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REVIEW

Yeast culture collections of the world: meeting the needs of industrial researchers

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Abstract The importance of selecting optimal yeast strains for research or industrial applications is often underestimated. For example, utilizing a strain background that already provides the desired stress tolerance or nutrient utilization profile can eliminate costly strain optimization. Yeast culture collections can provide not only the yeast strains but also data and curator expertise to help narrow the search for the optimal strain. While some collections are known for a broad range of cultures and services, other "boutique" collections can provide a broader selection of strains of certain categories, a surprising amount of characterization data, and assistance in selecting strains. This article provides information on dozens of yeast collections of the world, profiles of selected yeast culture collections, and the services that they provide: e.g., strain preservation for patent or safe deposit purposes, species identification service, training workshops, and consulting on yeast identification and physiology. Utilization of these services can save industrial researchers valuable time and resources.

Keywords Culture collections · Yeast · High-throughput screening · Biofuels · Species identification · Yeast ecology · Yeast taxonomy

Abbreviations

OECD	Organisation for Economic Co-operation and Development
CBD	Convention on Biological Diversity
WDCM	World Data Centre for Microorganisms
ORF	Open Reading Frame
DNA	Deoxyribonucleic acid
BLAST	Basic Local Alignment Search Tool
GBRCN	Global Biological Resource Centre Network
EMbaRC	European Consortium of Microbial Resources Centres

All culture collection acronyms are listed in Table 1.

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Introduction

In a recent report, the Organisation for Economic Co-operation and Development stated that, "Biological resource centers are an essential part of the infrastructure underpinning life sciences and biotechnology" [16]. Few would dispute the critical role that microbial culture collections play in life science research: they are the source of "bio" in biotechnology, the "life" in life science research. Though yeasts are a relatively small group of microbes, with roughly 1,500 known species, they play a disproportionately large role in industry, pathology, and life science research, and are responsible for producing some of our favorite foods and beverages. One could argue that yeasts are the most important "employees" in the winery, brewery, and bakery. Just as the prudent employer should interview multiple candidates for a job, the prudent yeast researcher should compare multiple yeast species or strains before selecting the best one for their application. Culture collections are arguably the best place to find these candidates.

Yeasts are defined as single-celled fungi. This simple definition tells us several useful traits of these organisms: they are heterotrophic, non-motile, have a relatively simple

morphology, and often function in nature as degraders. These properties make this class of microbes particularly useful for industrial applications, due to their genetic tractability, utilization of a broad variety of feedstocks, and production of numerous valuable products. It has been suggested that the yeast *Saccharomyces cerevisiae* was one of the first domesticated organisms [18], and that humans converted from a nomadic lifestyle to an agrarian one primarily to grow grains for brewing [5]. Regardless of whether yeasts are responsible for human civilization, they clearly have enormous industrial value.

Yeasts are found among two of the seven fungal phyla, Ascomycota and Basidiomycota, comprising a rather diverse group of organisms. There are approximately 1,500 yeast species known [19]. It is estimated that <1% of species have been discovered [4]. Thus, there is enormous potential for discovery, not just of new species, but for uses of these species. Yeasts are used in basic life science research such as studies of the cell cycle, regulation of gene expression, comparative genomics, metabolomics, and much more. The genomes of over 30 yeast species have been sequenced and the sequences published. Applied uses of yeasts include fermented foods and beverages, chemicals, nutraceuticals, pharmaceuticals, biofuels, and agricultural uses such as agents for biocontrol of plant pathogens [6, 17].

These discoveries have been facilitated by utilization of cultures that were deposited in culture collections. Culture collections serve to preserve biodiversity to allow development of new technologies. Though there are countless examples, a commonly referenced instance is the use of *Thermus aquaticus* in the discovery of Taq polymerase, 20 years after it had been deposited in ATCC. Another point that must be stressed is the importance of preserving multiple strains of a species, because there is physiological and genetic diversity within microbial species. This intraspecific diversity results in differences in antibiotic resistance, sterilization temperature, and other properties with important impacts for industrial fermentations, food preservation, and pathology.

Researchers working with yeasts can either isolate them themselves from nature, obtain them from colleagues such as their thesis advisor, or request them from culture collections. Researchers would be advised to utilize culture collections when possible. Service collections, especially, have the facilities and expertise to assure proper species identification, minimize genetic drift that often occurs with repeated transfer, and assure pure and viable cultures.

Comparison of yeast culture collections

There are numerous culture collections around the world, ranging from enormous and well-known collections, to smaller, more specialized "boutique" collections. Information collected from the World Data Center for Microorganisms online database (http://wdcm.nig.ac.jp/WDCHomePage_text.html) lists microbial collections with significant yeast holdings (Table 1). Most of these collections also carry other microbial taxa including bacteria and filamentous fungi. What these collections have in common is expertise in yeast cultivation, preservation and identification, and distribution of yeasts to researchers. Collections in Table 1 are located in over two dozen countries around the globe. Also, administrative oversight varies greatly. The collections are affiliated with government agencies, universities, or are privately operated.

The collections differ in their areas of focus, which often results from a history of expertise in a certain area. Surveys were sent to selected collections to help illustrate this point. The resulting information can convey to industrial yeast researchers the available range of both yeast cultures and services. This information is summarized in Table 2.

Survey respondents stressed the importance of adhering to the Convention on Biological Diversity (CBD), or the Budapest Treaty. The goals of this convention are [9]:

1. Recognize the sovereign rights of the country of origin
2. Prior informed consent
3. Conservation of biodiversity
4. Sustainable development of genetic resources
5. Fair sharing of benefits

While 193 countries are parties to this convention, the United States is a notable exception. Use of microbes isolated after the country of origin signed this treaty is subject to these terms. Culture collections must take measures to ensure that the treaty terms are followed, which can impact industrial uses of microbes of international origin.

The number of yeast strains and the number of yeast species held in a collection correlates closely with the historical mission of each collection. The mission of some collections such as NRRL, ATCC, and CBS includes accession of type cultures of all known species, hence the inclusion of "type culture" in the abbreviation ATCC. Other collections have a narrower range of species, but greater depth within these species, due to a historical focus on particular areas of research, such as wine (DBVPG and UCD-V&E), brewing (NCYC), or ecology (UCD-FST).

A common theme among the survey respondents was a broadening of the collection holdings and activities in recent decades. This can be traced to a new generation of curators, as well as a need to capture new funding sources. For example, NCYC in the United Kingdom, which formerly focused on brewing yeasts, has a very impressive array of brewing and distilling yeasts. This collection offers contract screening for brewing fermentation properties.

Table 1 Culture collections with at least 500 strains of yeasts, in descending order of the number of publicly available strains

Acronyms	Name	Country	Number of yeast strains	Website URL
NRRL	National Center for Agricultural Utilization Research, USDA	USA	14,500[a]	http://www.ncaur.usda.gov
ATCC	American Type Culture Collection	USA	10,000[b]	http://www.atcc.org/
CBS	Centraalbureau voor Schimmelcultures	Netherlands	7,000[a]	http://www.cbs.knaw.nl
UCD-FST	Phaff Yeast Culture Collection, University of California Davis	USA	6,108	http://www.phaffcollection.org
DBVPG	Department of Applied Biology, University of Perugia	Italy	5,160[b]	http://www.agr.unipg.it/dbvpg/home.html
UWO-PS	Department of Plant Sciences, University of Western Ontario	Canada	5,000[a]	n/a
NCYC	National Collection of Yeast Cultures	UK	4,000[b]	http://www.ncyc.co.uk
OUT	Department of Biotechnology, Graduate School of Engineering, Osaka University	Japan	3,803[a]	n/a
CCY	Culture Collection of Yeasts, Institute of Chemistry, Slovak ASCR	Slovakia	3,800[a]	http://www.chem.sk/activities/yeast/ccy/
CICIM	The Culture and Information Centre of Industrial Microorganisms of China Universities, Southern Yangtze University	China	3,600[a]	CICIM-CU.sytu.edu.cn
BCCM/IHEM	Scientific Institute of Public Health—Louis Pasteur	Belgium	3,453[a]	http://www.belspo.be/bccm
JCM	Japan Collection of Microorganisms, Bioresource Center	Japan	3,375[a]	http://www.jcm.riken.jp
YM	Yunnan Institute of Microbiology, Yunnan University	China	3,154[a]	n/a
NBRC (formerly IFO)	NITE Biological Resource Center	Japan	3,081[a]	http://www.nbrc.nite.go.jp
UCD-V&E	Wine Yeast and Bacteria Collection, University of California Davis	USA	2,600[b]	http://wineserver.ucdavis.edu/
PYCC	Portuguese Yeast Culture Collection, Universidade Nova de Lisboa	Portugal	2,600[b]	http://www.crem.fct.unl.pt/Research_Lines/Line_5/Line_5.htm
ACBR	Austrian Center of Biological Resources and Applied Mycology, University of Biological Resources and Applied Life Sciences	Austria	2,500[a]	http://www.acbr-database.at
CECT	Coleccion Espanola de Cultivos Tipo	Spain	2,495[b]	http://www.cect.org
VKM	All-Russia Collection of Microorganisms	Russia	2,300[a]	http://www.vkm.ru
BCCM/MUCL	Mycotheque de l'Universite catholique de Louvain	Belgium	2,200[a]	http://www.belspo.be/bccm
LCC	Labatt Culture Collection	Canada	2,000[a]	http://www.labatt.com
ZIM	Culture Collection of Industrial Microorganisms, University of Ljubljana	Slovenia	1,740[a]	http://www.bf.uni-lj.si/zt/bioteh/chair/index.html
KCTC	Korean Collection for Type Cultures	South Korea	1,735[a]	http://www.brc.re.kr
BCRC	Bioresource Collection and Research Center	Taiwan	1,564[a]	http://www.ccrc.firdi.org.tw
NCAIM	National Collection of Agricultural and Industrial Microorganisms	Hungary	1,540[a]	http://www.ncaim.uni-corvinus.hu
VTTCC	VTT Technical Center	Finland	1,400[a]	http://www.vtt.fi/bel/services/culture_collection.htm
USRCB	Ukrainian Scientific-Research Cell Bank	Ukraine	1,339[a]	n/a
AWRI MCC	The Australian Wine Research Institute	Australia	1,200[a]	http://www.awri.com.au
URM	Universidade Federal de Pernambuco, Micoteca do Departmento de Micologia	Brazil	946[a]	http://www.ufpe.br/micoteca

Table 1 continued

Acronyms	Name	Country	Number of yeast strains	Website URL
CICC	China Center for Industrial Culture Collection, China National Research Institute of Food and Fermentation Industries	China	747[a]	n/a
TISTR	TISTR Culture Collection Bangkok	Thailand	616[a]	http://www.biotec.or.th/tncc/tistr_dete.html
LYCC	Lallemand Yeast Culture Collection, Lallemand Yeast Inc.	Canada	600[a]	http://www.lallemand.com/
CSIR	National Collection of Industrial Microorganisms, National Chemical Laboratory (CSIR)	India	600[a]	n/a
MTCC	Microbial Type Culture Collection, Institute of Microbial Technology	India	575[a]	http://mtcc.imtech.res.in/
PROIMI	Planta Piloto de Procesos Industriales Microbiologicos (PROIMT)	Argentina	500[a]	n/a
DSMZ	Deutsche Sammulung von Mikroorganismen und Zellkulturen GmbH	Germany	500[a]	http://www.dsmz.de

[a] Data obtained from the World Data Centre for Microorganisms online database, http://wdcm.nig.ac.jp/CCINFO. *n/a* information not available

[b] Data from survey response

They also now interact with a broader range of biotechnology companies, and have expertise in yeast genomics. DBVPG in Italy previously focused on wine yeasts, and has an extraordinarily diverse portfolio of wine yeast strains. Like NCYC, they have expanded their mission to include interaction with biotechnology companies. UCD-FST initially focused on taxonomy and ecology research. This focus resulted in a collection with a remarkable assortment of yeast species from natural habitats including insects and decaying plant matter, particularly cacti. The collection now performs in-house screening for a range of biotechnology applications such as discovery of novel therapeutics, biofuels, and bulk and fine chemicals.

Services offered by yeast culture collections

Strain deposit and archive services

Strain distribution is a very important function of service culture collections. However, before they can distribute cultures, collections obviously must gather and authenticate them. Many culture collections, particularly those described as Biological Resource Centers using the classification developed by the Organisation for Economic Co-operation and Development [16], serve as public repositories of microbes. Strains deposited include type strains selected by taxonomists to represent a novel species, patented strains, strains cited in publications, and genetically modified strains used in research and industry. Many journals require that biological materials utilized in publications must be made available to the scientific public. However, a significant number of strains appearing in research articles are not deposited in culture collections. This limits their access by other researchers or companies for later studies or possible applications. Strain deposit serves the very important function of preserving biodiversity, allowing utilization in the future in ways that we cannot imagine today. Increasingly, this preservation becomes urgent as yeast-rich habitats, particularly in the tropics, are being destroyed. Culture collections serve as biodiversity archives, to ensure that materials will continue to be available. For example, they may preserve all or part of collections after academic researchers retire, or when government agencies shift their research focus and shut down programs.

Not all collections were built by acquisition of microbes from outside sources. UCD-FST and DBVPG are noteworthy examples of collections gathered in large part by a single eminent yeast microbiologist and their colleagues (Phaff and Castelli, respectively) during the course of their research careers. These collections differ from the public repositories in that the majority of strains are unique to

Table 2 Summary information of respondents to culture collection survey

Collection	CECT	PYCC	ATCC	NCYC	UFD-FST	UCD-V&E	DBVPG
Total number of yeast strains	2,495	2,600	Approx. 10,000	~4,000	6,105	2,300	5,160
Number of lab strains (GMO)	n/a	80 (mainly *S. cerevisiae*)	>30,000 strains belonging to 20 different species	1,500 (*S. cer* and *S. pombe*)	32	1,300	53 Hybrid
Number of yeast species	345	600 (120 genera)	Up to 1,000	500	750	50 (85% *S. cerevisiae* strains)	250 (1,100 *S. cerevisiae* strains)
Number/% of yeast strains unique to this collection	n/a	Approx. 30%	n/a	Approx. 60%	80%	50%	60%
Year established	1960	1952	1925	1948	1944	1930s	1906
Location	University of Valencia, Spain	Universidade Nova de Lisboa, Caparica, Portugal	Manassas, VA	Norwich, UK	University of California Davis	University of California Davis	Department of Applied Biology, University of Perugia, Italy
Other services	Deposit of strains Identification Consulting on strain preservation and taxonomy	Molecular identifications Consulting for research or industry Online strain database (in development)	Patent and safe deposit	Species identification Strain fingerprinting Patent deposit Confidential safe deposit Contract research	Consulting based on extensive strain database	Identification of wine spoilage yeasts	Identification, patent deposit, safe deposit. Consulting based on extensive strain database. Industry-funded research
In-house research areas	Taxonomy Phylogenetics	Yeast systematics and ecology; 50 species descriptions since 1990	Taxonomy, authentication, preservation, genomics, bioinformatics, reference materials	Taxonomy Phylogenetics Computational genomics	Ecology, taxonomy	Wine spoilage; metabolomic and genetic analysis of *Brettanomyces*	Taxonomy, biodiversity, and biotechnology
Users' research areas	Wine, food, biotechnology, QC for microbiology labs, academic teaching labs	CREM researchers: basic research; academic and industrial researchers	R&D projects in a broad variety of pure and applied areas	Food, brewing, pharmaceuticals, biotechnology, fundamental academic research	Biofuels, pharmaceutics, taxonomy, food ingredients, ecology	Commercial wine inoculants, biofuels, *S. cerevisiae* genetics and evolution	Ecology, taxonomy, food, industrial applications such as VOCs, pigments, fatty acids, enzymes

their collection. Also, most of the cultures are owned by their institutions. Strain ownership impacts the ability of the institution to license the strain for use in commercial applications.

Prior to distributing cultures, collections must confirm the species identity, which requires expertise in taxonomy and identification methods. The collection must also preserve each strain under conditions appropriate for the species. Collections such as ATCC and CBS have performed extensive research to identify methods appropriate for preservation and cultivation of various yeast species. This critical knowledge is passed along to users in the form of media recipes and detailed protocols for long-term preservation of cultures, available on many of the collections' Web sites.

Several of the collections surveyed offer patent deposit under terms of the Budapest Treaty. In fact, 78 culture collections registered in the World Data Centre for Microorganisms (WDCM) online database provide patent deposit services. The cost of this service varies widely among the collections surveyed. Several collections also offer archive, or safe deposit service, which can be guaranteed for up to 20 years.

Strain distribution

Yeast collections differ in their areas of emphasis. Type cultures of most or all known yeast species can be obtained from CBS, NRRL, or ATCC. While DBVPG and UCD-V&E have tremendous depth in wine yeasts, NCYC covers brewing yeasts. UCD-FST carries a great diversity of species associated with decaying plants, which is proving useful for conversion of lignocellulosic materials to biofuels.

Yeast culture collections have become very savvy in making their holdings available to the scientific public in user-friendly formats. Most collections listed in Table 1 have online catalogs and an online ordering system. Terms for Material Transfer Agreements (MTAs) are also available online or through the curators. Cultures also are marketed and packaged in sets in some cases. Examples include the *S. cerevisiae* ORF Deletion sets, generated by the *Saccharomyces* Genome Deletion Project, sold in 96-well format by ATCC. NCYC has made available "robot-ready" sets of strains of *S. cerevisiae* used in the *Saccharomyces* Genome Resequencing Project, including both parental strains and stable haploid derivatives. The European Saccharomyces Cerevisiae Archive for Functional Analysis (EUROSCARF, http://web.uni-frankfurt.de/fb15/mikro/euroscarf/), operated by the Institute of Microbiology at the University of Frankfurt, Germany, collects and distributes *Saccharomyces cerevisiae* strains and plasmids generated in the course of functional analysis projects, including *S. cerevisiae* knockouts.

Yeast strains have little value unless they are extensively characterized, and the information made available in a convenient format. CBS has an extremely impressive and useful online database of strain properties, including growth characteristics, morphology, photos, DNA sequences, and literature references. This database is useful for selecting CBS strains with specific properties, such as growth at specific temperatures or utilization of a specific carbon source. The online system also has polyphasic identification functions, based on physiological parameters and/or DNA sequences.

The cost per strain varies greatly among the various culture collections, so it is useful to shop around, particularly when one is purchasing a large number of cultures. Some collections offer a bulk discount when larger numbers of strains are purchased.

Industrial researchers also should shop around for curator expertise and existing strain characterization data when selecting cultures to use in research applications. For example, the NCYC collection is known for extensive data on fermentation profiles of their brewing strains. The collection can be screened on a contract basis for fermentation traits of interest. The NCYC Web site also has a search function to identify yeasts that can degrade a number of substrates such as whey, pectin, cellulose, or production of products such as enzymes or vitamins.

In addition to distributing strains, some collections offer other yeast-related research products. ATCC offers a variety of useful products such as purified genomic DNA, prepared media, reagents, kits, and clone sets.

Identification service

Because collections must confirm the species identification of cultures, the curators must have expertise in taxonomy and identification methods. Some of the collections offer identification service, as indicated in Table 2. This now is performed primarily by ribosomal DNA sequencing. Unlike the bacterial realm, yeasts are a more narrowly defined group of microorganisms, with a much smaller number of known species. Thanks to the work of forward-thinking yeasts taxonomists Kurtzman [13] and Fell [8] and colleagues, and subsequent authors of new species publications, the D1/D2 region of the large (26S) ribosomal RNA gene of virtually all know yeast species has been sequenced, and sequences have been deposited in public databases. For this reason, the sequence of a yeast strain can be compared to that of all known species by a simple BLAST search. However, discriminating the useful from the less useful sequences in the public databases requires a familiarity with the field and the personalities involved. Culture collection curators can serve this important function.

Research

Culture collections were often built in the course of basic and applied research programs. This contribution continues. Yeast taxonomy and systematics are common research areas for culture collections. They lead in this crucial function because few other laboratories have the large numbers of strains required to properly perform these studies. It is estimated that approximately 70% of new species description publications come out of culture collections (C. Kurtzman, pers. comm.). CBS, NRRL, and PYCC play key leadership roles in taxonomy, publishing numerous new species publications. Culture collections play a key role in improving the systematics of yeast. Examples are editing and contributing to the two major taxonomic yeast treatises, five editions of "The yeasts: a taxonomic study" [10–12, 14, 15] and three editions of "Yeasts: characteristics and identification" [1–3].

CECT and NCYC emphasize comparative and functional genomics, exemplified by tracking down the origin and pedigree of *Saccharomyces* species and developing novel yeast identification methods [7]. Yeast ecology is a major focus of PYCC and UCD-FST. For example, the UCD-FST collection is currently growing through an NIH-funded project by studying the ecology of yeasts in the guts of wood-feeding insects in Indonesia. PYCC on the other hand, has a relatively large collection of basidiomycetous yeasts. This collection resulted from yeast surveys in different terrestrial and aquatic habitats. Necessarily, the researchers of the host R&D unit have expertise in the systematics of those yeasts.

DBVPG research programs include molecular taxonomy, new species descriptions, strain fingerprinting, and isolation, identification, and characterization of non-*Saccharomyces* yeasts from previously unexplored habitats. New yeast strains were isolated recently in the course of several expeditions to tropical environments in Somalia, Brazil, and Argentina. Over 1,000 psychrophilic yeasts were isolated from glaciers in the Antarctic, Arctic, Himalayan, Andes, and Alps regions. This is perhaps the largest collection of psychrophilic yeasts. This collection serves to preserve these microbes as glaciers are disappearing. The collection also is of interest to industry for applications requiring a reduction of heating energy use.

These studies of yeast systematics and ecology, publication of descriptions of novel species, and improvements in protocols for species identification contribute to the scientific infrastructure used by all other yeast researchers.

Screening

Despite the impressive databases and curator expertise, the best strain for an industrial use may not be detected using pre-existing data. Selecting the best strain by screening a large pool of candidates can save countless hours of strain development and process optimization. For this reason, some collections now offer in-house screening service on behalf of biotechnology companies. UCD-FST, NCYC, and DBVPG have screened 100 or even 1,000 of strains for production of secondary metabolites such as killer proteins, carotenoids, and volatile organic compounds; production of enzymes; tolerance of stress conditions; or utilization of substrates. UCD-FST uses a subset of the collection, over 2,000 strains, in a 96-well format to facilitate these in-house screening projects.

Training and consultation

Many culture collections offer training workshops to the scientific public. CECT offers workshops on maintenance and characterization of microbial strains. CBS offers courses on fungal biodiversity, food and airborne fungi, and medical mycology. The ATCC Web page has links to a series of webcasts on cell culture techniques. PYCC periodically presents very informative and insightful workshops on yeast taxonomy and systematics.

Because collection curators must have expertise in numerous areas of yeast biology including taxonomy, ecology, and physiology, they often serve as consultants to various industries. Collections based at universities and government agencies often include an extension function as part of their mission. For example, the food industry consults with UCD-FST regarding food spoilage yeasts. The curator recently received a sample of a spoiled organic dried fruit and nut energy bar. The yeast responsible for spoilage was *Zygosaccharomyces rouxii*, an extremely osmotolerant yeast species. Armed with knowledge of yeast ecology and physiology, the curator was able to advise that the yeast most likely was harbored in the fruit rather than the nuts. Lowering the water activity of the product slightly would eliminate the ability of this yeast species to grow. As another example, a brewery recently contacted NCYC to determine why the flavor of their beer had changed. NCYC was able to utilize DNA fingerprinting to reveal that a slightly different yeast strain had crept into the brewing process. In 2004, CECT initiated an agreement with the Instituto Valenciano de Arte Moderno to identify the fungal strains causing damage to paintings belonging to the museum collections, and to test the sensitivity of the isolates to some antifungal compounds. A broad variety of industries and agencies can tap the knowledge of culture collection personnel in areas of yeast taxonomy and identification methods and yeast physiology to solve a variety of problems.

Collaborations and networks

In addition to recognizing their own role in preserving a portion of the world's microbial biodiversity, some collections have partnered with other institutions in this mission. CECT and seven other European culture collections have formed the European Consortium of Microbial Resources Centres (EMbaRC), with a mission to hold a significant part of the world's known microbial diversity (http://www.embarc.eu). The Global Biological Resource Centre Network (GBRCN) is an alliance of culture collections of 15 countries in Europe and Asia as well as the European Culture Collection Organisation and the Asian Consortium for Microorganisms (http://www.gbrcn.org). The goals of GBRCN include implementing the OECD Best Practices, ensuring preservation of microbial species, allowing controlled access to potentially hazardous microorganisms, and facilitating utilization of cultures for improvement of human health and the environment.

Conclusions

Yeast culture collections of the world comprise an important element of the infrastructure of yeast research for academic and industry researchers alike. In addition to the obvious function of providing strains, these collections offer a variety of other services and expertise that industrial researchers should utilize.

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