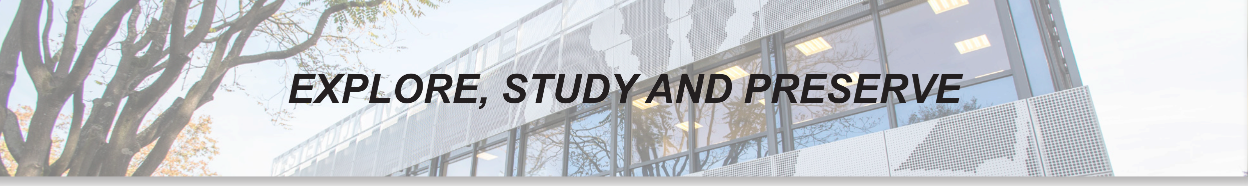
WESTERDIJK
FUNGALBIO
DIVERSITY
INSTITUTE

Progress Report

2019–2020

KONINKLIJKE NEDERLANDSE
AKADEMIE VAN WETENSCHAPPEN



EXPLORE, STUDY AND PRESERVE

Although 2020 was earmarked as the International Year of Plant Health, it was largely overshadowed by human health issues as the Covid-19 pandemic took the world by storm and significantly altered ‘normal’ life as we know it. As most international travel and field trips came to a halt, we had to postpone both our planned Spring Symposium “Rise of the Fungi” and the peer review of the institute to 2021. Despite the uncertainties and delays, we quickly adapted to our new ‘online’ reality and were able to accomplish a great deal in 2020.

The Westerdijk Fungal Biodiversity Institute (WI) became an “ESCMID Collaborative Centre” (ECC) to facilitate international training and collaboration, specifically for medical mycologists. The department of Medical Mycology is one of the few global ECC’s that has its focus on fungal infections and thus being an ECC is of great importance to position our institute within the European network of clinical microbiologists and infectious diseases specialists.

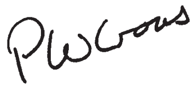
Following the national analysis of Dutch research institutes, a need was identified for the WI to collaborate more closely with the Netherlands Institute of Ecology (NIOO-KNAW) in soil microbiology. Our knowledge in fungal biodiversity together with the large number of soil fungi and their associated DNA data in the collection, as well as the current Citizen Science project make us an ideal candidate for this collaboration.

To combat biodiversity loss in the Netherlands, a new national approach was necessary in order to increase knowledge about Dutch biodiversity. To make this possible, the Naturalis Biodiversity Center, NIOO-KNAW, the Royal Netherlands Institute for Sea Research (NIOZ-NWO), and the WI joined forces. The aim is to work together to significantly increase integral knowledge of Dutch biodiversity in all environments: on land, in fresh and saltwater, in the air, and from genes to ecosystems. Together, the four institutes have launched BiodiversityXL, the Centre of Excellence for Netherlands Biodiversity Research. The centre forms the core for cooperation with universities and knowledge institutes of the Netherlands. This creates a hub of knowledge about biodiversity that is available to every scientist.

This cooperation also builds on NWO’s recent investments in the National Roadmap for Large-Scale Scientific Infrastructure. Awards were made for the ARISE project (including Naturalis and the WI) for the construction of a globally unique infrastructure to map all multi-cellular species within the Netherlands and to provide NIOZ’s research fleet with innovative, large-scale scientific equipment.

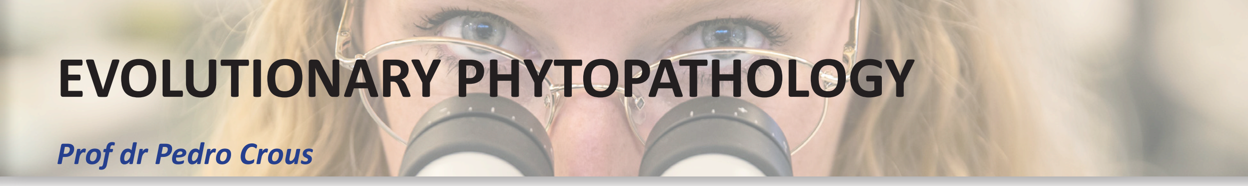
These important investments make it possible for us to jointly and efficiently obtain a more reliable picture of biodiversity throughout the Kingdom of the Netherlands including Aruba, Curaçao, and Sint Maarten. Biodiversity loss linked to global change remains one of the major aspects that impact our lives now and in the future, so initiatives like the ARISE project are essential to enable us to make a significant contribution to these new actions.

As scientific chair, Teun Boekhout has been making good progress with putting the IMC12 programme together. Seven themes were selected: Cell biology, biochemistry and physiology; Environment, ecology and interactions; Evolution, biodiversity and systematics; Fungal pathogenesis and disease control; Genomics, genetics and molecular biology; Nomenclature, and Applied mycology. The chairs have helped to select a stellar selection of keynote speakers to be announced during 2021. Furthermore, many “hands-on” workshops have been planned during IMC12. Despite the Covid-19 hindrances both the IMC12 in Amsterdam and IUMS meeting in Rotterdam promise to represent an exciting two weeks of “Mighty Microbes” in the Netherlands. I hope to see you there!



Prof dr Pedro W. Crous
Director: Westerdijk Fungal Biodiversity Institute

Scientific output		
Output type	**2019**	**2020**
Papers	155	113
Chapters in books	1	5
Books	2	-
Dissertations	2	2
Services		
Service type	**2019**	**2020**
Aquisition new strains	1 488	1 402
Identifications	254	172
Deposition patent strains	110	32
Dispatch of strains*	3 915	4 212
Dispatch of DNA samples	86	52
MycoBank		
Internet visits	**2019**	**2020**
MycoBank unique visitors	470K	326K**
*Fungi, bacteria/actinomycetes, yeasts.		
**Since 2020 new measuring software excludes crawlers and single page users from the total count.		



EVOLUTIONARY PHYTOPATHOLOGY

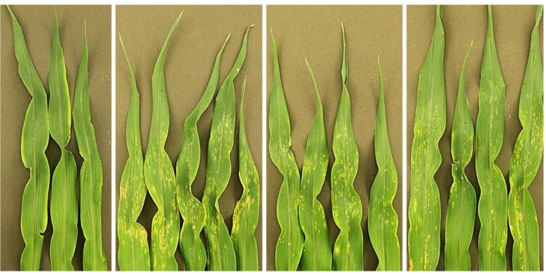
Prof dr Pedro Crous

Correct pathogen diagnoses is the key to success

In the coming 30 years the largest human population growth will be occurring in Africa. However, global climate change, linked to the increasing demand for food, also indicates that the fungal diseases occurring in certain regions will change. This shift in disease problems, and the emergence

of new diseases, will lead to ever increasing problems. Correct pathogen diagnosis is essential to mitigate effective management practices. Global trade in animal and plant products will continue to move pathogens around the globe, resulting in new introductions into areas where they are non-native. To ensure global food security, it is therefore essential that we develop the tools to rapidly detect plant pathogens, and to help understand and predict how they will interact with other organisms.

HIGHLIGHTS



Dothideomycetes is the largest class of kingdom *Fungi* and comprises an incredible diversity of lifestyles, many of which have evolved multiple times. Studying the ecology and evolution of *Dothideomycetes* significantly impacts our understanding of fungal evolution, effects of climate change, and adaptation to stress and host specificity. Using machine-learning techniques based on whole-genome sequences, we accurately classified fungi into lifestyle classes and identified a small number of gene families that positively correlate with these distinctions. Haridas *et al*. (2020). 101 *Dothideomycetes* genomes: a test case for predicting lifestyles and emergence of pathogens. *Studies in Mycology* **96**: 141–153.

Panama disease on banana is one of the major constraints in banana production worldwide. Indonesia is the centre of origin for wild and cultivated bananas, which likely co-evolved with *Fusarium oxysporum f. sp. cubense* (Foc). Although the disease has traditionally been attributed to Foc, we have shown that several species are able to

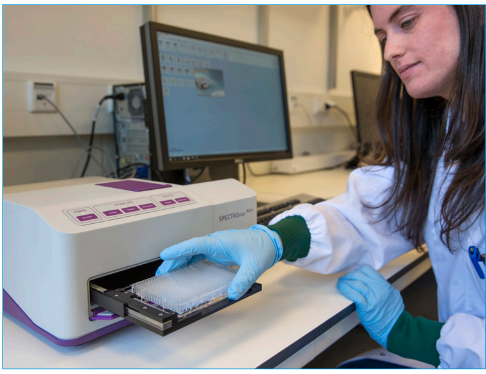
cause the disease, one of which has escaped Indonesia (TR4, named here as *F. odoratissimum*), causing havoc in Africa, Asia, and North, South America. Maryani *et al*. (2019). Phylogeny and genetic diversity of the banana Fusarium wilt pathogen *Fusarium oxysporum f. sp. cubense* in the Indonesian centre of origin. *Studies in Mycology* **92**: 155–194.

Species of eucalypts are commonly cultivated for solid wood and pulp products. Foliar fungal pathogens of eucalypts negatively impact commercial forest industries globally. To assist in evaluating this threat, the present study provides a global perspective on foliar pathogens of eucalypts, treating 110 different genera associated with foliar disease symptoms of these hosts. Crous *et al*. (2019). Foliar pathogens of eucalypts. *Studies in Mycology* **94**: 125–298.

FUNGAL NATURAL PRODUCTS

Dr Jérôme Collemare

Secondary metabolites provide solutions for healthcare, industry and agriculture



Fungi produce natural products known as secondary metabolites (SMs) that have significant impact on human societies. The most famous fungal SM is the broad-spectrum antibiotic penicillin, which provided the first effective treatment of bacterial infection and revolutionized modern medicine. Fungal SMs play important roles not only in healthcare, but also in agriculture and industry. Although fungi have provided us with life-changing compounds, the fungal kingdom has remained underexploited. The genomic era has revealed that fungal genomes encode many more biosynthetic pathways than the number of known SMs. This is due to the tight regulation of the expression of these pathways under very specific conditions that are difficult to reproduce in the laboratory. The Fungal Natural Products group aims to identify novel compounds and understand their biosynthesis in order to provide solutions for healthcare, industry and agriculture. More specifically, the objectives are to (i) exploit the biodiversity of the Westerdijk Institute's fungal bioresource and of fungal genomes to identify new compounds; (ii) elucidate their biosynthesis; (iii) determine the evolution of biosynthetic pathways; and (iv) characterize the role of SMs in fungal biology.

HIGHLIGHTS

For these purposes, we employ a multi-disciplinary approach that combines bioinformatics, genomics, molecular biology, bioassays and chemistry. On one hand, we are exploring genomes and have activated new biosynthetic pathways, focusing on specific ecosystems like lichens or specific applications like colourants; on the other hand, we have performed several screenings to identify novel antifungal compounds, and will develop a new method for the screening of antibiotics.

The Fungal Natural Products group co-organized the first European Fungal Secondary Metabolism symposium, together with Prof. Soizic Prado (Muséum National d'Histoire Naturelle, Paris) and Prof. Russell Cox (Leibniz Universität Hannover, Hannover), which was held in Hannover on September 30th and October 1st, 2019. This symposium was a first because it gathered biologists, chemists and bioinformaticians from different European countries, who are all experts in different aspects of fungal secondary metabolism. This interdisciplinary symposium thus made the bridge between these communities with the objective to connect them and new collaborations have already been stimulated. This symposium was organized with the help from the French Embassy in Berlin and the Institut Français in the Netherlands.

Focus on antimicrobial resistance: in collaboration with the Hubrecht Institute and Utrecht University, more than 10 000 fungal extracts were screened for antifungal activity against plant and human fungal pathogens. A few hundred hits have been obtained and determination of the chemical structures has started at the end of 2020 with the arrival of an organic chemist in the group.

The Fungal Natural Products group has released its first exploitation of fungal genomes with a comprehensive study of fungal type III polyketide synthases (PKSs). These particular enzymes are understudied in fungi despite their importance for the production of bioactive molecules like flavonoids and anthocyanins which exhibit antioxidant and antimicrobial properties. By combining phylogeny and comparative genomics, this study revealed a complex evolutionary history and has provided the fundamental knowledge required for the future characterization and engineering of these enzymes and biosynthetic pathways. Working hypotheses elaborated in this study are now under investigation in the laboratory. Navarro-Muñoz and Collemare (2020). *Frontiers in Microbiology* **10**: 3018.

FUNGAL PHYSIOLOGY

Prof dr ir Ronald de Vries

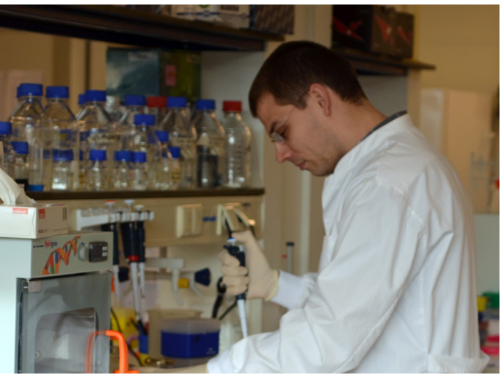
Answering fundamental questions of fungal biology through comparative studies across the fungal tree of life

The Fungal Physiology group aims to unravel the molecular mechanisms that affect fungal physiology on natural substrates (focusing on extracellular enzymes, regulatory systems and metabolism) and apply this knowledge to develop strains (e.g. cell factories) and enzymes to support the biobased economy. By answering fundamental questions of fungal biology, we generate insights that provide the basis for more applied projects, such as improving enzyme production, fungi as alternative protein sources, discovery of novel enzymes, or metabolic engineering. This is often performed in close collaboration with industrial partners. Our in-depth studies focus on a small number of model or reference species (*Aspergillus niger*, *A. nidulans*, *Trichoderma reesei*, *Dichomitus squalens*, *Penicillium subrubescens*) and results from those studies are subsequently used in comparative studies across the fungal tree of life. We use diverse methodologies, including comparative genomics, transcriptomics and proteomics, as well as traditional and cutting edge (e.g. CRISPR/Cas9) methods in molecular biology, genetics and biochemistry. The mature bioinformatics infrastructure of the group is the backbone of many of our research lines. The expertise of the group is further strengthened through strategic collaborations with researchers from several other academic institutions.

HIGHLIGHTS

2019 and 2020 marked the second half of the EU funded project FALCON (https://www.falcon-biorefinery.eu/), which was coordinated by Ronald de Vries. During this time the elucidation of the fungal aromatic resulted in realistic opportunities to use the related enzymes, as well as engineered fungal strains, to convert lignin-derived aromatic compounds into platform chemicals offering a realistic alternative for chemical synthesis. Related to this topic, four papers were published (see below), with several more in progress, and two patent applications were filed. Publications: Lubbers *et al*. (2019) *Biotechnology Advances* **37**: 107396; Lubbers *et al*. (2019) *Frontiers in Bioengineering and Biotechnology* **7**: 149; Lubbers *et al*. (2019) *ACS Sustainable Chemistry & Engineering* **7**: 19081–19089; Lubbers *et al*. (2020) *Journal of Applied Microbiology* **128**: 735–746.

Incorporation of CRISPR/Cas9 genome editing on our research lines has strongly extended the possibilities for a range of strain engineering, including gene deletions and point mutations, domain swapping, gene replacement, gene tagging, *etc*. While we have so far mainly implemented this in our main reference species, *Aspergillus niger*, successful CRISPR/Cas9 strain engineering has also been done for *A. nidulans* (not yet published) and *Penicillium subrubescens*. We should acknowledge the highly valuable support of our collaborators Prof. Adrian Tsang (Concordia University, Canada) and Prof. Uffe Mortensen (DTU, Denmark), who provided vectors and protocols that highly facilitated the implementation of this method in our research. Kun *et al*. (2020) *Enzyme and Microbial Technology* **136**: 109508; Salazar-Cerezo *et al.* (2020) *Enzyme and Microbial Technology* **133**: 109463; Chroumpi *et al.* (2020) *Microbiological Research* **234**: 126426.



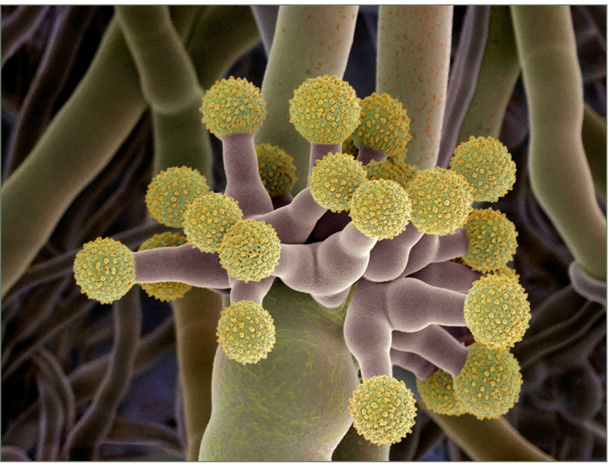
The project to obtain whole genome sequences of the genus *Aspergillus*, in which Ronald de Vries is a PI, continued with a comparison of the section *Flavi*, revealing both conservation and diversity within this section. Additional publications on other sections of the genus are in preparation. Kjærbølling *et al*. (2020). *Nature Communications* **11**: 1106.

FOOD AND INDOOR MYCOLOGY

Dr Jos Houbraken

Fungi may cause health issues and threaten food security

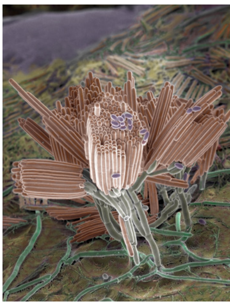
Fungi threaten the security of food supply to human populations in a number of ways. Firstly, they destroy up to 30% of crop products through disease and spoilage. Secondly, mycotoxin-production of food spoiling fungi leads to acute or long-term exposure to poisonous substances. Thirdly, some food or indoor fungi are opportunistic pathogens, which may lead to dangerous infection, mostly in immunocompromised persons. Fungi are also present in the indoor environment, where people spend the majority of their life. Fungal growth occurs when moisture is available and causes material deterioration and disfiguration. It can also lead to health issues such as allergic reactions and even infections. The species that colonise food as well as live in indoor environments (the mycobiota) are partially the same. In our group we perform research on fungi that occur in food and the indoor environment at a fundamental and applied level.

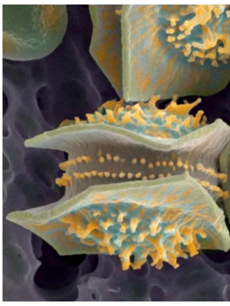


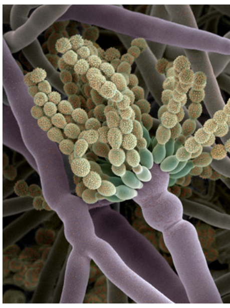
HIGHLIGHTS

The research group activities and highlights are centered on three main themes:

1. **Taxonomy and biodiversity**: In 2019–2020, we continued our polyphasic taxonomic research of fungi occurring in food and the indoor environment and used in biotechnology (e.g. *Penicillium*, *Aspergillus* and related genera, *Chaetomium*) using genomics, phenotypic treats and extrolite analysis, including mycotoxins. Important papers on classification and identification have been published and lists of accepted names were updated and expanded. Progress was made in linking this fundamental taxonomic research with rapid identification, typing and detection tools, such as wgMLST, STR and qPCR detection methods.
2. **Fundamental projects**: In order to understand the biology of food and indoor fungi, the fungal cell is studied, in particular on the topic of cell stress, with the aim to find novel solutions for prevention of food spoilage and fungal growth in the harsh indoor environment. In a TiFN funded project in collaboration with Utrecht University, Leiden University and Wageningen University & Research, we investigate the intraspecific variation for various stresses such as heat and antifungal compounds.
3. **Applied projects for industry and government**: Within the Service Unit, projects on food and indoor mycology were conducted varying from prevention of food spoilage, development of (rapid) identification tools and biodeterioration testing. Over 400 small and large projects for a diversity of clients (government, industrial, pharmaceutical, food and beverage, and commercial sectors) were performed on various mycological issues. These smaller projects regularly lead to larger grant proposals, and in 2020 NWO-TTW funded a project with the aim to study the cause leading to natamycin resistance of the cheese spoiling agent *Penicillium discolor*.







Houbraken *et al*. (2020). Classification of *Aspergillus*, *Penicillium*, *Talaromyces* and related genera (*Eurotiales*): An overview of families, genera, subgenera, sections, series and species. *Studies in Mycology* **95**: 5–169.

Van den Brule *et al*. (2020). The most heat-resistant conidia observed to date are formed by distinct strains of *Paecilomyces variotii*. *Environmental Microbiology* **2020**: 986–999.

Dijksterhuis *et al*. (2019). The preservative propionic acid differentially affects survival of conidia and germ tubes of feed spoilage fungi. *International Journal of Food Microbiology* **306**: 108–258.

MEDICAL MYCOLOGY

Dr Ferry Hagen

Antifungal resistance and rise of number of novel pathogens in the clinic - improving fungal diagnostics is key

Fungal infections impact the health of over a billion people, ranging from skin infections to serious life-threatening invasive infections that result each year in more than 1.5 million hospitalizations. Optimal treatment of invasive infections is restricted to a handful of antifungal compounds, which is increasingly complicated by the emergence of antifungal resistance and the rise of novel pathogens in the clinic, such as the multidrug-resistant yeast *Candida auris*. In addition to the ever-increasing resistance problem there is a need to further improve fungal diagnostics. For common fungal pathogens, like *Aspergillus* and *Pneumocystis*, molecular diagnostics is the standard, while there is a lack of fast and inexpensive detection and identification methods for the majority of clinically relevant yeasts and molds. We investigate how these new fungal pathogens emerge in a clinical environment and how they can be better detected and identified. This is studied by using a host-pathogen model, comparative genomics and large-scale epidemiological studies. To reach our goal to improve fungal diagnostics we collaborate with diagnostic laboratories worldwide.

HIGHLIGHTS

The multidrug-resistant yeast *Candida auris* was described a decade ago as a new species. Since then it rapidly dispersed globally causing large nosocomial outbreaks. We studied which typing method works most efficiently for this emerging pathogen. Siblings of *C. auris* emerge in the clinic too, which might be difficult to identify. Hence we apply nanopore genome sequencing in our laboratory to provide sequence data for molecular diagnostic assay design. To study the virulence potential of *Candida* species we have implemented the *Galleria mellonella* (greater wax moth) host-pathogen interaction model system. This was done in collaboration with the team of Prof. dr. Astrid Groot (IBED, University of Amsterdam).

Vatanshenassan *et al*. 2020. Evaluation of microsatellite typing, ITS sequencing, AFLP fingerprinting, MALDI-TOF MS, and Fourier-Transform Infrared Spectroscopy analysis of *Candida auris*. *Journal of Fungi* **6**: 146.

Extraordinary fungal infections, or those caused by atypical species, are part of our routine identification activities. Some notable examples are those of transplant-related infections, either caused by an infected transplanted organ or due to immune-suppression of the organ-recipient. *Cryptococcus neoformans* is well-known to cause infections in this patient-group. We described a cluster of cryptococcal infections among organ-recipients who developed cryptococcosis due to *Cryptococcus deuterogattii*. Using molecular tools we were able to link these cases to a single donor who was retrospectively diagnosed with cryptococcal meningitis as cause of death.

Santos *et al*. (2020). Donor-derived transmission of *Cryptococcus gattii sensu lato* in kidney transplant recipients. *Emerging Infectious Diseases* **26**: 1329–1331.

Fungal outbreaks are increasingly reported, mostly due to endemic mycoses like *Coccidioides* and *Histoplasma* but also due to antifungal resistant yeasts such as *Candida glabrata*. We use a wide variety of molecular typing tools to investigate fungal outbreaks and antifungal resistance, ranging from AFLP fingerprinting, microsatellite typing, multi-locus sequence typing to state-of-the-art nanopore sequencing.

Caceres *et al*. (2020). Detection and control of fungal outbreaks. *Mycopathologia* **185**: 741–745.

Dr Gerard Verkley

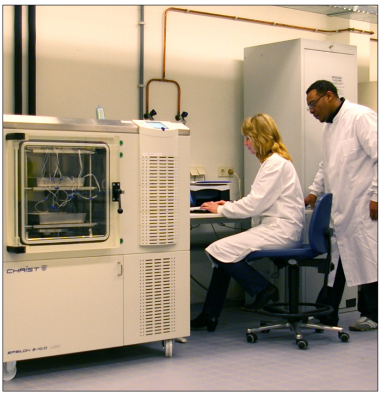
Our Collection is renowned for its high number of fungal ex-type strains

The Biological Resource Centre (BRC) of the Westerdijk Institute maintains the public CBS Collection of living fungi (established 1904), and the NCCB Collection of wild-type and mutant bacteria, plasmids and phages. In the period 2019–2020 the BRC acquired 2 890 new cultures and supplied 8 127 strains to scientists worldwide. The collection is renowned for its high number of ex-type strains, and 1 053 of these were added in 2019–2020, including new deposits and strains designated as epitype or neotype. Holdings of clinical fungi (>5 000 BSL-2 and BSL-3 strains) and fungi from unique environments around the globe are extensive. The online strain catalogue provides access to information on available cultures, as well as tools to identify fungi and yeasts by sequence BLAST and phenotypic analyses. The closed CBS Collection is an International Depository Authority under the Budapest Treaty for patent strains, and also offers the service of safe deposit. The BRC has been ISO 9001 certified since 2007.

Number of strains preserved in the BRC at December 31, 2020	
CBS strains	
Filamentous fungi	74 546
Yeasts	13 157
Oomycota	1 935
NCCB strains	
Bacteria	8 765
Actinobacteria	1 474
Plasmids	563
Total	**100 440**
Type strains	
Filamentous fungi	10 329
Oomycota	282
Yeasts	2 939
Total	**13 550**

Strain characterization for up-to-date identification and rapid selection for certain purposes

For all strains in the CBS Collection ITS and LSU rDNA sequences are generated and many have been made available on GenBank and the identification tool on the WI collection website (https://wi.knaw.nl/page/Pairwise_alignment). In addition, MALDI profiles are generated for CBS yeast strains. The CBS Collection is collaborating with the Joint Genome Institute and other partners to provide reference material for new Whole Genome Sequencing projects. The number of CBS strains for which genomes are available is rapidly increasing and by the end of 2020 amounted to 650. In the past two years, we have seen a strong increase in interest from industry to use our strains for screening on bioactive properties and other potential applications.



International collaboration

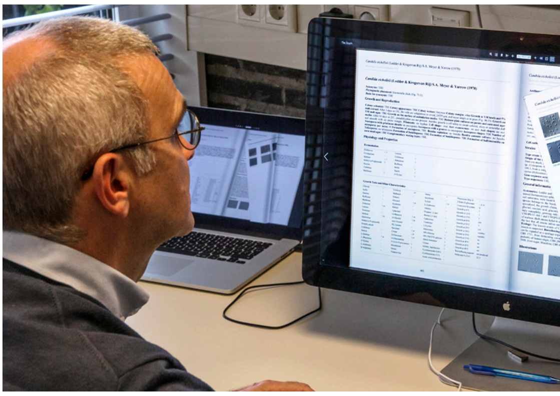
Our curators are actively involved in international fora for the implementation of the Nagoya Protocol (EU Consultation Forum, EU Guidance development for EU Regulation 511/214), and in further improving tools for compliance, such as best practice for culture collections (MIRRI Manual for ABS) and material deposit & transfer agreements (new ECCO models for MDA, MTA). In 2019, Gerard Verkley was elected President of the European Culture Collections' Organization (ECCO, www.eccosite.org), of which presently 76 collections from 26 European countries are member. Marizeth Groenewald serves as Secretary on the board of the World Federation of Culture Collection (WFCC, www.wfcc.info). From the start we have been involved in building the Microbial Resource Research Infrastructure (MIRRI, www.mirri.org), a pan-european RI of microbial BRCs. With 15 other collections and associated partners the Collection participates in the IS_MIRRI21 project (2020–2023), ismirri21.mirri.org, to work on common standards and improve BRC services in Europe.

BIOINFORMATICS, SOFTWARE DEVELOPMENT AND DATABASING

Dr Vincent Robert

Our databases and algorithms allow fast and reliable identifications and data analyses of large datasets

The Bioinformatics, Software development and Databasing group works on the creation and the maintenance of reference databases and websites including CBS collections, ISHAM Barcoding and MLST, MycoBank, MIRRI, Q-Bank and other fungal molecular databases. Specific software has been created for the management, analysis and publication of large and complex collections of scientific data that are being used at the Westerdijk Institute as well as in many research groups or companies distributed globally. We also develop algorithms that allow fast and reliable identifications and data analyses of large datasets. We create new clustering and comparison algorithms that are much faster and more accurate than the existing ones. Currently we are developing new methods to store and analyze large amounts of data, including MALDI-TOF MS profiles or complete genomes. These are huge challenges given the complexity and the diversity of fungal genomes. We are working on the establishment of a new workflow management system and the integration of data analyses pipelines.

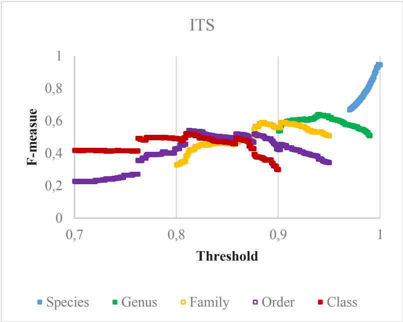


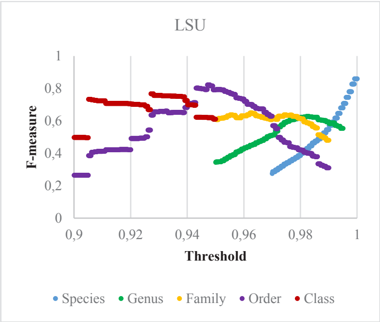
HIGHLIGHTS

We participate in several international initiatives and projects. One of them is the EOSC-Life project that intends to create an open collaborative digital space for life science in the European Open Science Cloud (EOSC). We are also actively working on the construction of the Microbial Resource Research Infrastructure for which we are building the database, website, web services and creating scripts to import and maintain data.

One of our long-term research subjects related to microbial growth temperatures and the rise of *Candida auris* received a lot of media attention in 2019. We hypothesize that global warming is a major driver in the emergence of new fungal pathogens.

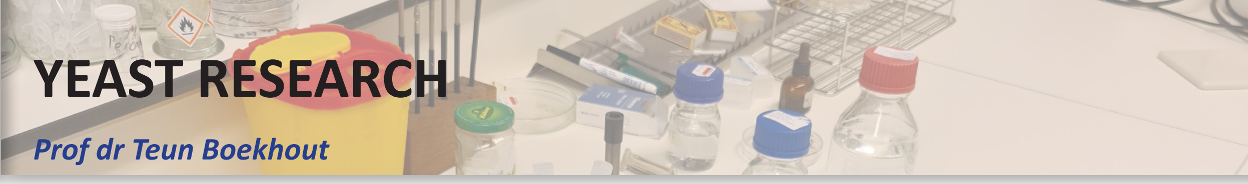
Casadevall *et al*. (2019). On the emergence of *Candida auris*: climate change, azoles, swamps, and birds. *mBio* **10**(4) e01397-19.





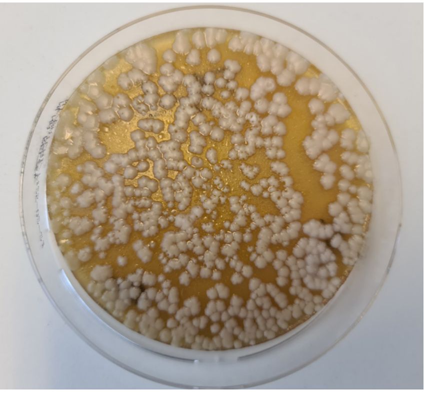
Another highlight was the release and analysis of more than 24 000 DNA barcode sequences of 12 000 ex-type and manually validated filamentous fungal strains of 7 300 accepted species. This was a result of a project funded in the Netherlands to barcode specimens of major national biobanks in which sequences of two nuclear ribosomal genetic markers, the Internal Transcribed Spaces and (ITS) and the D1/D2 domain of the 26S Large Subunit (LSU), were generated as DNA barcode data for *ca*. 100 000 fungal strains originally assigned to *ca*. 17 000 species in the CBS fungal biobank maintained at the Westerdijk Institute. Based on the large amount of released barcodes, we were able to reveal thresholds and accuracy for fungal species and higher taxon delimitation. The DNA barcodes have been submitted to GenBank and are available at the Westerdijk Institute's website as reference sequences for fungal identification, marking an unprecedented data release event in global fungal barcoding efforts to date.

Vu *et al*. (2019). Large-scale generation and analysis of filamentous fungal DNA barcodes boosts coverage for kingdom fungi and reveals thresholds for fungal species and higher taxon delimitation. *Studies in Mycology* **92**: 135–154.



Malassezia*: The most predominant fungal genus of the human skin microbiome - friend or foe?*

The genus *Malassezia* has increasingly become one of the focal points in the yeast research group. From an evolutionary perspective, this yeast is unique in its lipid-dependence, a likely result of a host-shift from plant to animal skin, including humans. There, it resides as a ubiquitous commensal but can also cause various skin diseases, such as dandruff/seborrheic dermatitis, pityriasis versicolor and atopic dermatitis. In recent years, an even more striking role in pathogenesis has been reported for this yeast: i.e., as an emerging pathogen in (neonatal) bloodstream infections (Rhimi *et al*. 2020), linked with gut health and disease (e.g. Inflammatory Bowel Diseases), and promoting pancreatic cancer. We aim to link observed genetic/genomic variation to evolutionary processes, such as mating and hybridization, and explore how this may affect pathogenicity and adaptation to new niches. In recent years, hybrid origins for multiple yeast species have been identified, including the opportunistic pathogen *Candida inconspicua* (Mixão *et al*. 2019). We found proof of multiple unique hybridization events in the *Malassezia furfur* species complex, a phenomenon frequently associated with speciation, adaptation and pathogenicity.



HIGHLIGHTS

The impact of *Malassezia furfur* in deep-seated infections has especially been observed in premature neonates receiving parenteral lipid-rich nutrition and its emergence may in part be the result of unintended selection through fluconazole prophylaxis in the clinic. Together with clinicians from hospitals in Italy and Russia we are studying the epidemiology of this phenomenon.

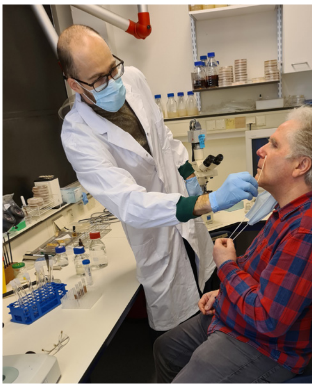
Considering the above-mentioned new areas of clinical relevance, we are utilizing novel DNA target regions for the development of sensitive diagnostic tools, applicable in complex clinical samples such as blood and gut.

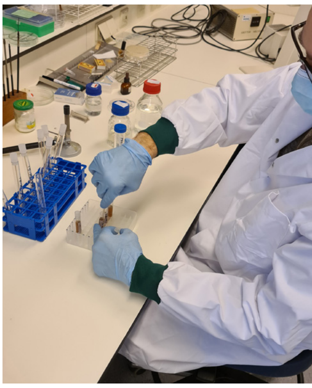
Another approach to gather insight in the fascinating dual role of *Malassezia* - that of harmless or even beneficial commensal *vs* disease causing state - is to consider *Malassezia* as a member of the (skin) microbiome. Sampling of the yeast from a well-controlled study group and from both healthy and diseased skin, may reveal new information about the conditions under which this yeast can become a problem for human health, and may help in finding novel treatment solutions. For this, we collaborate with a Dutch clinical research center, also adding to increased knowledge about the role of *Malassezia* in Dutch populations.

In 2020, Teun Boekhout co-organized with Thomas Dawson (Singapore) and Wonhee Jung (Korea) the fourth International Workshop on *Malassezia*, due to the corona pandemic for the first time held on a virtual platform, hosted in Korea. Over a period of two weeks, 240 scientists from 37 countries shared content through discussions, 16 oral presentations and 21 posters, dealing only with *Malassezia* research. Bart Theelen chaired one of the topics/sessions and gave a plenary talk on part of his PhD research.

Rhimi *et al*. (2020). *Malassezia* spp. yeasts of emerging concern in fungemia. *Frontiers in Cellular and Infection Microbiology* **10**: 370.

Mixão *et al*. (2019). Whole-genome sequencing of the opportunistic yeast pathogen *Candida inconspicua* uncovers its hybrid origin. *Frontiers in Genetics* **10**: 383.





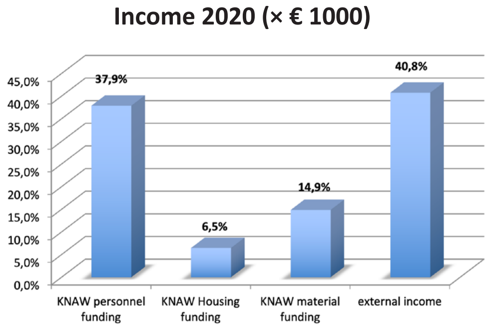
Pictures to the right show Bart Theelen sampling Teun Boekhout for *Malassezia* spp., the most predominant fungal genus of human skin microbiota.

FINANCES AND STAFF

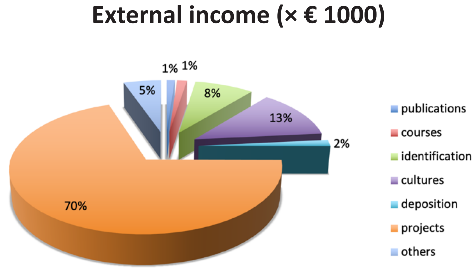
The low rate of absenteeism in the institute is indicative of a healthy workplace environment

INCOME

The Westerdijk Institute has a total income of € 6.69 M. Of this amount, 56% is funded by the KNAW (€ 3.9 M).



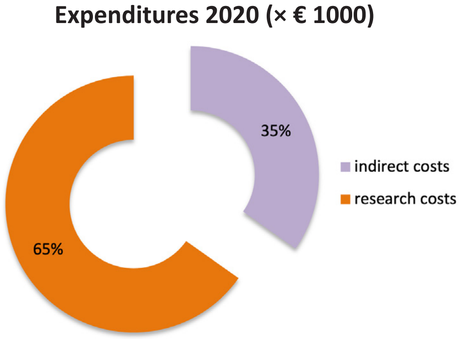
Of the external income, 70% is related to projects (€ 1.9 M). 26% (€ 699 K) of the external income is directly or indirectly derived from the collections and activities such as book sales, training and courses, as well as identification/sales of fungi and bacteria. The Odo van Vloten Foundation finances one postdoc research project.



EXPENDITURES

The total expenditure of the Westerdijk Institute (€ 6.7 M) consists mainly of salaries (60%). Non-personnel costs are costs of materials, housing, and depreciation of durable equipment and intangible assets, e.g. software.

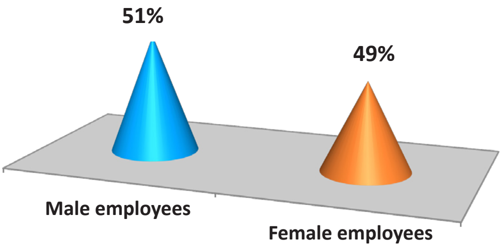
65% of the expenditures can be indicated as direct research costs. Indirect costs (35%) are for management, maintenance of the collection and for the collective support division of the Westerdijk Institute and the Hubrecht Institute.



STAFF

In December 2020 the Westerdijk Institute employed 53 FTE, of which 27 FTE research staff; 22 FTE analytical and technical support staff (for the research groups and preservation and digitalization of the collection); and 4 FTE administrative support staff. 33 FTE (62%) are employed with an appointment for an indefinite period of time.

The gender division of the staff was: female 25 FTE (47%) and male 28 FTE (53%). In headcount: female 29 (49%) and male 30 (51%).



The Westerdijk Institute employs three full professors. Ultimo 2020 the Westerdijk Institute hosted 24 promovendi.

The Westerdijk Institute has a happy working environment with a low rate of sick leave: at 0.98% annually, it is one of the lowest rates within the Royal Netherlands Academy of Arts and Sciences (KNAW).

Westerdijk Fungal Biodiversity Institute

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“Studies in Mycology” online via Elsevier (www.studiesinmycology.org)
“Fungal Systematics and Evolution” online via Ingenta (http://fuse-journal.org)
"Persoonia" online via Ingenta (https://www.persoonia.org)

Pictures by Westerdijk Fungal Biodiversity Institute & Photographers Thijs Rooimans and Christopher Paul