

The U.S. Culture Collection Network Lays the Foundation for Progress in Preservation of Valuable Microbial Resources

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ABSTRACT

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The U.S. Culture Collection Network was formed in 2012 by a group of culture collection scientists and stakeholders in order to continue the progress established previously through efforts of an ad hoc group. The network is supported by a Research Coordination Network grant from the U.S. National Science Foundation (NSF) and has the goals of promoting interaction among collections, encouraging the adoption of best practices, and protecting endangered or orphaned collections. After prior meetings to discuss best practices, shared data, and synergy with genome programs, the network held a meeting at the U.S. Department of Agriculture (USDA)-Agricultural Research Service (ARS) National Center for Genetic Resources Preservation (NCGRP) in Fort Collins, Colorado in October 2015 specifically to discuss collections that are vulnerable because of changes in funding programs, or are at risk of loss because of retirement or lack of funding. The meeting allowed collection curators who had already backed up their resources at the USDA NCGRP to visit the site, and brought collection owners, managers, and stakeholders together. Eight formal collections have established off-site backups with the USDA-ARS, ensuring that key material will be preserved for future research. All of the collections with backup at the NCGRP are public distributing collections including U.S. NSF-supported genetic stock centers, USDA-ARS collections, and university-supported collections. Facing the retirement of several pioneering researchers, the community discussed the value of preserving personal research collections and agreed that a mechanism to preserve these valuable collections was essential to any future national culture collection system. Additional input from curators of plant and animal collections emphasized that collections of every kind face similar challenges in developing long-range plans for sustainability.

Living microbe collections, historically called culture collections, have established networks in many countries (Miyazaki and Sugawara 2002) to take advantage of shared expertise, to promote best practices (OECD 2007), and to have a common voice in discussions of funding (Smith et al. 2014), regulation (Dedeurwaerdere et al. 2013), and infrastructure support (Parsons and Duke 2013). The diverse stakeholder communities associated with these collections

represent some of the most important and impactful communities in modern research (Stromberg et al. 2013). Bringing U.S. collection communities together is the goal of the National Science Foundation (NSF) sponsored Research Coordination Network for a community of ex situ microbial germplasm repositories, or as it is more commonly known, the U.S. Culture Collection Network (USCCN) (<http://www.usccn.org/Pages/default.aspx>). Because collection curators typically participate in meetings closely tied to the research communities they support, this goal is foundational to progress in preserving and sharing microbial resources utilized in cutting edge research. Notably, before the 2012 meeting at the Fungal Genetics Stock Center (FGSC), most active U.S. culture collection curators had never visited another collection. Additional goals of the USCCN are to promote best practices, to develop shared data access, and to work

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*The e-Xtra logo stands for "electronic extra" and indicates that one supplementary file is published online.

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toward sustainability of the network and the collections that comprise the network. This review presents the results of the October 2015 meeting that addressed specifically the challenges to collection sustainability.

FORMATION OF U.S. CULTURE COLLECTION NETWORK

The U.S. Culture Collection Network has its roots in an ad hoc committee of scientists (Babcock et al. 2007; Kang et al. 2006), with support and participation from the U.S. Department of Agriculture (USDA), Agricultural Research Service (ARS), and Animal and Plant Health Inspection Service (APHIS). Two meetings were held to discuss the development of a National Plant Microbial Germplasm System (Bennett 2010; Gold et al. 2008). These meetings defined the core components of a system to preserve and share microbial resources to promote standardization, reproducibility, and collaboration. The meetings sponsored by The American Phytopathological Society (APS) and APHIS took place during a time of transition for all scientific collections in the United States and built upon a foundation put in place by the report of the National Science and Technology Council Interagency Working Group on Scientific Collections (IWGSC) which was published in 2009 and found that scientific collections “provide an excellent return on the taxpayers’ investments” (National Science and Technology Council 2009). It also emphasized that scientific collections are “composed of items acquired for scientific study rather than simply for historic or artistic value.” The IWGSC report made direct recommendations that were communicated in the 6 October 2010 U.S. White House Office of Science and Technology Policy (OSTP) memorandum to the heads of executive departments and agencies on the subject of “Policy on Scientific Collections.” The specific goals mentioned here, and expanded in an update by the OSTP on 20 March 2014, on the subject of “Improving the Management of and Access to Scientific Collections,” included a mandate that every federal agency that held scientific collections develop a draft policy for scientific collection management. They explicitly included federally owned and supported collections, but excluded project collections that were developed for a specific use and with a defined life-span. Key issues were collection-

specific budgeting, insuring that all regulatory requirements were met, and a strategy for making collections accessible online. Further noted in the 2014 memorandum was a legal requirement for a formal federal agency review process for de-accessioning, transferring, or disposing of scientific collections. This part of the OSTP memo was enacted by section 104 of the 2010 America COMPETES Act (Gordon 2010).

Among the major agencies with scientific collections, the USDA, the U.S. NSF and the U.S. National Institutes of Health (NIH) were responsible for most living collections. Medical collections have mostly been consolidated into a centralized resource known as BEI resources (<https://www.beiresources.org/>), incorporating several smaller collections into one program, most recently called Microbiology and Infectious Diseases Biological Resources Repository (RFP-NIAID-DMID-NIHAI201503, 3/30/2015). These are generally outside the scope of the present review.

The U.S. NSF supported living collections for many years through a program originally called Living Stock Collections for Biological Research (LSCBR) within the NSF Division on Biological Infrastructure. This program provided long-term salary support for genetic and biodiversity collections including research microbes, invertebrates, plants, and animals. As a partner in the IWGSC, the NSF conducted a review of its collections (Skog et al. 2009) and found that while biological collections comprised more than half of all 611 NSF collections described in the survey, only 3% (18) were living collections.

Because of the high impact and value of these collections, the Ecological Society of America (ESA), with support from the NSF, held a series of workshops to bring living collection workers together (Parsons and Duke 2011, 2013). These meetings began a process that culminated in the present RCN group (although the USCCN includes diverse collections not part of the NSF cohort). In 2013 LSCBR was merged with a program supporting field stations and natural history collections to form the program now called Collections in Support of Biological Research (CSBR). Unlike the historical LSCBR program, which provided long-term salary support, CSBR supports project-based proposals that emphasize collection improvement, stabilization, or relocation (<http://www.nsf.gov/pubs/2015/nsf15577/nsf15577.htm>, accessed 1/12/16). On March 16, 2016 the NSF announced that the CSBR program

TABLE 1
Living collections receiving National Science Foundation (NSF) support^a

Collection	End date	Host institution	URL
Peromyscus Genetic Stock Center	05/31/2017	University of South Carolina at Columbia	http://stkctr.biol.sc.edu/
The <i>E. coli</i> Genetic Stock Center	08/31/2018	Yale University	http://cgsc.biology.yale.edu/
University of Texas Culture Collection of Algae	04/30/2016	University of Texas	https://utex.org/
The Drosophila Species Stock Center	03/31/2018	University of California, San Diego	https://stockcenter.ucsd.edu/info/welcome.php
Provasoli-Guillard National Center for Marine Algae and Microbiota	05/31/2018	Bigelow Laboratory for Ocean Sciences	https://ncma.bigelow.org/
The Arabidopsis Biological Resource Center	03/31/2016	Ohio State University	https://abrc.osu.edu/
The <i>Bacillus</i> Genetic Stock Center	04/30/2017	Ohio State University	http://www.bgsc.org/
The Chlamydomonas Resource Center	08/31/2016	University of Minnesota (grant with Carnegie Institution of Washington)	http://www.chlamycollection.org/
International Culture Collection of Arbuscular Mycorrhizal Fungi (INVAM)	04/30/2017	West Virginia University	http://invam.wvu.edu/
Duke Lemur Center	03/31/2016	Duke University	http://lemur.duke.edu/
Phaff Yeast Culture Collection	05/31/2017	University of California, Davis	http://phaffcollection.ucdavis.edu/

^a From the NSF award database (http://www.nsf.gov/funding/pgm_summ.jsp?pims_id=503651, accessed 1/13/16).

TABLE 2
U.S. Culture Collection Network (USCCN) participating collections^a

Collection name	Host institution	Emphasis	Number of strains
Pacific Bacterial Collection	University of Hawaii, College of Tropical Agriculture and Human Resources	Bacterial plant pathogens	6,171
The Samuel Roberts Noble Foundation culture collection	The Samuel Roberts Noble Foundation	Endophytes	Unspecified
Phaff Yeast culture collection	University of California, Davis, Food Science	Yeast biodiversity	>7,000
The Mollicutes Collection of Cultures and Antisera	University of Florida	Mollicutes	>12,000 strains and 18,000 antibody specimens
Bull Penn Collection	Penn State University, Department of Plant Pathology and Environmental Microbiology	Bacterial plant pathogens	3,000
World <i>Phytophthora</i> Genetic Resource Collection	University of California, Riverside, Department of Plant Pathology	Oomycetes	>15,000
USDA FS Cronartium collection	USDA FS SRS	<i>Cronartium quercuum</i> f. sp. <i>fusiforme</i>	9
PSU <i>Fusarium</i> Resource Center	Penn State University, Department of Plant Pathology and Environmental Microbiology	<i>Fusarium</i>	>20,000
Center for Forest Mycology Research	USDA CFMR, Madison, WI	Wood inhabiting fungi	>20,000
USDA-ARS Collection of Entomopathogenic Fungal Cultures	USDA RWH Center, Cornell University, Ithaca, NY	Insect infecting fungi	>13,000
Fungal Genetics Stock Center	Kansas State University, Department of Plant Pathology	Filamentous fungi and yeast, plasmids	>25,000 (plus 50,000 in archival collection)
UTEX Culture Collection of Algae	University of Texas	Freshwater algae	3,000
OSU Culture Collection	Applied Mycology Lab, Department Of Wood Science and Engineering, Oregon State University	Wood Spalting fungi	>10
Moscow Fungal Archive Collection	USDA Forest Service – Rocky Mountain Research Station, Moscow, ID	Forest fungi	15,000
The Chlamydomonas Resource Center	Department of Plant Biology, University of Minnesota, St. Paul, MN	Chlamydomonas	4,000
Vidaver Bacteria Collection	University of Nebraska, Lincoln, NE	Plant Pathogenic and nitrogen fixing bacteria	3,000
USDA-ARS NRRL Culture Collection	National Center for Agricultural Utilization Research, Peoria, IL	Bacteria and fungi, IDA	93,000
<i>E. coli</i> Genetic Stock Center	Yale University, Department of Molecular, Cellular, and Developmental Biology. New Haven, CT	<i>E. coli</i>	10,000 (plus 15,000 in archival collection)
National Center for Marine Algae and Microbiota	Bigelow Laboratory for Ocean Sciences, East Boothbay, ME	Marine algae, IDA	>2,700
Guest Collections			
CABI Genetic Resources Collection	CABI, Surrey, UK	Diverse microbes	28,000
Duke Lemur Center	Duke University	Prosimian primates	250 individuals, 10,000 derived samples
Montgomery Botanical Center		Palms and Cycads	>3,000 accessions
CDC Arbovirus Collection	CDC	Arboviruses	>120,000 vials

(continued on next page)

^a IDA denotes a collection that serves as a patent collection (International Depository Authority) under the Budapest treaty of 1985 (WIPO 1980).
^b At risk indicates a collection with no formal, guaranteed institutional support.

TABLE 2
(continued from preceding page)

Collection name	Status	Catalog	Support	Representative citation
Pacific Bacterial Collection	Endangered	Not available	Informal	(Sueno et al. 2014)
The Samuel Roberts Noble Foundation culture collection	Institutional	Not available	Institutional	(Herrera et al. 2013)
Phaff Yeast culture collection	Institutional	http://phaffcollection.ucdavis.edu/	Institutional, sale, grants	(Sitepu et al. 2014)
The Mollicutes Collection of Cultures and Antisera	At risk ^b	http://gcm.wfcc.info/858	International Organization for Mycoplasmaology	(Brown et al. 2011)
Bull Penn Collection	Individual/ institutional	Under development	PSU, USDA, ad hoc	(Bull and Koike 2015)
World <i>Phytophthora</i> Genetic Resource Collection	Institutional, at risk	http://phytophthora.ucr.edu/default.html	Institutional, sale, grants	(Martin et al. 2014)
USDA FS Cronartium collection	At risk	Not available	USDA FS FRS, individual	(Amerson et al. 2015)
PSU <i>Fusarium</i> Resource Center	At risk	http://www.fusariumdb.org/index.php?a=guestlogin&r=/index.php	Research support, individual	(Aoki et al. 2014)
Center for Forest Mycology Research	Institutional, at risk	http://www.fpl.fs.fed.us/research/centers/mycology/culture-collection.shtml	USDA, individual	(Palmer et al. 2014)
USDA-ARS Collection of Entomopathogenic Fungal Cultures	Institutional, at risk	http://www.ars.usda.gov/Main/docs.htm?docid=12125	USDA-ARS	(Kepler et al. 2014)
Fungal Genetics Stock Center	Institutional, at risk	http://www.fgsc.net	Institutional, sales, grants	(McCluskey 2011)
UTEX Culture Collection of Algae	Institutional	https://utex.org/	Institutional, sales, grants	(Brand et al. 2013)
OSU Culture Collection	Informal	http://www.northernspalting.com	Sales, individual	(Weber et al. 2014)
Moscow Fungal Archive Collection	At risk	Not available	Research support, individuals	(Kim et al. 2010)
The Chlamydomonas Resource Center	At risk	http://www.chlamycollection.org/	Institutional, sales, grants	(Tam et al. 2013)
Vidaver Bacteria Collection	Endangered	Not available	Individual, research grants	(Agarkova et al. 2011)
USDA-ARS NRRL Culture Collection	Institutional	http://nrll.ncaur.usda.gov/	USDA-ARS	(Geiser et al. 2013)
<i>E. coli</i> Genetic Stock Center	At risk	http://cgsc.biology.yale.edu/	Sales, grant	(Turner et al. 2014)
National Center for Marine Algae and Microbiota	Institutional	https://ncma.bigelow.org/	Grants, sales, contract	
Guest Collections				
CABI Genetic Resources Collection		http://cabi.bio-aware.com	Institutional, sale, services	(Broughton et al. 2012)
Duke Lemur Center	Institutional, at risk	http://lemur.duke.edu/	Institutional, sale, grants	(Zehr et al. 2014)
Montgomery Botanical Center	Independent	http://www.montgomerybotanical.org/Pages/Collection_Database.htm	Endowment, sale, grants	(Griffith et al. 2015)
CDC Arbovirus Collection	Federal	http://www.cdc.gov/ncepid/dvbd/	Federal	(Cleton et al. 2015)

would be officially “in hiatus” and is not accepting proposals in 2016. The CSBR program has different categories for natural history collections and for living collections, although only a few living collections receive support. As of 13 January 2016, the NSF award database for this program (“element code 1197”) listed 95 active awards of which 12 were to living collections, one supports

this RCN and the remaining 82 grants are to natural history collections, predominantly for once-living collections. The living collections receiving support are diverse and not all include microbes (Table 1). Among these, many collections including the *Bacillus* Genetic Stock Center, Chlamydomonas Resource Center, and the *E. coli* Genetic Stock Center (CGSC) (Table 2) are in

the process of transitioning from NSF support to independent long-term sustainability. The FGSC has already begun this transition and is no longer receiving sustenance support from the NSF. The transition to independence is supported by the continued high numbers of strain distributions and the impact of these collections. The FGSC is cited in hundreds of articles every year. The CGSC stock center continues to distribute over 6,000 strains per year. All of these collections are embracing the impact of molecular genetic resources. The FGSC has distributed over half of a million gene deletion strains arrayed in 96-well format and both the *E. coli* and *Chlamydomonas* stock centers are developing arrayed sets for distribution.

One challenge facing these collections is the question of who owns the material. While the NSF is formally a U.S. government agency, they do not own the collections they support and this is one of the key differences between USDA, NIH, and NSF collections. NSF-supported collections are owned by their hosting institution and most consider their strains to be held in trust for the public. Most USDA and NIH federal collections, by way of contrast, are explicitly owned by the U.S. government. The ARS NRRL collection (including the patent collection) is one of the world's leading microbe collections with nearly 100,000 accessions (<http://nrrl.ncaur.usda.gov/>). The ARS Entomopathogenic Fungal (ARSEF) collection holds over 13,000 strains valuable for taxonomy, research, and agriculture, including materials not available elsewhere (<http://www.ars.usda.gov/Main/docs.htm?docid=12125>). University-based collections, including public collections such as the Phaff Yeast Culture Collection, and also private or research collections generated by individual researchers or groups, such as the Pacific Bacteria Collection (Sueno et al. 2014) or the Vidaver Research Collection at the University of Nebraska, Lincoln (Agarkova et al. 2011), are typically owned by the host institution. While these may be formally distributing collections with established Material Transfer Agreements and defined fees, or ad hoc collections which share isolates on an exchange or collaboration basis, all hold valuable materials with high impact in published research.

THE U.S. CULTURE COLLECTION NETWORK MEETINGS

The diversity of resources held by U.S. living microbe collections (Table 2) has been a barrier to interaction for collection curators and staff because they participate in research community specific activities, rather than collection activities. Building upon the momentum established by the APS and ESA efforts, the present Research Coordination Network was formed and has held five meetings or workshops in the 3 years since the network was established. Following on the success of meetings at the Fungal

Genetics Stock Center (2012) and the USDA NRRL collection (2013), which emphasized community building, workshops at Penn State University (McCluskey et al. 2014), and at the University of California, Davis (Boundy-Mills et al. 2015), addressed the topics of national and international regulations and genome program engagement, respectively. To discuss the shared goal of implementing off-site back up for active collections, including the identification of a mechanism to preserve endangered or orphaned collections, the most recent meeting of the USCCN was held at the USDA-ARS National Center for Genetic Resources Preservation (NCGRP) in Ft. Collins, Colorado, which has established a security back-up storage program for U.S. living microbe collections. Held on 13 to 14 October 2015, this meeting provided an opportunity for collection curators and stakeholders to meet and share experiences, challenges, and opportunities.

The meeting began with an introduction to the scope and practices of the USDA-ARS NCGRP, which is expanding its holdings of microbial resources. At present this is primarily a nondistributing, back-up role that is limited to formal public collections. The NCGRP already holds 32,000 isolates, although this is a small fraction of the total microbe resources presently available through USCCN participating collections (Table 3). Among the resources at the NCGRP, the plant pathogen differential sets organized through the APS-International Seed Foundation are the only microbe sets that are available directly to clients (<http://www.cppi.org/>). These important pathogen sets allow unambiguous characterization of genetic host resistance and provide for standardization among corporate entities or across national boundaries.

APPROACHES AND CHALLENGES TO SUSTAINING COLLECTIONS

Because collections are rarely economically self-supporting (Smith et al. 2014), basic support is essential and a number of presentations emphasized this (Supplementary File). Typically supplemented by user fees, basic support can include grant support, institutional funds, or endowment income. While some collections may relocate to maintain affiliation with their research community (Brown et al. 2011; McCluskey and Leslie 2015), maintenance in situ is often the best option for collection preservation. Transfer of responsibility for the UTEX Collection of Algae to the curator following retirement of long time director Jerry Brand (Day et al. 2004) exemplified this approach to collection continuity. Algal collections have enjoyed a recent resurgence of interest and this allows collections with validated isolates of known provenance to generate significant revenue through strain distribution and

TABLE 3
Microbial collections with back-up holdings at the National Center for Genetic Resources Preservation (NCGRP)^a

Collection	Holdings	Number of strains at NCGRP (total holdings)	Description
Fungal Genetics Stock Center (FGSC)	Fungi	13,000 (23,000)	Gene deletion mutants and plant pathogens
International Culture Collection of Arbuscular Mycorrhizal Fungi (INVAM)	Fungi	81 (1,112)	Mycorrhizae
<i>Bacillus</i> Genetic Stock Culture (BGSC)	<i>Bacillus</i>	2,058 (2,500)	<i>Bacillus</i>
<i>E. coli</i> Genetic Stock Center (CGSC)	<i>E. coli</i>	5,723 (9,700)	<i>E. coli</i>
ARS Entomopathogenic Fungal (ARSEF)	Fungi	2,997 (9,000)	Entomopathogenic fungi
NRRL	Bacteria	1,597 (93,000)	<i>Listeria</i> (broad emphasis)
Phaff Yeast Culture Collection	Yeast	3,854 (7,000)	Yeast
UTEX Culture Collection of Algae	Algae	1,095 (3,000)	Algae
Other	Various	2,952	USDA lab collections

^a The NCGRP was renamed the National Laboratory for Genetic Resources Preservation on 15 December 2015.

other fee-based products and services (Sitepu et al. 2013). Algal collections, however, face the unique challenge that cryopreservation is often not possible and so the challenge of limiting genetic drift incurred by serial strain subculture (Brand et al. 2013) becomes a significant hurdle to genetic stability (Lakeman et al. 2009) and the extent of genetic drift is not known. Because this issue is foundational to all living collection curators, an invited presentation by Christopher M. Richards of the NCGRP described approaches to prioritizing collecting activities to maximize genetic diversity among crop wild relatives (Reeves et al. 2012). This presentation described how ex situ preservation impacted the genetic diversity of a collection. Although some aspects of this emphasize the fundamental simplicity of preserving microbial germplasm as compared with outbreeding plant species, the core question of how many individual isolates are necessary to represent a population is similar. While not microbial in nature, presentations that described living biodiversity collections of palms and cycads or of lemurs were valuable in their emphasis of both the shared challenges, and the significant differences between microbe and plant or animal collections. The Duke University Lemur collection is descended from a small founder population (Zehr et al. 2014) and unlike microbe collections, individual lemurs are ephemeral and cannot be preserved. In the case of a plant collection, significant endowments and revenue from public participation can support conservation goals (Griffith et al. 2015). The engagement of living vertebrate and plant collection curators showed how both microbe and macro flora or fauna collections are similar in that they are all vulnerable to down-turns in research funding.

PRESERVING ENDANGERED COLLECTIONS

The Phaff Yeast Culture Collection at UC Davis is a leading collection for discovery and development of biotechnological applications of environmental yeasts. Nearly lost following the retirement of the founder, H. Phaff, the recent identification of strains capable of producing biofuel from agricultural waste was an unanticipated benefit (Sitepu et al. 2014) from a collection that was established for taxonomy and biodiversity studies. Because of the visionary investment in this collection by the University of California, this valuable resource was preserved. Not all institutions are willing to support historical collections and some, such as the Pacific Bacteria Collection (Sueno et al. 2014), or the Vidaver Research Collection at the University of Nebraska, Lincoln (Agarkova et al. 2011), are at immediate risk of loss.

Logistic issues can make collection preservation difficult. Within the United States, permitting for interstate movements is perhaps the most significant. Permit requirements differ depending on the types of material being moved. For wild-type, classical, or molecular genetic mutants of non-plant pathogen strains, no permits are normally required (for example, yeast for research, baking, or brewing). Wild type and classical mutant plant pathogen strains require prior approval of the USDA APHIS (PPQ526), while movements of mutant plant pathogen strains generated by molecular technology require specific strain-by-strain permits from the USDA Biotechnology Regulatory Service in addition to PPQ526 permits. In many cases it is easier to reconstruct a mutant strain than to obtain necessary permits, although this may lead to proliferation of diverse strain lineages, complicating direct comparison and challenging reproducibility. Regardless of permit requirements, guidelines for shipping perishable material established by the International Air Transport Authority need to be observed.

SPECIAL PURPOSE COLLECTIONS

Among the collections participating in USCCN activities, some are associated with specific research questions. The *Cronartium*

quercuum f. sp. *fusiforme* collection at the USDA Forest Service, Southern Research Station (Amerson et al. 2015) is comprised of isolates used in the characterization of resistance genes important to the forest industry. Similarly, a presentation on virus isolates maintained by the U.S. Centers for Disease Control and Prevention, Division of Vector-Borne Diseases emphasized the similarities among collections. This presentation showcased world leading research and development relevant to human pathogen viruses all of which are transmitted by arthropods (Johnson et al. 2014). While its impact is huge, this collection, which includes diverse diagnostic reagents in addition to historical pathogen isolates, faces many of the same challenges to information resources and long-term stability faced by plant and environment microbe collections.

BIOSECURITY AND INTERNATIONAL OBLIGATIONS

While individual researchers' collections may be ephemeral, formal collections have both permanence and a public presence. Addressing a possibility that this could expose collection materials to intentional misuse, a formal discussion of how culture collections had been misused in a number of high profile actual or threatened biological attacks was included (Astuto-Gribble et al. 2009) in the meeting agenda. Most of the collections represented at the meeting neither hold high-risk agents nor distribute material to the general public and as such most meeting participants were confident that material from their collections could not be utilized for intentional harm. One issue shared by collections that hold pathogenic microorganisms is the observation that many microbes in culture lose pathogenicity and so individuals with mal-intent who are interested in obtaining highly pathogenic material would more likely obtain them directly from nature (Janbon et al. 2014; Jeon et al. 2013; Songe et al. 2014). Whatever the risk, it was clear that culture collection biosecurity is at the same time important and also understood differently by collection managers and outside observers. It was generally agreed among meeting participants that scientists who collaborate with colleagues in developing nations face additional challenges. Infrastructure elements that are common in developed nations may not be available for collections in developing nations. Overall, formal living microbe collections are able to identify and comply with evolving regulations more readily than individual researchers who may rely on peer-to-peer exchanges which have the potential to be vulnerable to exploitation due to lack of procedural oversight.

Emphasizing the similar processes being undertaken around the world, EU scientists are working to establish a multinational network of living microbe collections to facilitate access and to increase the impact of microbial technology for industry, agriculture, and society (Schüngel et al. 2014). Called Microbial Research Resource Infrastructure (MIRRI), this comes at an important time as the legal framework for establishing rights to genetic resources under the Nagoya Protocol on Access and Benefit Sharing to the Convention on Biological Diversity (CBD) entered into force in 2014 (Schindel and Du Plessis 2014). The CBD deals with genetic resources accessioned into collections after 1993 (Secretariat of the Convention on Biological Diversity 1992). The codification of the role of ex situ microbial germplasm repositories in the CBD emphasizes the benefit of long-term sustainability plans for both long-established as well as newly established collections and offers both hope and also concern for the future. Similarly, although the USCCN is fundamentally about U.S. collections, frequent scientific collaboration among U.S. and Canadian scientists emphasized the importance of microbe collections in Canada. Frequently utilized by U.S. researchers, the University of Alberta Microfungus collection was in the process of relocation in late 2015 and is now established in a new home at the Gage Research Institute (associated with the University of Toronto) (Table 2).

CONCLUSION

Emphasizing the interconnectedness of living collections, the USCCN has held several meetings allowing collection scientists from diverse backgrounds to interact, including the most recent meeting on 13 to 14 October 2015 at the USDA National Center for Genetic Resources Preservation. With this continued engagement by the USDA, the USCCN continues to make progress toward its stated goals of holding workshops and meetings to promote best practices, to share information and protocols, to enable international engagement, to explore strategies for long term sustainability of collections and a collection network, and as discussed at the most recent meeting held at the USDA National Center for Genetic Resources Preservation in October 2015, to establish a formal off-site back-up program for public collections and collections that are at risk of loss. Among the observations made at this most recent meeting was that even within a narrow community like the USCCN, there are distinct collection types. The historically NSF-supported stock centers are deeply aligned with their respective research communities. Among these collections, the CGSC, the Chlamydomonas Resource Center, and the FGSC, as well as the *Bacillus* Stock Center and the Arabidopsis Resource Center are all taxonomically narrow and hold genetically defined variants with reduced background genetic variation. Other collections emphasize biodiversity and engage a broader research community. Collections like the Phaff yeast collection as well as numerous phytopathogen collections, such as the World Oomycete collection, the Bull Penn Collection (which includes the Bull Salinas collection and additional materials), the Pacific Bacteria collection, and the Vidaver phyto bacteria collections, all hold diverse organisms, most of which have been utilized in published research by the lab director and their collaborators. Similarly, the fungal collections at the USDA Center for Forest Mycology Research, the USDA-ARS Collection of Entomopathogenic Fungal Cultures, and the Moscow fungal archive collection represent tremendous biological diversity, although they have different support and distribution models. Among USDA-supported collections in the network, only the NRRL and the ARSEF collections are publicly distributing collections. The American Type Culture Collection (ATCC) historically received public support, but became self-supporting many years ago through modern marketing and intellectual property management (Simione et al. 2012). To leverage open access policies many recent microbial whole genome sequencing programs have partnered with overseas collections such as the German Deutsche Sammlung von Mikroorganismen und Zellkulturen (DSMZ) collection which contributed to the project to generate a genomic encyclopedia of bacteria and archae (Kyrpidis et al. 2014) or the Dutch Centraalbureau voor Schimmelcultures (CBS) collection which has provided strains for the thousand fungal genome project (Grigoriev et al. 2014).

Another area where collections differ greatly is in the support they receive. Collections historically supported by the U.S. NSF have long been encouraged to become self-sustaining and while the FGSC has identified independent university support through the Kansas State University College of Agriculture, other collections are still greatly dependent upon NSF support. Fees charged by these collections differ, ranging from a low fee of \$8 per strain (plus a per-order fee of \$35) at the CGSC to \$20 per strain at the Chlamydomonas center or \$50 per strain from the FGSC. These are all a fraction of the fees charged by some of the largest international collections. The ATCC in the United States and the CBS in the Netherlands ask fees of \$250 to \$350; CABI in the UK and DSMZ in Germany ask fees of \$100 to \$150. Meanwhile the USDA public collections are prohibited from charging recipients and must limit the number of isolates available outside of formal collaborations. Most research collections provide strains with colleagues on an exchange basis, as an obligation of having received federal funding, or to satisfy the requirements of

journals. By way of contrast, many medically relevant collections in the United States are managed as a central non-research active facility under contract from the U.S. National Institutes of Allergies and Infectious Diseases and do not charge fees. The recent solicitation for bids to operate the Microbiology and Infectious Diseases Biological Resource Repository included support for as many as 46 full time scientists, technicians, and support staff (NIAID 2015) to manage just over 13,000 strains, most of which are biosafety level one or two. Many fewer of their isolates are biosafety level three and a very small number are high-risk, biosafety level four. By way of contrast, most collections that participate in the USCCN activities have one or two dedicated staff members and manage thousands to tens of thousands of strains and related materials (Boundy-Mills 2012; McCluskey and Boundy-Mills 2014; Stackebrandt 2010).

Research progresses at a greatly accelerated rate when authentic research materials are available from quality-controlled public collections (Furman et al. 2010). Such collections are part of the research infrastructure and as such the cost and benefit are separate and it is not always possible to demonstrate clearly the impact of materials from supporting living repositories. A clear message from the expanded participation in the 2015 meeting of the U.S. Culture Collection Network is that living research collections face similar challenges regardless of their history, holdings, or research emphasis. To overcome this, robust support for foundational infrastructure elements, based on historical and on-going impact, is essential. Much as the impact of individual resources is enhanced by being publicly shared, the research endeavor in the broadest sense receives benefits, including accelerated productivity, reproducibility, and in translation into practical applications, when validated and quality controlled materials are openly available (Stern 2004). Potential approaches to promoting expansion of resources to assure that important microbial resources are openly available include a requirement by funders or journal publishers that strains be deposited in public collections (Stackebrandt et al. 2014). This is highly desirable and follows precedent established by the requirement that accession numbers be provided for DNA sequences in published articles (Cinkosky et al. 1991). To meet this demand, the living microbe collection community needs long-term support to develop the necessary infrastructure to manage the large numbers of isolates this could generate (Kang et al. 2006). Preservation of existing collections, including those maintained by individual researchers, provides opportunity for studies not possible with only newly isolated modern materials. Continual availability of archival, curated living cultures should be considered to be of the highest priority.

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