Yeast Diversity in Human Welfare

Tulasi Satyanarayana · Gotthard Kunze
Editors

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Editors
Tulasi Satyanarayana
Division of Biological Sciences and Engineering
Netaji Subhas Institute of Technology
Dwarka, Delhi
India

Gotthard Kunze
Yeast Genetics, Department of Physiology and Cell Biology
Leibniz Institute of Plant Genetics and Crop Plant Research
Gatersleben, Sachsen-Anhalt
Germany

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Preface

Yeasts are eukaryotic microbes placed in the kingdom Fungi, under the phyla Ascomycota and Basidiomycota with approximately 2000 species described till date. These are estimated to constitute 1–1.5% of the fungal species described, and the number of existing yeast species is expected to exceed that of the described ones. In case yeasts make up 1–1.5% of the estimated fungal species extant on Earth of three million species, the yeast species would be between 30,000 and 45,000. Extensive efforts are needed to understand the diversity of yet to be cultured yeast species. Yeasts are mostly unicellular, although some species develop multicellular characteristics by forming pseudohyphae. Most yeasts reproduce asexually by mitosis, and many do so by the asymmetric division process called budding and a few by fission.

By fermentation, the yeast species *Saccharomyces cerevisiae* and others have been converting carbohydrates to carbon dioxide and alcohols for thousands of years, and carbon dioxide has been used in baking and the alcohol in alcoholic beverages. It is also a centrally important model organism in modern cell biology research, and is one of the most thoroughly investigated eukaryotic microbes. Researchers have used it to gather information about the biology of the eukaryotic cell and ultimately human biology. Other species of yeasts like *Candida albicans* are opportunistic pathogens and known to cause infections to humans. Yeasts have recently been used to generate electricity in microbial fuel cells, and to produce ethanol for the biofuel industry.

Certain strains of some yeast species produce proteins called yeast killer toxins, which allow them to eliminate competing strains. This may cause problems for wine making, but could potentially be used to advantage by using killer toxin-producing strains to make wine. Yeast killer toxins may find medical applications in the treatment of yeast infections.

Yeasts occur in the environment, and particularly in sugar-rich materials. For instance, naturally occurring yeasts are found on the skins of fruits and berries and plant exudates. Some yeasts are also found in association with soil and insects. The ecological function and biodiversity of yeasts have not yet been adequately understood. Yeasts are also present in the gut flora of mammals and some insects.

Even deep-sea environments also host some yeasts. An Indian investigation on 7 bee species and 9 plant species found 45 yeast species belonging to 16 genera to colonize the nectaries of flowers and honey stomachs of bees. Most were members of the genus *Candida*; the most common species in honey was *Dekkera intermedia* and in flower nectaries, *Candida blankii*. Yeast-colonizing nectaries of the stinking hellebore have been found to raise the temperature of the flower, which may aid in attracting pollinators by increasing the evaporation of volatile organic compounds. Black yeast has been observed as a partner in a complex relationship between ants, their mutualistic fungus, a fungal parasite of the fungus and a bacterium that kills the parasite. The yeast has a negative effect on the bacteria that normally produce antibiotics to kill the parasite, so may affect the ants' health by allowing the parasite to spread.

Some species of yeasts are opportunistic pathogens, which can cause infection in people with compromised immune systems. *Cryptococcus neoformans* and *Cryptococcus gattii* are significant pathogens of immuno-compromised individuals. They are the species primarily responsible for cryptococcosis, a fungal disease that occurs in about one million HIV/AIDS patients, causing over 600,000 deaths annually. Yeasts of the genus *Candida* cause oral and vaginal infections in humans called candidiasis. The pathogenic yeasts of candidiasis in probable descending order of virulence for humans are: *C. albicans*, *C. tropicalis*, *C. stellatoidea*, *C. glabrata*, *C. krusei*, *C. parapsilosis*, *C. guilliermondii*, *C. viswanathii*, *C. lusitaniae*, and *Rhodotorula mucilaginosa*. *Candida glabrata* is the second most common pathogenic yeast after *C. albicans*, causing infections of the urogenital tract, and of the bloodstream (candidemia).

The useful physiological properties of yeast have led to their use in the field of biotechnology. Fermentation of sugars by yeast is the oldest and largest application of this technology. Many types of yeasts are used for making many foods: baker's yeast in bread production, brewer's yeast in beer fermentation, and yeast in wine fermentation and the production of xylitol.

Some yeasts can find potential application in the field of bioremediation. One such yeast, *Yarrowia lipolytica*, is known to degrade palm oil mill effluent, TNT (an explosive material), and other hydrocarbons such as alkanes, fatty acids, fats, and oils. It can also tolerate high concentrations of salt and heavy metals, and is being investigated for its potential as a heavy metal biosorbent. *Saccharomyces cerevisiae* has potential to bioremediate toxic pollutants like arsenic from the industrial effluents. Bronze statues are known to be degraded by certain species of yeast. Different yeasts from Brazilian gold mines accumulate free and complexed silver ions.

Yeast is used in nutritional supplements popular with health-conscious individuals and those following vegetarian diets. It is often referred to as "nutritional yeast" when sold as a dietary supplement. Nutritional yeast is deactivated yeast, usually *S. cerevisiae*. It is an excellent source of protein and vitamins, especially B-complex vitamins as well as other minerals and cofactors required for growth. It is also naturally low in fat and sodium. Some brands of nutritional yeast, though not all, are fortified with vitamin B_{12}, which is produced separately by bacteria.

In 1920, the Fleischmann Yeast Company began promoting yeast cakes in a successful "Yeast for Health" campaign. They initially emphasized the importance of yeast as a source of vitamins, good for skin and digestion. Their advertising later claimed a much broader range of health benefits. Nutritional yeast has a nutty, cheesy flavor that makes it popular as an ingredient in cheese substitutes. It is often used by vegetarians in the place of Parmesan cheese. Another popular use is as a topping for popcorn. It can also be used in mashed and fried potatoes, as well as in scrambled eggs. It comes in the form of flakes or as a yellow powder similar in texture to cornmeal. In Australia, it is sometimes sold as "savory yeast flakes." Though "nutritional yeast" usually refers to commercial products, inadequately fed prisoners have used "home-grown" yeast to prevent vitamin deficiency.

Some probiotic supplements use the yeast *Saccharomyces boulardii* for maintaining and restoring the natural flora in the gastrointestinal tract. *S. boulardii* has been shown to reduce the symptoms of acute diarrhea, reduce the chance of infection by *Clostridium difficile*, reduce bowel movements in diarrhea patients, and reduce the incidence of antibiotic-, traveler's-, and HIV/AIDS-associated diarrheas.

Yeasts are able to grow in foods with a low pH (5.0 or lower) and in the presence of sugars, organic acids, and other easily metabolized carbon sources. During their growth, yeasts metabolize some food components and produce metabolic end products. This causes the physical, chemical, and sensible properties of a food to change, and the food is spoiled. The growth of yeast within food products is often seen on their surfaces, as in cheeses or meats, or by the fermentation of sugars in beverages, such as juices, and semi-liquid products, such as syrups and jams. The yeast of the genus *Zygosaccharomyces* has had a long history as spoilage yeasts within the food industry. This is mainly because these species can grow in the presence of high sucrose, ethanol, acetic acid, sorbic acid, benzoic acid, and sulphur dioxide, representing some of the commonly used food preservation methods. The major spoilage yeast in enology is *Brettanomyces bruxellensis*.

Several yeasts, in particular *S. cerevisiae*, have been widely used in genetics and cell biology, largely because this is a simple eukaryotic cell, serving as a model for all eukaryotes including humans, for studying fundamental cellular processes such as the cell cycle, DNA replication, recombination, cell division, and metabolism. Yeasts are easily manipulated and cultured in the laboratory, which has allowed the development of powerful standard techniques, such as yeast two-hybrid, synthetic genetic array analysis, and tetrad analysis. Many proteins important in human biology were first discovered by studying their homologues in yeast, which include cell cycle proteins, signaling proteins and protein-processing enzymes.

Saccharomyces cerevisiae was announced to be the first eukaryote to have its genome on April 24, 1996, comprising 12 million base pairs, fully sequenced as part of the Genome Project. At that time, this was the most complex organism to have its full genome sequenced at that time, and took 7 years with the efforts of more than 100 laboratories. The second yeast species to have its genome sequenced was *Schizosaccharomyces pombe*, which was completed in 2002. It was the sixth eukaryotic genome sequenced that comprised 13.8 million base pairs. By 2012, over 30 yeast species have had their genomes sequenced and published. A total of

approximately 24,200 novel genes were identified, the translation products of which were classified together with *S. cerevisiae* proteins into about 4700 families, forming the basis for interspecific comparisons. The analysis of chromosome maps and genome redundancies revealed that the different yeast lineages have evolved through a marked interplay between several distinct molecular mechanisms, including tandem gene repeat formation, segmental duplication, a massive genome duplication, and extensive gene loss.

Yeast species have been genetically engineered to efficiently produce various drugs by a technique called metabolic engineering. *S. cerevisiae* is easy to genetically engineer; its physiology, metabolism, and genetics are well known, and it is amenable for use in harsh industrial conditions. A wide variety of chemicals in different classes can be produced by engineered yeast, including phenolics, isoprenoids, alkaloids, and polyketides. About 20 biopharmaceuticals are produced in *S. cerevisiae*, including insulin, vaccines for hepatitis, and human serum albumin.

The advances in modeling and synthetic biology tools and how these tools can speed up the development of yeast cell factories have been recently made. Metabolic engineering strategies for developing yeast strains for the production of polymer monomers: lactic, succinic, and cis, cis-muconic acids have been attempted. *S. cerevisiae* has already firmly established itself as a cell factory in industrial biotechnology and the advances in yeast strain engineering will stimulate the development of novel yeast-based processes for production of chemicals in the near future. Strategies are being developed for metabolic engineering of ethanologenic yeasts for the production of bioethanol from complex lignocellulosic residues. Recent examples of yeast metabolic engineering have shown that evolutionary potential of cells should not be underestimated in strain improvement. Evolutionarily evolved strains can form suitable starting points for inverse metabolic engineering approaches too. For developing an understanding of the cell as a whole, sophisticated computational methods capable of integrating copious amounts of data/information are required.

This book is an attempt in bringing together the scattered information on various aspects of the utility of yeast diversity for human welfare into one volume. This includes recent developments made in the past few decades on these aspects. The chapters have been written by experts, who have done a commendable job of reviewing the developments made in recent years. We wish to thank all the contributors. The views expressed by authors are their own. We sincerely hope and wish that the book will be useful for teachers, scientists, researchers and students of biology, microbiology, mycology, and biotechnology.

We wish to appreciate and thank the efforts made by Springer in publishing the book for disseminating knowledge on the utility of yeast diversity for human welfare.

New Delhi, India — Prof. Tulasi Satyanarayana
Gatersleben, Germany — Prof. Gotthard Kunze

Contents

Editors and Contributors

About the Editors

Tulasi Satyanarayana after obtaining M.Sc. and Ph.D. at the University of Saugar (India), Tulasi Satyanarayana had postdoctoral stints at the Paul Sabatier University and National Institute of Applied Sciences, Toulouse, France. In 1988, he joined the Department of Microbiology, University of Delhi South Campus as Associate Professor and became Professor in 1998. His research efforts have been focused on understanding the diversity of yeasts, and thermophilic fungi and bacteria, their enzymes and potential applications, heterotrophic carbon sequestration and metagenomics. He has published over 250 scientific papers and reviews and edited six books. He has two Indian patents to his credit. He has been conferred with Dr. G.B. Manjrekar award of the Association of Microbiologists of India in 2004, Dr. V.S. Agnihotrudu award of Mycological Society of India in 2009 and Malaviya award of Biotech Research Society of India in 2012 for his distinguished contributions.

Gotthard Kunze studied biology at the Ernst Moritz Arndt University in Greifswald. He got a postdoctoral fellowship and a position as scientific assistant at the Department of Biology of the University. In 1986 he joined as a research associate at the Institute of Plant Genetics and Crop Plant Research (IPK), Gatersleben. Since 1998, he has been a Visiting Professor at the University of Greifswald and Professor at the Technical University Anhalt at Köthen since 1998. During this period, he focused his research activities on yeast genetics (construction of new yeast host vector systems, heterologous gene expression, thermo- and osmo-resistance in nonconventional yeasts and microbial yeast biosensors). Professor Gotthard Kunze is the author of about 182 publications, editor of two books, and teaches at the universities of Greifswald and Köthen.

Contributors

Adivitiya Department of Microbiology, University of Delhi South Campus, New Delhi, India

Bijender Kumar Bajaj School of Biotechnology, University of Jammu, Jammu, India

Tek Chand Bhalla Department of Biotechnology, Himachal Pradesh University, Shimla, Himachal Pradesh, India

Felix Bischoff Leibniz Institute of Plant Genetics and Crop Plant Research (IPK), Gatersleben, Germany

Bruno Blondin SPO, INRA, SupAgro, Université Montpellier, Montpellier, France

Erik Böer Leibniz Institute of Plant Genetics and Crop Plant Research (IPK), Gatersleben, Germany

Carole Camarasa SPO, INRA, SupAgro, Université Montpellier, Montpellier, France

Alexandre Chamas Leibniz Institute of Plant Genetics and Crop Plant Research (IPK), Gatersleben, Germany

V. Choudhary Department of Microbiology, Institute of Home Economics, University of Delhi, New Delhi, India

Preeti Dabas School of Biotechnology, G.G.S. Indraprastha University, Dwarka, Delhi, India

Vikas Kumar Dagar Department of Microbiology, University of Delhi South Campus, New Delhi, India

Sylvie Dequin SPO, INRA, SupAgro, Université Montpellier, Montpellier, France

Mukund V. Deshpande Biochemical Sciences Division, National Chemical Laboratory, Pune, India

Kostyantyn Dmytruk Institute of Cell Biology, NAS of Ukraine, Lviv, Ukraine

Sonali Kashinath Doke School of Pharmacy, SRTM University, Nanded, Maharashtra, India

Virginie Galeote SPO, INRA, SupAgro, Université Montpellier, Montpellier, France

Loughlin Gethins School of Microbiology, University College Cork, Cork, Ireland; Teagasc Research Centre, Fermoy, Co. Cork, Ireland

Vandana Ghormade Nanobioscience Group, Agharkar Research Institute, Pune, India

Shivkrupa Devrao Halbandge DST-FIST & UGC-SAP Sponsored School of Life Sciences, SRTM University NAAC Accredited with 'A' Grade, Nanded, Maharashtra, India

Olena Ishchuk Department of Biology, Lund University, Lund, Sweden

Kumaraswamy Jeyaram Microbial Resources Division, Institute of Bioresources and Sustainable Development (IBSD), Imphal, Manipur, India

Swati Joshi National Institute of Occupational Health (NIOH), Ahmedabad, Gujarat, India

Sankunny Mohan Karuppayil DST-FIST and UGC-SAP Sponsored School of Life Sciences, SRTM University (NAAC Acredited with a Grade), Nanded, Maharashtra, India

Yogender Pal Khasa Department of Microbiology, University of Delhi South Campus, New Delhi, India

Deepak Kumar School of Biotechnology, G.G.S. Indraprastha University, Dwarka, Delhi, India

Gotthard Kunze Leibniz Institute of Plant Genetics and Crop Plant Research (IPK), Gatersleben, Germany

Olena Kurylenko Institute of Cell Biology, NAS of Ukraine, Lviv, Ukraine

Jean-Luc Legras SPO, INRA, SupAgro, Université Montpellier, Montpellier, France

Ina Lemke Leibniz Institute of Plant Genetics and Crop Plant Research (IPK), Gatersleben, Germany

Katarzyna Litwińska Leibniz Institute of Plant Genetics and Crop Plant Research (IPK), Gatersleben, Germany

A. Madan Department of Microbiology, Institute of Home Economics, University of Delhi, New Delhi, India

Sarika S. Mane Biochemical Sciences Division, National Chemical Laboratory, Pune, India

Falko Matthes Leibniz Institute of Plant Genetics and Crop Plant Research (IPK), Gatersleben, Germany

John P. Morrissey School of Microbiology, University College Cork, Cork, Ireland

Volkmar Passoth Department of Molecular Sciences, Swedish University of Agricultural Sciences, Uppsala, Sweden

Reinhard Pätz Bioprocess Technology, University of Applied Sciences, Köthen, Germany

Amit Kumar Rai Institute of Bioresources and Sustainable Development, Sikkim Centre, Tadong, Sikkim, India

Jayant Shankar Raut UGC Center for Advanced Study, University Institute of Pharmaceutical Sciences (UIPS), Panjab University, Chandigarh, India

Jau-Henryk Richter-Listewnik Bioprocess Technology, University of Applied Sciences, Köthen, Germany

Paul Ross School of Microbiology, University College Cork, Cork, Ireland; Alimentary Pharmabiotic Centre, Microbiome Institute, University College Cork, Cork, Ireland

Justyna Ruchala Rzeszow University, Rzeszow, Poland

Tulasi Satyanarayana Division of Biological Sciences and Engineering, Netaji Subhas Institute of Technology, Dwarka, Delhi, India

Savitri Department of Biotechnology, Himachal Pradesh University, Shimla, Himachal Pradesh, India

Frieder Schauer Institute of Microbiology, Ernst-Moritz-Arndt-University of Greifswald, Greifswald, Germany

Rabea Schlüter Institute of Microbiology, Ernst-Moritz-Arndt-University of Greifswald, Greifswald, Germany

Nimisha Sharma School of Biotechnology, G.G.S. Indraprastha University, Dwarka, Delhi, India

Andriy Sibirny Institute of Cell Biology, NAS of Ukraine, Lviv, Ukraine; Rzeszow University, Rzeszow, Poland

Satbir Singh School of Biotechnology, University of Jammu, Jammu, India

Catherine Stanton Teagasc Research Centre, Fermoy, Co. Cork, Ireland; Alimentary Pharmabiotic Centre, Microbiome Institute, University College Cork, Cork, Ireland

Santosh G. Tupe Biochemical Sciences Division, National Chemical Laboratory, Pune, India

Javier A. Varela School of Microbiology, University College Cork, Cork, Ireland

Pandit B. Vidyasagar SRTM University, NAAC Accredited with 'A' Grade, Nanded, Maharashtra, India

A. Vohra Department of Microbiology, Institute of Home Economics, University of Delhi, New Delhi, India

Sebastian Worch Leibniz Institute of Plant Genetics and Crop Plant Research (IPK), Gatersleben, Germany