1 Genomics and the Making of Yeast Biodiversity

2
3 Running Title: The Evolution of Yeast Genomes

4
5 For the "Genomes and Evolution" Special Issue of *Current Opinion in Genetics and*
6 *Development*

7
8 2545 words

9 2 figures, 1 box

10 105 references with 10 each of *special and **outstanding interest

11
12 Chris Todd Hittinger^{1,2@}, Antonis Rokas³, Feng-Yan Bai⁴, Teun Boekhout⁵, Paula Gonçalves⁶,
13 Thomas W. Jeffries⁷, Jacek Kominek¹, Marc-André Lachance⁸, Diego Libkind⁹, Carlos A.
14 Rosa¹⁰, José Paulo Sampaio⁶, Cletus P. Kurtzman¹¹

15
16 @Corresponding author: cthittinger@wisc.edu

17
18 ¹Laboratory of Genetics, Genome Center of Wisconsin, Wisconsin Energy Institute, J. F. Crow
19 Institute for the Study of Evolution, University of Wisconsin-Madison, Madison, WI 53706, USA

20
21 ²DOE Great Lakes Bioenergy Research Center, University of Wisconsin-Madison, Madison, WI
22 53706, USA

23
24 ³Department of Biological Sciences, Vanderbilt University, Nashville, TN 37235, USA

25
26 ⁴State Key Laboratory of Mycology, Institute of Microbiology, Chinese Academy of Sciences,
27 Beijing 100101, China

28
29 ⁵CBS-KNAW Fungal Biodiversity Centre, Utrecht, The Netherlands; State Key Laboratory of
30 Mycology, Institute of Microbiology, Chinese Academy of Sciences, Beijing, China; Shanghai
31 Key Laboratory of Molecular Medical Mycology, Changzheng Hospital, Second Military Medical
32 University, Shanghai, China

33
34 ⁶UCIBIO-REQUIMTE, Departamento de Ciências da Vida, Faculdade de Ciências e Tecnologia,
35 Universidade Nova de Lisboa, 2829-516 Caparica, Portugal

36
37 ⁷Department of Bacteriology, University of Wisconsin-Madison, Madison, WI 53706, USA

38
39 ⁸Department of Biology, University of Western Ontario, London, ON N6A 5B7, Canada

40
41 ⁹Laboratorio de Microbiología Aplicada y Biotecnología, Instituto de Investigaciones en
42 Biodiversidad y Medioambiente (INIBIOMA), UNComahue-CONICET, Bariloche, Argentina

43
44 ¹⁰Department of Microbiology, ICB, Federal University of Minas Gerais, C.P. 486, Belo
45 Horizonte, MG, 31270-901, Brazil

46
47 ¹¹Bacterial Foodborne Pathogens and Mycology Research Unit, National Center for Agricultural
48 Utilization Research, Agricultural Research Service, US Department of Agriculture, Peoria, IL,
49 USA

Abstract

Yeasts are unicellular fungi that do not form fruiting bodies. Although the yeast lifestyle has evolved multiple times, most known species belong to the subphylum Saccharomycotina (syn. Hemiascomycota, hereafter yeasts). This diverse group includes the premier eukaryotic model system, *Saccharomyces cerevisiae*; the common human commensal and opportunistic pathogen, *Candida albicans*; and over 1,000 other known species (with more continuing to be discovered). Yeasts are found in every biome and continent and are more genetically diverse than angiosperms or chordates. Ease of culture, simple life cycles, and small genomes (~10-20 Mbp) have made yeasts exceptional models for molecular genetics, biotechnology, and evolutionary genomics. Here we discuss recent developments in understanding the genomic underpinnings of the making of yeast biodiversity, comparing and contrasting natural and human-associated evolutionary processes. Only a tiny fraction of yeast biodiversity and metabolic capabilities has been tapped by industry and science. Expanding the taxonomic breadth of deep genomic investigations will further illuminate how genome function evolves to encode their diverse metabolisms and ecologies.

66

67 **A brief history of yeast evolutionary genomics**

68 The *Saccharomyces cerevisiae* genome was the first eukaryotic genome sequenced [1], a
69 collaborative feat that enabled two decades of innovation and discovery. *C. albicans* soon
70 followed [2], as well as a handful of relatives in both clades and a smattering of taxonomically
71 diverse species [3–8]. *S. cerevisiae* became a proving ground for new genomic technologies,
72 such as deleting and barcoding genes for functional profiling [9]. Early comparative studies
73 pioneered the now commonplace use of genome sequencing to address specific functional and
74 evolutionary hypotheses, such as using conserved genomic regions to identify functional DNA
75 sequence elements [3,4]. These genomes began to catalyze research in many other fields,
76 resulting in important advances to our understanding of the evolution of genome content and
77 organismal traits [10,11], phylogenetics [12], and cis-regulatory element prediction [13]. By the
78 last comprehensive review of yeast evolutionary genomics in 2010 [14], the genomes of 26
79 yeast species had been sequenced, still mostly in the two clades containing *S. cerevisiae* and
80 *C. albicans*. With the popularization of next-generation sequencing, the genomes of 40
81 additional species have been published in the last five years, while 20 more are publicly
82 available but await formal publications (Figure 1). Nonetheless, most yeast biodiversity remains
83 unexplored at the genomic level (Figure 2).

84

85 **Yeast mating systems**

86 Most yeasts have true sexual cycles, but some manifest complex parasexual cycles (non-
87 meiotic processes involving mitotic recombination and chromosome loss), whereas others are
88 thought to be asexual. This multiplicity of forms and sexual cycles led to a byzantine
89 nomenclature system that is undergoing a radical simplification, which will ultimately result in a
90 taxonomy based on phylogeny (Box 1). Although asexual strains achieve higher laboratory
91 fitness [15], they seem not to persist or undergo frequent cladogenesis. Sex may increase the

rate of adaptation to novel environments and help purge deleterious alleles [16,17]. Thus, most yeast clades harbor at least some sexual taxa, which likely reflect their ancestral states. Sexual cycles exist in both obligately outcrossing (heterothallic) species, where mating types reside in different individuals, as well as in species that can self-fertilize (homothallic).

Self-fertilization in *S. cerevisiae* and relatives is achieved through the tight regulation of the *HO* gene, which encodes a homing endonuclease co-opted from an intein selfish element [18]. The Ho protein cuts the active mating cassette, allowing for homology repair by one of two silent mating cassettes, thereby switching the mating type and enabling clonal mother-daughter mating. Interestingly, *Kluyveromyces lactis* *HO* has been replaced by *MAT α 3*, another selfish element co-opted from a DNA transposon [19,20]. A simpler two-locus system that switches mating types by inversion has evolved in the clade containing *Ogataea (Hansenula) polymorpha* and *Komagataella (Pichia) pastoris* [21]. Here inversion simply switches which of the two mating loci is present in active chromatin, and thus determines which is expressed. These genetic systems have profound effects on maintaining local genetic variation [22] and generating genome instability [23] at the mating-type locus.

The genetic regulatory networks that control the batteries of genes necessary for each mating type have been investigated extensively in several species, establishing a paradigm for both the logic and molecular mechanisms by which such networks evolve. Several genetic changes can facilitate the evolutionary rewiring of regulatory networks, including the duplication of regulators and partitioning of target genes [24], intercalation of new regulators [25], and alteration of binding site specificity [26]. Most such changes are thought to occur through selectively neutral mechanisms, often resulting in the same network output. These studies have established rewiring as a common feature in regulatory network evolution and have shown how neutral changes can profoundly shape evolutionary outcomes.

Metabolic diversity, ecology, and biotechnology

Thanks to their diverse metabolisms, yeasts exhibit a remarkable range of ecologies, including methanol consumption in *O. polymorpha* and *K. pastoris*; xylose fermentation in *Scheffersomyces (P.) stipitis* and *Spathaspora passalidarum*; lipid production in *Yarrowia lipolytica* and *Lipomyces starkeyi*; human pathogenesis in *C. albicans* and *C. (Nakaseomyces) glabrata*; and cotton pathogenesis in *Eremothecium (Ashbya) gossypii* [27] (Figure 1). Many of these metabolic capabilities are exploited in various biotechnological, food, and beverage industries. For example, *S. cerevisiae* is the workhorse of the multibillion-dollar brewing, wine-making, baking, and biofuel industries, but other commonly used species include *Kazachstania exigua* (sourdough), *Cyberlindnera jadinii* (syn. *C. utilis*, food additives), *K. pastoris* (heterologous protein production), and *E. gossypii* (riboflavin). Nonetheless, these well-known yeasts represent a scant slice of yeast metabolisms and ecologies, and most species remain unharnessed by industry and only modestly explored by science.

Yeast ecological niches require more study, especially in natural settings, but what limited information exists suggests that yeast niches are partitioned by many parameters, including temperature, pH, radiation, insect and plant hosts, and metabolism [27–29]. For example, *Saccharomyces* and relatives have evolved an extreme preference for fermenting glucose into ethanol, even in the presence of oxygen, a process known as Crabtree-Warburg Effect or aerobic fermentation. This “make-accumulate-consume” strategy provides a powerful ecological advantage by exploiting the rich reserves of simple sugars in sap, fruit, and other sources [30–33]. Other genera, such as *Scheffersomyces* and *Spathaspora*, have adapted to living in the guts of wood-consuming beetles and are capable of fermenting xylose, the second most abundant monosaccharide in woody plant material, which is of critical importance to the lignocellulosic biofuel industry [11,34,35]. Some traits are unique, such as a requirement for

carbon dioxide in *Cyniclomyces* [36], while others, such as temperature preferences, evolve quickly [27–29]. A handful of lineages have evolved into commensals and/or pathogens of mammals and birds, exhibiting increased thermophily, the loss of key metabolic functions, increased biofilm-forming ability, and the acquisition of new traits to evade the host immune system [2,7,8,37].

The genetic outlines underlying some of these remarkable innovations are beginning to be understood. Some differences evolve rapidly and can be explained by one or two genes. For example, there is widespread variation in the catabolism of disaccharides, perhaps because extracellular cleavage often sets up a “prisoner’s dilemma” where competitors can consume the monosaccharide intermediates [29]. Other traits, such as galactose catabolism, seem to be lost frequently [10,38] (and potentially regained [39]), correlating with the loss of several genes. Aerobic fermentation is thought to involve many genetic changes in glycolytic and mitochondrial pathways and has evolved only a handful of times [30–33]. Strikingly, many of these pathways underwent parallel evolutionary changes during the acquisition of aerobic fermentation by the lineage leading to *S. cerevisiae* and the highly divergent lineage leading to *Brettanomyces (Dekkera) bruxellensis* [30,32].

Much remains to be understood about the forces driving most yeast radiations (Figure 2). For example, dozens of species evolved from clades associated with fruit-rot and tree-flux habitats to exploit the diverse chemistries associated with different species of cacti, which, in turn, have been exploited by several different cactophilic *Drosophila* and sap beetle species that feed on these yeasts [27,28]. Most species of the *Starmerella* clade are associated with Hymenoptera species, while yeasts of the genus *Ogataea* frequently inhabit leaf litter where methanol consumption may be beneficial [21,27,40]. Little is known about the genetic underpinnings of these ecological innovations, except that they must rely, at least partly, on metabolism.

Metabolic traits, which can be easily studied in the lab and whose genetic basis is often well understood from model organisms, are therefore uniquely suited to provide the thin end of a wedge to open an understanding of yeast diversification.

Hybridization, introgression, and horizontal gene transfer

One of the most important paradigm shifts catalyzed by broader yeast genome sequencing is a realization of the prevalence of gene sharing through hybridization, introgression, and horizontal gene transfer (HGT), especially among domesticated strains. Perhaps the most iconic examples are the lager-brewing yeasts, which were recently shown to be allopolyploids of *S. cerevisiae* and the recently discovered species *S. eubayanus* [41,42]. Allopolyploids of *S. cerevisiae* x *S. kudriavzevii* are also used in brewing, wine fermentation, and cider fermentation [43]. Conversely, strains of *S. uvarum* used in cider and champagne fermentation have acquired genes from several *Saccharomyces* species, but most wild strains lack these introgressions [44].

Fewer allopolyploids are known outside of the genus *Saccharomyces*, and all are from industrial or clinical settings. In the genus *Zygosaccharomyces*, a miso production strain [45] and a sparkling wine contaminant [46] are allopolyploids. Echoing the recent status of *S. eubayanus*, genome sequencing showed *Millerozyma (P.) sorbitophila*, a sorbitol contaminant, to be an interspecies hybrid of *Millerozyma (P.) farinosa* and a yet-to-be-identified congeneric species [47]. Similarly, genome sequencing of a wine spoilage strain purported to be *B. bruxellensis* revealed it to be allotriploid [48]. Several clinical isolates from the *C. parapsilosis* species complex are also interspecies hybrids [49].

In addition to hybridization, many strains of *S. cerevisiae* used in industry have picked up genes through introgression from various *Saccharomyces* species [44,50,51], as well as from more

distantly related yeasts through HGT [52–54]. HGT is not restricted to strains grown in artificial environments but also occurs at a low, but significant, rate across the yeast phylogeny, influencing the content of both the nuclear [55] and mitochondrial genomes [56]. For example, a recent examination of fungal metabolic pathways inferred that 1.8% of yeast metabolic genes have undergone HGT at some point in their history [57]. HGT has influenced individual genes, sometimes repeatedly [33,53,58]; entire metabolic pathways [59]; and larger genomic fragments [52], although the latter has only been observed in industrial strains [52,55]. Although it is thought that conjugation, transformation, and viral transduction are involved in filamentous fungi [60], less is known about the mechanisms that facilitate yeast HGT. Interestingly, a recent study showed that experimental rates of bacteria-to-yeast HGT can be strongly influenced by gene presence/absence polymorphisms in non-essential yeast genes [61].

Resequencing dynamic genomes

Yeast genomics has greatly enhanced our understanding of the evolutionary dynamics of natural populations, among domesticated strains, during infections, and during laboratory experiments. Aside from *S. cerevisiae* [51], population genomic studies have characterized the metabolic, genetic, and biogeographic diversity of *S. paradoxus* [62], *S. kudriavzevii* [38], and *S. uvarum* [44], making this genus one of the few where population genomic datasets exist for the majority of known species [63]. Large-scale population genomic studies in other yeasts remain rare, but a recent investigation of the stability of the unusual GC content of a chromosome-arm in *Lachancea kluyveri* is an undeniable harbinger of the future [64]. Remarkably, estimates of the frequency of outcrossing ($\sim 10^{-5}$) in *L. kluyveri* are similar to *Saccharomyces* [22], suggesting that key lifestyle parameters may be conserved across vast timespans, different ecologies, and different mating-type control systems.

Genome resequencing has allowed experimental evolution studies in *S. cerevisiae* to rapidly move from identifying specific adaptive mutations [15,65,66] to examining pools of variants undergoing clonal interference [67,68] to massively parallelized tracking of individually tagged lineages [69]. Although the most advanced genetic tricks are not available for other yeasts, some of these approaches have even been extended to study the evolution of clinical isolates of *C. albicans* during the course of infection [70,71]. Collectively, these studies paint the portrait of a dynamic genome that can be pushed easily toward evolving a variety of traits. Indeed, a provocative corollary is that the trillions of scattered cells belonging to each yeast species are being exposed to potentially quite different selective pressures, ultimately engendering different genomic outcomes that must be reconciled.

Which microevolutionary processes explain macroevolutionary patterns?

Juxtaposing data from laboratory evolution and population genomic studies to the data from comparisons of distantly related genomes raises an interesting paradox: rapid, radical, and sometimes irreversible changes regularly occur across microevolutionary timescales, and yet, relative stability persists over macroevolutionary ones. Some common types of mutations, such as aneuploidy [66], are unlikely to be fixed in a species because these low frequency polymorphisms are easily reversed. Others, such as interspecies hybridization and the loss of mating pathways, can expose lineages to Muller's Ratchet and eventual extinction. Many of the most readily acquired mutations are further predicted to reduce or eliminate gene activity, especially in regulatory genes [15,65,66,71].

Certainly, many lineages have lost specific genes, networks, and traits, but even when they arise as conditionally advantageous mutations, several forces likely act to limit the impact of the most radical changes over geological timescales. First, species are seldom exposed to static environments that allow conditionally useful genes to be tossed aside. Rather, they must be

able to thrive and complete their life cycles in fluctuating environments. Second, individuals exchange genes with other members of their species, which may exist across a range of environments, allowing genes to be reintroduced if a loss was only transiently beneficial. Third, although the mutations may be rarer than nonsense or frameshift mutations, more specific regulatory mutations are likely to arise eventually [72]. Fourth, horizontal gene transfer (HGT) may allow genes to be reacquired from other organisms [55,59]. Finally, lineages that have lost key functions may be less likely to undergo cladogenesis or be more susceptible to extinction.

Given the currently limited sampling of yeast genomes, one might justly ask whether we are missing a trend of widespread, but undetected, gene loss and gene sharing that will be revealed as all the branches of the phylogeny are filled in. Many additional congeneric hybrids at the tips of the phylogeny will undoubtedly be discovered. Nonetheless, as with most gene loss events, hybridization events are generally neutral or short-lived adaptations to extreme conditions. Allopolyploidization results in whole genome duplications (WGDs) [73], which are relatively easy to detect, thanks to pioneering work that inferred the WGD in the lineage leading to *S. cerevisiae* by comparing this genome to itself [74]. Although that solitary WGD event had a tremendous and lasting impact on duplicate gene function and genome structure in over 50 species of Saccharomycetaceae, including *S. cerevisiae* [75], the frequency with which yeast WGD descendants persist is clearly much lower than in angiosperms, where most lineages have undergone multiple rounds of WGD [76]. Finally, HGT is responsible for a non-trivial number of yeast adaptations, but the rate remains much lower than in bacteria [57].

Prospects for the future

As with all organisms, yeast genome sequences comprehensively describe their genetic makeups, but historical and genetic processes that have sculpted their evolution are best understood through a comparative lens. Remarkably, several ambitious projects promise to

enhance dramatically the genome sampling of fungal biodiversity at both the population and species levels, including the 1KFG Project surveying the entire spectrum of fungal diversity (<http://1000.fungalgenomes.org>), the 1002 Yeast Genomes Project focusing on *S. cerevisiae* (<http://1002genomes.u-strasbg.fr>), the Dikaryome Consortium (<http://dikaryome.org>), the iGénolevures Consortium (<http://gryc.inra.fr>), and the Y1000+ Project focusing on the subphylum Saccharomycotina (<http://y1000plus.org>).

At least for the yeasts, these projects stand a chance of saturating two key dimensions of known biodiversity: genetic depth and taxonomic breadth. Just as a genome sequence definitively describes what genes are present in an organism, only a complete clade of genomes can fully chronicle their evolution and enable the study of genetic and functional diversification across taxa, niches, and time. With these projects underway and with perhaps the most advanced armamentarium for functional dissection at hand, the genetic features that cause some species to make beer, others to inhabit cacti, and still others to cause lethal blood infections are finally coming into focus. The yeasts are rising to the challenge to create an unparalleled model of eukaryotic genome evolution.

Acknowledgements

We thank the many colleagues who alerted us to relevant literature and apologize to those whose work was excluded due to space limitations or oversight. Mention of trade names or commercial products in this publication is solely for the purpose of providing specific information and does not imply recommendation or endorsement by the U.S. Department of Agriculture. USDA is an equal opportunity provider and employer. Research in the Hittinger Lab is supported in part by the National Science Foundation (Grant Nos. DEB-1442148 to CTH and CPK, DEB-1253634 to CTH); the DOE Great Lakes Bioenergy Research Center (DOE Office of Science BER DE-FC02-07ER64494); the USDA National Institute of Food and Agriculture

299 (Hatch project 1003258); the Alexander von Humboldt Foundation (CTH is an Alfred Toepfer
300 Faculty Fellow); and the Pew Charitable Trusts (CTH is a Pew Scholar in the Biomedical
301 Sciences). Research in the Rokas Lab is supported by the National Science Foundation (DEB-
302 1442113); the National Institutes of Health (NIAID, AI105619); and the March of Dimes.
303 Research in the Lachance Lab is supported by the Natural Science and Engineering Research
304 Council of Canada. Research in the Libkind Lab is supported by CONICET, Universidad
305 Nacional del Comahue (B171), and FONCyT (PICT 2014-2542). Research in the Rosa Lab is
306 supported by the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq)-
307 Brazil.

Figure Legends

Figure 1. Key traits and phylogenetic relationships of the 86 yeasts of the subphylum

Saccharomycotina whose genomes have been sequenced. The topology of the cladogram has been estimated conservatively from previous analyses using genome [12,23] or multi-locus sequence data [27,36]. Major clades [36] are color-coded (clade names are shown in Figure 2). Only one reference genome per species is included with preference given to the highest quality and/or most widely used reference genome. Only publicly available genome assemblies are included. Interspecies hybrids are discussed in the text but are not shown here. WGD, whole genome duplication; recent work has shown that the WGD was caused by an allopolyploidization event that occurred between an early member of the *Zygosaccharomyces/Torulaspora* clade and an early member of the *Kluyveromyces/Lachancea/Emmenthycium* clade, thus making this part of the phylogeny a network, rather than a tree [73]. CTG clade, yeasts using an alternate codon table where CTG encodes serine, instead of leucine. JGI, genomes publicly available on MycoCosm at <http://genome.jgi-psf.org/programs/fungi/index.jsf>, which are subject to the usage terms of the DOE Joint Genome Institute until formal publication. GB1, GenBank Accession CCBQ000000000; GB2, Genbank Accession JPPO000000000; GB3, GenBank Accession AEOI000000000; GB4, GenBank Accession LCTY000000000.

Figure 2. Most yeast clades remain underrepresented by genome sequence data.

Estimated species counts for each major yeast clade [36] (light colors) are compared with the number of publicly available genomes from each clade (dark sliver within larger triangles). In addition to the 807 species shown, approximately 400 anamorphic species (e.g. *Candida* spp.) currently lack a clear phylogenetic placement. As the phylogeny is resolved, these species will

be reassigned to genera and higher taxonomic ranks consistent with their phylogeny (Box 1).

Color codes are the same as in Figure 1.

Box 1. One Fungus, One Name (1F1N) and the Phylogenomic Future of Yeast Taxonomy

Despite the considerable progress made classifying yeasts using multi-locus DNA sequence data, critical gaps remain. Many genera are paraphyletic or polyphyletic, while many taxonomic circumscriptions at or above the family level are poorly supported or completely lacking. Further complicating matters, many species are assigned to large, polyphyletic, anamorphic (no known sexual state) genera (e.g. *Candida*), rather than to allied teleomorphic (sexual) genera. Due to a recent revision in the International Code of Nomenclature for algae, fungi, and plants (formerly the International Code of Botanical Nomenclature), anamorphs and teleomorphs can now, for the first time, be reassigned to monophyletic genera that contain species both with and without known sexual cycles. This long-overdue change presents a timely opportunity to formulate a comprehensive and stable yeast taxonomy based on complete genetic data. Well-circumscribed monophyletic genera (and higher order taxa) will finally provide evolutionary geneticists, mycologists, biotechnologists, and clinicians with phylogenetically informative names to aid in the design of experiments and the interpretation of data. In this review, the current, formally recognized genus names are shown first with alternative names in parentheses. In some cases, such as the affinity of *C. glabrata* with *Nakaseomyces*, there is strong phylogenomic support and a virtual certainty that the species will be ultimately reassigned to a particular genus; in other cases, phylogenomic analyses and further taxonomic consensus will be required.

354

355 **Reference Highlights (COPY EDITOR: Thanks for incorporating these per journal style.)**

356

357 **Wohlbach et al. 2011

358 The first comparative genomics study of xylose-fermenting yeasts revealed several common
359 genetic pathways and physiological strategies that have evolved to enable xylose fermentation.

360

361 *Salichos and Rokas 2013

362 The latest in a series of phylogenomic methodological advances catalyzed by yeast genome
363 sequences. This paper introduced the internode certainty and tree certainty indices, which
364 formally measure phylogenetic conflict.

365

366 **Hanson et al. 2014

367 Discovered and investigated an inversion-based mechanism for mating-type switching that may
368 represent the ancestral state for many yeasts, likely indicating that the use of homing
369 endonucleases co-opted from selfish elements, as in *S. cerevisiae*, is evolutionarily derived.

370

371 *Gordon et al. 2011

372 Sequenced several phylogenetically well-distributed Saccharomycetaceae to show that genes
373 adjacent to the mating-type locus are prone to loss or translocation in species with homing
374 endonuclease-based switching mechanisms.

375

376 *Baker et al. 2011

377 An excellent example of hypothesis-driven genome sequencing where two species were
378 sequenced to study the evolution of the binding site motifs of a mating-type transcription factor.

379

380 **Thompson et al. 2013

381 Landmark study that explored the evolution of aerobic fermentation across several species of
382 yeasts by examining the genetic regulatory networks governing diauxic shift, the transition from
383 the consumption of fermentable to respiratory carbon sources.

384

385 *Hagman et al. 2013

386 This physiological study of several yeasts suggested that the timing and trajectory of the
387 evolution of aerobic fermentation by the lineage leading to *S. cerevisiae* was much more
388 complex than has been assumed.

389

390 **Rozpedowska et al. 2011

391 Demonstrated that *B. bruxellensis* independently evolved aerobic fermentation in part through
392 the same molecular mechanisms as in *S. cerevisiae*, including the massive loss of a cis-acting
393 element regulating genes involved in respiration.

394

395 **Libkind et al. 2011

396 Discovered the naturally occurring species that hybridized with *S. cerevisiae* to form lager-
397 brewing yeasts (*S. pastorianus* syn. *S. carlsbergensis*). The new species was formally
398 described as *S. eubayanus* in part using genome sequence data, a first for yeasts that was also
399 recently adopted in the description of *E. aceri* [84].

400

401 *Almeida et al. 2014

Genome sequence data from over 50 strains showed that many cider and champagne yeasts are domesticated strains of *S. uvarum*, which have often acquired genes from other species of *Saccharomyces*. Wild strains of *S. uvarum* generally lacked introgressions.

*Pryszcz et al. 2014

Genome sequence data showed that several clinical isolates from the *C. parapsilosis* species complex are interspecies hybrids, extending the possible link between humans and interspecies hybridization to a clinical setting.

**Strope et al. 2015

Landmark study of 100 *S. cerevisiae* genome sequences, which includes considerable evidence of introgression and horizontal gene transfer.

*Coelho et al. 2013

Demonstrated the repeated HGT of the *FSY1* fructose symporter into multiple divergent clades of yeasts, including wine-associated lineages of *S. cerevisiae*.

*Marsit et al. 2015

Determined that the *FOT* oligopeptide transporters conferred a fitness advantage in grape musts. Along with *FSY1* [53], two of three major HGT events from other yeasts into wine-associated lineages of *S. cerevisiae* have now been shown to confer conditional fitness advantages.

**Wisecaver et al. 2014

Quantified the rate of horizontal gene transfer across various fungal lineages and showed it to be lower in the Saccharomycotina than in several clades of Pezizomycotina, the subphylum to which most filamentous ascomycetes belong.

*Liti et al. 2009

The first population genomics study in yeasts, which included a comparison of *S. cerevisiae* with its many domesticated lineages to its sister species, *S. paradoxus*, whose natural history and genetic makeup have been much less impacted by humans.

**Friedrich et al. 2015

The first yeast population genomics study outside of the *Saccharomyces* suggested that the frequency of outcrossing may be conserved across vast timescales.

**Kvitek et al. 2013

This experimental evolution study showed that loss-of-function alleles, especially in regulatory pathways, frequently evolve in constant environmental conditions. Conditional fitness experiments verified the tradeoffs under selection.

*Levy et al. 2015

Developed a highly parallelized system that tracks the evolution of cellular lineages through next-generation sequencing of DNA barcodes.

**Marcet-Houben and Gabaldón 2015

Provided the first concrete phylogenomic evidence that the WGD in the lineage leading to *S. cerevisiae* was due to an allopolyploidization event, rather than an autopolyploidization event.

451
452

Literature Cited

- 453 1. Goffeau A, Barrell BG, Bussey H, Davis RW, Dujon B, Feldmann H, Galibert F, Hoheisel
454 JD, Jacq C, Johnston M, et al.: **Life with 6000 genes**. *Science* 1996, **274**:546,563–567.
- 455 2. Jones T, Federspiel NA, Chibana H, Dungan J, Kalman S, Magee BB, Newport G,
456 Thorstenson YR, Agabian N, Magee PT, et al.: **The diploid genome sequence of**
457 ***Candida albicans***. *Proc Natl Acad Sci U S A* 2004, **101**:7329–7334.
- 458 3. Cliften P, Sudarsanam P, Desikan A, Fulton L, Fulton B, Majors J, Waterston R, Cohen
459 BA, Johnston M: **Finding functional features in *Saccharomyces* genomes by**
460 **phylogenetic footprinting**. *Science* 2003, **301**:71–76.
- 461 4. Kellis M, Patterson N, Endrizzi M, Birren B, Lander ES: **Sequencing and comparison of**
462 **yeast species to identify genes and regulatory elements**. *Nature* 2003, **423**:241–254.
- 463 5. Kellis M, Birren BW, Lander ES: **Proof and evolutionary analysis of ancient genome**
464 **duplication in the yeast *Saccharomyces cerevisiae***. *Nature* 2004, **428**:617–624.
- 465 6. Dietrich FS, Voegeli S, Brachat S, Lerch A, Gates K, Steiner S, Mohr C, Pohlmann R,
466 Luedi P, Choi S, et al.: **The *Ashbya gossypii* genome as a tool for mapping the**
467 **ancient *Saccharomyces cerevisiae* genome**. *Science* 2004, **304**:304–307.
- 468 7. Butler G, Rasmussen MD, Lin MF, Santos MA, Sakthikumar S, Munro CA, Rheinbay E,
469 Grabherr M, Forche A, Reedy JL, et al.: **Evolution of pathogenicity and sexual**
470 **reproduction in eight *Candida* genomes**. *Nature* 2009, **459**:657–662.
- 471 8. Dujon B, Sherman D, Fischer G, Durrens P, Casaregola S, Lafontaine I, De Montigny J,
472 Marck C, Neuveglise C, Talla E, et al.: **Genome evolution in yeasts**. *Nature* 2004,
473 **430**:35–44.
- 474 9. Giaever G, Chu AM, Ni L, Connelly C, Riles L, Veronneau S, Dow S, Lucau-Danila A,
475 Anderson K, Andre B, et al.: **Functional profiling of the *Saccharomyces cerevisiae***
476 **genome**. *Nature* 2002, **418**:387–391.
- 477 10. Hittinger CT, Rokas A, Carroll SB: **Parallel inactivation of multiple *GAL* pathway**
478 **genes and ecological diversification in yeasts**. *Proc Natl Acad Sci U S A* 2004,
479 **101**:14144–14149.
- 480 11. Wohlbach DJ, Kuo A, Sato TK, Potts KM, Salamov AA, Labutti KM, Sun H, Clum A,
481 Pangilinan JL, Lindquist EA, et al.: **Comparative genomics of xylose-fermenting fungi**
482 **for enhanced biofuel production**. *Proc Natl Acad Sci U S A* 2011, **108**:13212–13217.
- 483 12. Salichos L, Rokas A: **Inferring ancient divergences requires genes with strong**
484 **phylogenetic signal**. *Nature* 2013, **497**:327–31.

- 485 13. Maclsaac KD, Wang T, Gordon DB, Gifford DK, Stormo GD, Fraenkel E: **An improved**
486 **map of conserved regulatory sites for *Saccharomyces cerevisiae*.** *BMC*
487 *Bioinformatics* 2006, **7**:113.
- 488 14. Dujon B: **Yeast evolutionary genomics.** *Nat Rev Genet* 2010, **11**:512–524.
- 489 15. Lang GI, Murray AW, Botstein D: **The cost of gene expression underlies a fitness**
490 **trade-off in yeast.** *Proc Natl Acad Sci U S A* 2009, **106**:5755–5760.
- 491 16. Goddard MR, Godfray HCJ, Burt A: **Sex increases the efficacy of natural selection in**
492 **experimental yeast populations.** *Nature* 2005, **434**:636–40.
- 493 17. Gray JC, Goddard MR: **Sex enhances adaptation by unlinking beneficial from**
494 **detrimental mutations in experimental yeast populations.** *BMC Evol Biol* 2012, **12**:43.
- 495 18. Butler G, Kenny C, Fagan A, Kurischko C, Gaillardin C, Wolfe KH: **Evolution of the *MAT***
496 **locus and its *Ho* endonuclease in yeast species.** *Proc Natl Acad Sci U S A* 2004,
497 **101**:1632–1637.
- 498 19. Fabre E, Muller H, Therizols P, Lafontaine I, Dujon B, Fairhead C: **Comparative**
499 **genomics in hemiascomycete yeasts: evolution of sex, silencing, and**
500 **subtelomeres.** *Mol Biol Evol* 2005, **22**:856–73.
- 501 20. Barsoum E, Martinez P, Aström SU: ***Alpha3*, a transposable element that promotes**
502 **host sexual reproduction.** *Genes Dev* 2010, **24**:33–44.
- 503 21. Hanson SJ, Byrne KP, Wolfe KH: **Mating-type switching by chromosomal inversion**
504 **in methylotrophic yeasts suggests an origin for the three-locus *Saccharomyces***
505 ***cerevisiae* system.** *Proc Natl Acad Sci U S A* 2014, **111**:E4851–8.
- 506 22. Tsai IJ, Bensasson D, Burt A, Koufopanou V: **Population genomics of the wild yeast**
507 ***Saccharomyces paradoxus*: Quantifying the life cycle.** *Proc Natl Acad Sci U S A*
508 2008, **105**:4957–4962.
- 509 23. Gordon JL, Armisen D, Proux-Wera E, OhEigeartaigh SS, Byrne KP, Wolfe KH:
510 **Evolutionary erosion of yeast sex chromosomes by mating-type switching**
511 **accidents.** *Proc Natl Acad Sci U S A* 2011, **108**:20024–20029.
- 512 24. Pérez JC, Fordyce PM, Lohse MB, Hanson-Smith V, DeRisi JL, Johnson AD: **How**
513 **duplicate transcription regulators can diversify to govern the expression of**
514 **nonoverlapping sets of genes.** *Genes Dev* 2014, **28**:1272–7.
- 515 25. Booth LN, Tuch BB, Johnson AD: **Intercalation of a new tier of transcription**
516 **regulation into an ancient circuit.** *Nature* 2010, **468**:959–963.
- 517 26. Baker CR, Tuch BB, Johnson AD: **Extensive DNA-binding specificity divergence of a**
518 **conserved transcription regulator.** *Proc Natl Acad Sci U S A* 2011, **108**:7493–8.

- 519 27. Kurtzman CP, Fell JW, Boekhout T: *The Yeasts: A Taxonomic Study*. Elsevier Science;
520 2011.
- 521 28. Lachance M: **The Biodiversity, Ecology, and Biogeography of Ascomycetous**
522 **Yeasts**. In *The Ecological Genomics of Fungi*. Edited by Martin F. Wiley-Blackwell;
523 2014:355–370.
- 524 29. Greig D, Travisano M: **The Prisoner's Dilemma and polymorphism in yeast *SUC***
525 **genes**. *Proc Biol Sci* 2004, **271** Suppl :S25–6.
- 526 30. Thompson DA, Roy S, Chan M, Styczynsky MP, Pfiffner J, French C, Socha A, Thielke A,
527 Napolitano S, Muller P, et al.: **Evolutionary principles of modular gene regulation in**
528 **yeasts**. *Elife* 2013, **2**:e00603.
- 529 31. Hagman A, Säll T, Compagno C, Piskur J: **Yeast “make-accumulate-consume” life**
530 **strategy evolved as a multi-step process that predates the whole genome**
531 **duplication**. *PLoS One* 2013, **8**:e68734.
- 532 32. Rozpedowska E, Hellborg L, Ishchuk OP, Orhan F, Galafassi S, Merico A, Woolfit M,
533 Compagno C, Piskur J: **Parallel evolution of the make-accumulate-consume strategy**
534 **in *Saccharomyces* and *Dekkera* yeasts**. *Nat Commun* 2011, **2**:302.
- 535 33. Gojkovic Z, Knecht W, Zameitat E, Warneboldt J, Coutelis JB, Pynyaha Y, Neuveglise C,
536 Moller K, Löffler M, Piskur J: **Horizontal gene transfer promoted evolution of the**
537 **ability to propagate under anaerobic conditions in yeasts**. *Mol Genet Genomics*
538 2004, **271**:387–393.
- 539 34. Lobo FP, Gonçalves DL, Alves SL, Gerber AL, de Vasconcelos ATR, Basso LC, Franco
540 GR, Soares MA, Cadete RM, Rosa CA, et al.: **Draft Genome Sequence of the D-**
541 **Xylose-Fermenting Yeast *Spathaspora arborariae* UFMG-HM19.1A^T**. *Genome*
542 *Announc* 2014, **2**:e01163–13.
- 543 35. Jeffries TW, Grigoriev I V, Grimwood J, Laplaza JM, Aerts A, Salamov A, Schmutz J,
544 Lindquist E, Dehal P, Shapiro H, et al.: **Genome sequence of the lignocellulose-**
545 **bioconverting and xylose-fermenting yeast *Pichia stipitis***. *Nat Biotechnol* 2007,
546 **25**:319–326.
- 547 36. Kurtzman CP, Robnett CJ: **Relationships among genera of the Saccharomycotina**
548 **(Ascomycota) from multigene phylogenetic analysis of type species**. *FEMS Yeast*
549 *Res* 2013, **13**:23–33.
- 550 37. Gabaldón T, Martin T, Marcet-Houben M, Durrens P, Bolotin-Fukuhara M, Lespinet O,
551 Arnaise S, Boissard S, Aguilera G, Atanasova R, et al.: **Comparative genomics of**
552 **emerging pathogens in the *Candida glabrata* clade**. *BMC Genomics* 2013, **14**:623.
- 553 38. Hittinger CT, Gonçalves P, Sampaio JP, Dover J, Johnston M, Rokas A: **Remarkably**
554 **ancient balanced polymorphisms in a multi-locus gene network**. *Nature* 2010,
555 **464**:54–8.

- 556 39. Slot JC, Rokas A: **Multiple *GAL* pathway gene clusters evolved independently and**
557 **by different mechanisms in fungi.** *Proc Natl Acad Sci U S A* 2010, **107**:10136–10141.
- 558 40. Ramezani-Rad M, Hollenberg CP, Lauber J, Wedler H, Griess E, Wagner C, Albermann
559 K, Hani J, Piontek M, Dahlems U, et al.: **The *Hansenula polymorpha* (strain CBS4732)**
560 **genome sequencing and analysis.** *FEMS Yeast Res* 2003, **4**:207–15.
- 561 41. Libkind D, Hittinger CT, Valerio E, Goncalves C, Dover J, Johnston M, Goncalves P,
562 Sampaio JP: **Microbe domestication and the identification of the wild genetic stock**
563 **of lager-brewing yeast.** *Proc Natl Acad Sci U S A* 2011, **108**:14539–14544.
- 564 42. Nakao Y, Kanamori T, Itoh T, Kodama Y, Rainieri S, Nakamura N, Shimonaga T, Hattori
565 M, Ashikari T: **Genome sequence of the lager brewing yeast, an interspecies hybrid.**
566 *DNA Res* 2009, **16**:115–129.
- 567 43. Peris D, Lopes CA, Belloch C, Querol A, Barrio E: **Comparative genomics among**
568 ***Saccharomyces cerevisiae* x *Saccharomyces kudriavzevii* natural hybrid strains**
569 **isolated from wine and beer reveals different origins.** *BMC Genomics* 2012, **13**:407.
- 570 44. Almeida P, Goncalves C, Teixeira S, Libkind D, Bontrager M, Albertin W, Durrens P,
571 Sherman D, Marullo P, Masneuf-pomare I, et al.: **A Gondwanan imprint on global**
572 **diversity and domestication of wine and cider yeast *Saccharomyces uvarum*.** *Nat*
573 *Commun* 2014, **5**:4044.
- 574 45. Gordon JL, Wolfe KH: **Recent allopolyploid origin of *Zygosaccharomyces rouxii***
575 **strain ATCC 42981.** *Yeast* 2008, **25**:449–56.
- 576 46. Mira NP, Münsterkötter M, Dias-Valada F, Santos J, Palma M, Roque FC, Guerreiro JF,
577 Rodrigues F, Sousa MJ, Leão C, et al.: **The genome sequence of the highly acetic**
578 **acid-tolerant *Zygosaccharomyces bailii*-derived interspecies hybrid strain ISA1307,**
579 **isolated from a sparkling wine plant.** *DNA Res* 2014, **21**:299–313.
- 580 47. Louis VL, Despons L, Friedrich A, Martin T, Durrens P, Casarégola S, Neuvéglise C,
581 Fairhead C, Marck C, Cruz JA, et al.: ***Pichia sorbitophila*, an Interspecies Yeast**
582 **Hybrid, Reveals Early Steps of Genome Resolution After Polyploidization.** *G3*
583 *(Bethesda)* 2012, **2**:299–311.
- 584 48. Curtin CD, Borneman AR, Chambers PJ, Pretorius IS: **De-Novo Assembly and**
585 **Analysis of the Heterozygous Triploid Genome of the Wine Spoilage Yeast *Dekkera***
586 ***bruxellensis* AWRI1499.** *PLoS One* 2012, **7**:e33840.
- 587 49. Pryszcz LP, Németh T, Gácsér A, Gabaldón T: **Genome comparison of *Candida***
588 ***orthopsilosis* clinical strains reveals the existence of hybrids between two distinct**
589 **subspecies.** *Genome Biol Evol* 2014, **6**:1069–78.
- 590 50. Dunn B, Richter C, Kvitek DJ, Pugh T, Sherlock G: **Analysis of the *Saccharomyces***
591 ***cerevisiae* pan-genome reveals a pool of copy number variants distributed in**
592 **diverse yeast strains from differing industrial environments.** *Genome Res* 2012,
593 **22**:908–924.

- 594 51. Strobe PK, Skelly DA, Kozmin SG, Mahadevan G, Stone EA, Magwene PM, Dietrich FS,
595 McCusker JH: **The 100-genomes strains, an *S. cerevisiae* resource that illuminates
596 its natural phenotypic and genotypic variation and emergence as an opportunistic
597 pathogen.** *Genome Res* 2015, **25**:762–74.
- 598 52. Novo M, Bigey F, Beyne E, Galeote V, Gavory F, Mallet S, Cambon B, Legras JL,
599 Wincker P, Casaregola S, et al.: **Eukaryote-to-eukaryote gene transfer events
600 revealed by the genome sequence of the wine yeast *Saccharomyces cerevisiae*
601 EC1118.** *Proc Natl Acad Sci U S A* 2009, **106**:16333–16338.
- 602 53. Coelho MA, Gonçalves C, Sampaio JP, Gonçalves P: **Extensive intra-kingdom
603 horizontal gene transfer converging on a fungal fructose transporter gene.** *PLoS
604 Genet* 2013, **9**:e1003587.
- 605 54. Marsit S, Mena A, Bigey F, Sauvage F-X, Couloux A, Guy J, Legras J-L, Barrio E, Dequin
606 S, Galeote V: **Evolutionary advantage conferred by an eukaryote-to-eukaryote gene
607 transfer event in wine yeasts.** *Mol Biol Evol* 2015, **32**:1695–707.
- 608 55. Fitzpatrick DA: **Horizontal gene transfer in fungi.** *FEMS Microbiol Lett* 2012, **329**:1–8.
- 609 56. Wu B, Buljic A, Hao W: **Extensive Horizontal Transfer and Homologous
610 Recombination Generate Highly Chimeric Mitochondrial Genomes in Yeast.** *Mol Biol
611 Evol* 2015, doi:10.1093/molbev/msv127.
- 612 57. Wisecaver JH, Slot JC, Rokas A: **The evolution of fungal metabolic pathways.** *PLoS
613 Genet* 2014, **10**:e1004816.
- 614 58. Bruto M, Prigent-Combaret C, Luis P, Moënne-Loccoz Y, Muller D: **Frequent,
615 independent transfers of a catabolic gene from bacteria to contrasted filamentous
616 eukaryotes.** *Proc Biol Sci* 2014, **281**:20140848.
- 617 59. Wisecaver JH, Rokas A: **Fungal metabolic gene clusters-caravans traveling across
618 genomes and environments.** *Front Microbiol* 2015, **6**:161.
- 619 60. Soanes D, Richards TA: **Horizontal gene transfer in eukaryotic plant pathogens.**
620 *Annu Rev Phytopathol* 2014, **52**:583–614.
- 621 61. Moriguchi K, Yamamoto S, Tanaka K, Kurata N, Suzuki K: **Trans-kingdom horizontal
622 DNA transfer from bacteria to yeast is highly plastic due to natural polymorphisms
623 in auxiliary nonessential recipient genes.** *PLoS One* 2013, **8**:e74590.
- 624 62. Liti G, Carter DM, Moses AM, Warringer J, Parts L, James SA, Davey RP, Roberts IN,
625 Burt A, Koufopanou V, et al.: **Population genomics of domestic and wild yeasts.**
626 *Nature* 2009, **458**:337–341.
- 627 63. Lawrie DS, Petrov DA: **Comparative population genomics: power and principles for
628 the inference of functionality.** *Trends Genet* 2014, **30**:133–9.

- 629 64. Friedrich A, Jung P, Reisser C, Fischer G, Schacherer J: **Population genomics reveals**
630 **chromosome-scale heterogeneous evolution in a protoploid yeast.** *Mol Biol Evol*
631 2015, **32**:184–92.
- 632 65. New AM, Cerulus B, Govers SK, Perez-Samper G, Zhu B, Boogmans S, Xavier JB,
633 Verstrepen KJ: **Different Levels of Catabolite Repression Optimize Growth in Stable**
634 **and Variable Environments.** *PLoS Biol* 2014, **12**:e1001764.
- 635 66. Selmecki AM, Maruvka YE, Richmond PA, Guillet M, Shores N, Sorenson AL, De S,
636 Kishony R, Michor F, Dowell R, et al.: **Polyploidy can drive rapid adaptation in yeast.**
637 *Nature* 2015, **519**:349–52.
- 638 67. Kvitek DJ, Sherlock G: **Whole genome, whole population sequencing reveals that**
639 **loss of signaling networks is the major adaptive strategy in a constant**
640 **environment.** *PLoS Genet* 2013, **9**:e1003972.
- 641 68. Lang GI, Rice DP, Hickman MJ, Sodergren E, Weinstock GM, Botstein D, Desai MM:
642 **Pervasive genetic hitchhiking and clonal interference in forty evolving yeast**
643 **populations.** *Nature* 2013, **500**:571–4.
- 644 69. Levy SF, Blundell JR, Venkataram S, Petrov DA, Fisher DS, Sherlock G: **Quantitative**
645 **evolutionary dynamics using high-resolution lineage tracking.** *Nature* 2015,
646 **519**:181–6.
- 647 70. Ford CB, Funt JM, Abbey D, Issi L, Guiducci C, Martinez DA, Delorey T, Li BY, White TC,
648 Cuomo C, et al.: **The evolution of drug resistance in clinical isolates of *Candida***
649 ***albicans*.** *Elife* 2015, **4**:e00662.
- 650 71. Hirakawa MP, Martinez DA, Sakthikumar S, Anderson MZ, Berlin A, Gujja S, Zeng Q,
651 Zisson E, Wang JM, Greenberg JM, et al.: **Genetic and phenotypic intra-species**
652 **variation in *Candida albicans*.** *Genome Res* 2015, **25**:413–25.
- 653 72. Stern DL, Orgogozo V: **The loci of evolution: how predictable is genetic evolution?.**
654 *Evolution (N Y)* 2008, **62**:2155–2177.
- 655 73. Marcet-Houben M, Gabaldón T: **Beyond the whole genome duplication: phylogenetic**
656 **evidence for an ancient inter-species hybridization in the baker's yeast lineage.**
657 *PLoS Biol* 2015, **13**:e1002220.
- 658 74. Wolfe KH, Shields DC: **Molecular evidence for an ancient duplication of the entire**
659 **yeast genome.** *Nature* 1997, **387**:708–713.
- 660 75. Conant GC, Wolfe KH: **Turning a hobby into a job: how duplicated genes find new**
661 **functions.** *Nat Rev Genet* 2008, **9**:938–50.
- 662 76. Soltis DE, Bell CD, Kim S, Soltis PS: **Origin and early evolution of angiosperms.** *Ann*
663 *N Y Acad Sci* 2008, **1133**:3–25.

- 664 77. Scannell DR, Zill OA, Rokas A, Payen C, Dunham MJ, Eisen MB, Rine J, Johnston M,
665 Hittinger CT: **The awesome power of yeast evolutionary genetics: new genome**
666 **sequences and strain resources for the *Saccharomyces sensu stricto* genus.** *G3*
667 *Genes Genomes Genet* 2011, **1**:11–25.
- 668 78. Liti G, Nguyen Ba AN, Blythe M, Müller CA, Bergström A, Cubillos FA, Dafnis-Calas F,
669 Khoshraftar S, Malla S, Mehta N, et al.: **High quality de novo sequencing and**
670 **assembly of the *Saccharomyces arboricolus* genome.** *BMC Genomics* 2013, **14**:69.
- 671 79. Baker E, Wang B, Bellora N, Peris D, Hulfachor AB, Koshalek JA, Adams M, Libkind D,
672 Hittinger CT: **The genome sequence of *Saccharomyces eubayanus* and the**
673 **domestication of lager-brewing yeasts.** *Mol Biol Evol* 2015, **32**:2818–31.
- 674 80. Scannell DR, Frank AC, Conant GC, Byrne KP, Woolfit M, Wolfe KH: **Independent**
675 **sorting-out of thousands of duplicated gene pairs in two yeast species descended**
676 **from a whole-genome duplication.** *Proc Natl Acad Sci U S A* 2007, **104**:8397–8402.
- 677 81. Souciet JL, Dujon B, Gaillardin C, Johnston M, Baret P V, Cliften P, Sherman DJ,
678 Weissenbach J, Westhof E, Wincker P, et al.: **Comparative genomics of protoploid**
679 ***Saccharomycetaceae*.** *Genome Res* 2009, **19**:1696–1709.
- 680 82. Galeote V, Bigey F, Devillers H, Neuvéglise C, Dequin S: **Genome Sequence of the**
681 **Food Spoilage Yeast *Zygosaccharomyces bailii* CLIB 213^T.** *Genome Announc* 2013,
682 **1**:e00606–13.
- 683 83. Sarilar V, Devillers H, Freel KC, Schacherer J, Neuvéglise C: **Draft Genome Sequence**
684 **of *Lachancea lanzarotensis* CBS 12615^T, an Ascomycetous Yeast Isolated from**
685 **Grapes.** *Genome Announc* 2015, **3**:e00292–15.
- 686 84. Dietrich FS, Voegeli S, Kuo S, Philippsen P: **Genomes of *Ashbya* fungi isolated from**
687 **insects reveal four mating-type loci, numerous translocations, lack of transposons,**
688 **and distinct gene duplications.** *G3 (Bethesda)* 2013, **3**:1225–39.
- 689 85. Wendland J, Walther A: **Genome evolution in the *Eremothecium* clade of the**
690 ***Saccharomyces* complex revealed by comparative genomics.** *G3 (Bethesda)* 2011,
691 **1**:539–48.
- 692 86. Wendland J, Walther A: **Chromosome number reduction in *Eremothecium coryli* by**
693 **two telomere-to-telomere fusions.** *Genome Biol Evol* 2014, **6**:1186–98.
- 694 87. Lertwattanasakul N, Kosaka T, Hosoyama A, Suzuki Y, Rodrussamee N, Matsutani M,
695 Murata M, Fujimoto N, Suprayogi, Tsuchikane K, et al.: **Genetic basis of the highly**
696 **efficient yeast *Kluyveromyces marxianus*: complete genome sequence and**
697 **transcriptome analyses.** *Biotechnol Biofuels* 2015, **8**:47.
- 698 88. Giorello FM, Berná L, Greif G, Camesasca L, Salzman V, Medina K, Robello C, Gaggero
699 C, Aguilar PS, Carrau F: **Genome Sequence of the Native Apiculate Wine Yeast**
700 ***Hanseniaspora vineae* T02/19AF.** *Genome Announc* 2014, **2**:e00530–14.

- 701 89. Freel KC, Sarilar V, Neuvéglise C, Devillers H, Friedrich A, Schacherer J: **Genome**
702 **Sequence of the Yeast *Cyberlindnera fabianii* (*Hansenula fabianii*)**. *Genome*
703 *Announc* 2014, **2**:e00638–14.
- 704 90. Tomita Y, Ikeo K, Tamakawa H, Gojobori T, Ikushima S: **Genome and transcriptome**
705 **analysis of the food-yeast *Candida utilis***. *PLoS One* 2012, **7**:e37226.
- 706 91. Schneider J, Rupp O, Trost E, Jaenicke S, Passoth V, Goesmann A, Tauch A, Brinkrolf
707 K: **Genome sequence of *Wickerhamomyces anomalus* DSM 6766 reveals genetic**
708 **basis of biotechnologically important antimicrobial activities**. *FEMS Yeast Res*
709 2012, **12**:382–6.
- 710 92. Schneider J, Andrea H, Blom J, Jaenicke S, Rückert C, Schorsch C, Szczepanowski R,
711 Farwick M, Goesmann A, Pühler A, et al.: **Draft genome sequence of**
712 ***Wickerhamomyces ciferrii* NRRL Y-1031 F-60-10**. *Eukaryot Cell* 2012, **11**:1582–3.
- 713 93. De Schutter K, Lin Y-C, Tiels P, Van Hecke A, Glinka S, Weber-Lehmann J, Rouzé P,
714 Van de Peer Y, Callewaert N: **Genome sequence of the recombinant protein**
715 **production host *Pichia pastoris***. *Nat Biotechnol* 2009, **27**:561–6.
- 716 94. Liu X, Kaas RS, Jensen PR, Workman M: **Draft genome sequence of the yeast**
717 ***Pachysolen tannophilus* CBS 4044/NRRL Y-2460**. *Eukaryot Cell* 2012, **11**:827.
- 718 95. Morales L, Noel B, Porcel B, Marcet-Houben M, Hullo M-F, Sacerdot C, Tekaia F, Leh-
719 Louis V, Despons L, Khanna V, et al.: **Complete DNA sequence of *Kuraishia***
720 ***capsulata* illustrates novel genomic features among budding yeasts**
721 **(*Saccharomycotina*)**. *Genome Biol Evol* 2013, **5**:2524–39.
- 722 96. Piškur J, Ling Z, Marcet-Houben M, Ishchuk OP, Aerts A, LaButti K, Copeland A,
723 Lindquist E, Barry K, Compagno C, et al.: **The genome of wine yeast *Dekkera***
724 ***bruxellensis* provides a tool to explore its food-related properties**. *Int J Food*
725 *Microbiol* 2012, **157**:202–9.
- 726 97. Chan GF, Gan HM, Ling HL, Rashid NAA: **Genome sequence of *Pichia kudriavzevii***
727 **M12, a potential producer of bioethanol and phytase**. *Eukaryot Cell* 2012, **11**:1300–1.
- 728 98. Riccombeni A, Vidanes G, Proux-Wéra E, Wolfe KH, Butler G: **Sequence and Analysis**
729 **of the Genome of the Pathogenic Yeast *Candida orthopsilosis***. *PLoS One* 2012,
730 **7**:e35750.
- 731 99. Kim J-S, Baek J-H, Park N-H, Kim C: **Complete Genome Sequence of Halophilic**
732 **Yeast *Meyerozyma caribbica* MG20W Isolated from Rhizosphere Soil**. *Genome*
733 *Announc* 2015, **3**:e00127–15.
- 734 100. Chatterjee S, Alampalli SV, Nageshan RK, Chettiar ST, Joshi S, Tatu US: **Draft genome**
735 **of a commonly misdiagnosed multidrug resistant pathogen *Candida auris***. *BMC*
736 *Genomics* 2015, **16**:686.

101. HersHKovitz V, Sela N, Taha-Salaime L, Liu J, Rafael G, Kessler C, Aly R, Levy M, Wisniewski M, Droby S: **De-novo assembly and characterization of the transcriptome of *Metschnikowia fructicola* reveals differences in gene expression following interaction with *Penicillium digitatum* and grapefruit peel.** *BMC Genomics* 2013, **14**:168.
102. Kunze G, Gaillardin C, Czernicka M, Durrens P, Martin T, Böer E, Gabaldón T, Cruz JA, Talla E, Marck C, et al.: **The complete genome of *Blastobotrys (Arxula) adenivorans* LS3 - a yeast of biotechnological interest.** *Biotechnol Biofuels* 2014, **7**:66.
103. Polev DE, Bobrov KS, Eneyskaya E V, Kulminskaya AA: **Draft Genome Sequence of *Geotrichum candidum* Strain 3C.** *Genome Announc* 2014, **2**:e00956–14.
104. Vega-Alvarado L, Gómez-Angulo J, Escalante-García Z, Grande R, Gschaedler-Mathis A, Amaya-Delgado L, Sanchez-Flores A, Arrizon J: **High-Quality Draft Genome Sequence of *Candida apicola* NRRL Y-50540.** *Genome Announc* 2015, **3**:e00437–15.
105. Matsuzawa T, Koike H, Saika A, Fukuoka T, Sato S, Habe H, Kitamoto D, Morita T: **Draft Genome Sequence of the Yeast *Starmerella bombicola* NBRC10243, a Producer of Sophorolipids, Glycolipid Biosurfactants.** *Genome Announc* 2015, **3**:e00176–15.

Figure 1

Figure 2