but also to retain the mitochondria from this species. Phylogenetic reconstruction of mitochondria based on the cytochrome-c oxidase subunit II (*COX2*) sequence showed that mitochondrial DNA often recombines in a region between *COX2* and the *ORF1* sequence (a large ORF related to the group I introns), and that introgression from *S. paradoxus* is present.

Serge Casaregola (CIRM-Levures, INRA, France) carried out a population genomics study of two species of the CTG clade (yeasts that translate CTG as serine instead of leucine), *Millerozyma farinosa* and *Debaryomyces hansenii*, and showed that several cryptic species, which could not be distinguished using ribosomal DNA analysis, were present. New hybrids, such as those between *M. farinosa* and *Millerozyma miso*, were also discovered. These hybrids seemed to undergo loss of heterozygosity readily during sporulation. Casaregola concluded that the diversity among yeasts of the CTG clade is wider than previously thought, with the coexistence of many cryptic species, haploids, heterozygote diploids and hybrids.

Yeast has long been used as model to study the phenotypic effects of copy number variation and mitochondrial diseases. Maitreya Dunham (University of Washington, USA) analyzed the origins and consequences of copy number variation in yeast strains grown in a chemostat under different nutritional limitations. By introducing a collection of barcoded plasmids containing a copy of every gene into the yeast cells, she was able to study the effect of duplications. She identified a set of genes whose copy number increase was beneficial to the cell in all the conditions tested, and others that were environment-dependent. Dunham also reported a new inverted tandem repeat structure that is inconsistent with the currently accepted mechanisms of DNA repair. She proposed a new model for origin-dependent inverted repeat amplification, suggesting that such tandem architecture can be caused by an error in the DNA replication fork.

Monique Bolotin-Fukuhara (Université Paris Sud, France) described the generation of a collection of yeast strains with mutations in mitochondrial transfer RNAs that mimicked human pathological diseases. She showed that the severity of the human phenotype was recapitulated in yeast, and that the nature of the mitochondrial sequence neighboring the engineered mutations affected the severity of the phenotype.

## Biogeography

Significant advances on the ecology and natural distribution of *Saccharomyces sensu stricto* species were made recently. José Paulo Sampaio (Universidade Nova de Lisboa, Portugal), explained how the belief that *Saccharomyces* was a purely domesticated organism, living mainly in human-made environments such as fermenting grapes, has hampered the detection of truly ecological species for several years. Improvements in the isolation methodologies from natural substrates are gradually changing this situation, allowing the identification of several new yeast isolates. In fact, yeasts are widely distributed on oaks and on species of the closely related *Nothofagus* genus, found in Patagonia, the Philippines, South Australia and New Zealand. The cryotolerant species *Saccharomyces arboriculus*, *Saccharomyces eubayanus* and *Saccharomyces uvarum* have all been isolated from *Nothofagus* species. Sampaio's study of *S. uvarum* biogeography has shown the existence of three different populations, found in Europe, South America and Australasia, respectively. Interestingly, the Australasian population is highly divergent, and hybrid crosses of Australasian strains with those from the South American populations have as little as 36% spore viability. Although *Saccharomyces paradoxus* and *S. cerevisiae* seem to have a global distribution, other lineages such as *S. kudriavzevii* and *Saccharomyces mikatae* were isolated from restricted geographical areas.

Christopher Hittinger (University of Wisconsin, USA) reported on the discovery and the genome analysis of *S. eubayanus* (isolated from *Nothofagus* sp. in Patagonia), the missing parental contributor to the lager-brewing yeast *Saccharomyces pastorianus*. A total of 200 *S. eubayanus* and *S. uvarum* strains were isolated in Argentina and were sequenced to determine the genetic diversity and population structure of this species. Interestingly, Hittinger pointed out that both *S. eubayanus* and *S. uvarum* have retained some parts of the RNA interference machinery in their genomes, such as the *Dicer 1* (*DCR1*) gene, which are lost in the other *Saccharomyces sensu stricto* species. Hittinger also mentioned the *Saccharomyces sensu stricto* consortium (SSS), which includes improved and assembled genome sequences for these yeasts (<http://www.saccharomycessensustricto.org>).

## Taxonomy

The theme of taxonomy was an important part of the meeting given the rapid and increasing number of newly discovered yeast species. In his plenary lecture, Teun Boekhout (CBS-KNAW, Utrecht, The Netherlands) called for a revision of the phylogenetic classification not only of the basidiomycetous yeasts, but also of the highly polyphyletic *Candida* genus, in which the majority of species are harmless and have no relation to the human pathogen *Candida albicans*. The systematics of yeast

species taxonomy should be carried out using refined multigene phylogenies or whole genome analysis, because the morphological and physiological criteria are often misleading, conflicting with the gene tree. It follows that there is a need for whole genome sequencing projects at the species level, building on from the existing genomic characterization of several strains belonging to *S. cerevisiae* and *S. paradoxus* species (<http://www.sanger.ac.uk/research/projects/genomeinformatics/sgrp.html>). Boekhout also discussed his large-scale effort to determine unusual phenotypes in less explored non-conventional yeasts that may be of industrial relevance (the EU Cornucopia project).

Vincent Robert (CBS-KNAW, Utrecht, the Netherlands) gave an update on the DNA barcoding of all the 9,000 strains in the CBS collection by sequencing the D1/D2 and ITS region of the ribosomal DNA. This barcode method is useful to revise identifications and select strains for further exploration. Moreover, MALDI-TOF (matrix-assisted laser desorption/ionization time-of-flight mass spectrometry) techniques, based on differential peptide fingerprinting patterns, are being developed and applied for strain classification and quality control analysis of the CBS collection.

The recent discovery of the new species *S. eubayanus*, one of the original parents of *S. pastorianus*, necessitated a revision of the nomenclature and phylogeny of the *sensu strictu* species, with the old *Saccharomyces bayanus*

var. *uvarum* becoming a recognized species called *S. uvarum*, and the old *S. bayanus* var. *bayanus* becoming *S. bayanus*, presenting a hybrid genome from different strains and species belonging to *S. uvarum*, *S. eubayanus* and *S. cerevisiae*. Huu-Vang Nguyen (INRA, AgroParisTech, Thiverval-Grignon, France) showed that a small number of specific markers (*NTS2*, *MAL31*, *MEL1*, *MTY1*) are sufficient to discriminate between pure lines of *S. uvarum* and *S. eubayanus* and the hybrids *S. bayanus* and *S. cerevisiae*. By PCR and restriction fragment length polymorphism analysis, he was able to reclassify the *S. bayanus* strains CBS 424, CBS 425 and CBS 3008, showing that they were inbred lines of *S. uvarum* and *S. eubayanus*, and that they did not contain the *S. cerevisiae* portion of the genome usually present in *S. bayanus* strains. This method is a quick and reliable approach to differentiating between different hybrids and species belonging to the *Saccharomyces sensu stricto* group.

In conclusion, the ICY meeting showed that there is an exciting future for yeast research, with an ever expanding repertoire of species and strains to study and set of genomics tools with which to do so.

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