Project Details	
Project Code	MRCIIAR26Ex Yvon-Durocher
Title	Quantifying Rapid Evolution of Thermal Tolerance in the Novel Pathogenic Fungus Candida auris (Candidozyma auris)
Research Theme	IIAR
Project Type	Wet lab
Summary	Periodic episodes of high temperature associated with global climate change may be driving changes in the host range of pathogens, potentially enabling high temperature adapted fungi to make host jumps into human and warm-blooded animals. In this project we will explore how and whether the recently emerged drug-resistant fungal pathogen Candida auris, (now renamed Candidozyma auris) has adapted to rising temperatures. We will compare human fungal pathogens of the Candida and related genera for their thermal tolerance profiles and use serial in vitro adaptation experiments to assess the physiological traits that correlate with thermal adaptation.
Description	Candida auris has rapidly emerged as a significant global health threat due to its remarkable capacity to cause superficial and invasive infections, its resistance to antifungal drugs, and its ability to persistently colonize healthcare environments. It is now known why multiple clades of C. auris have emerged almost simultaneously on multiple continents in the last 15-20 years. This highlights major gaps in our understanding of its evolutionary and ecological adaptation. Recent research underscores the critical role of environmental changes, including global warming and widespread fungicide usage, in promoting the emergence and adaptation of fungal pathogens capable of overcoming mammalian thermal barriers. Given the escalating incidence and severity of invasive fungal infections, it is essential to understand the limits and mechanisms underlying thermal tolerance in C. auris to predict and manage its potential threats. This project addresses crucial gaps by comprehensively investigating how C. auris and related environmental Candida species respond to elevated temperatures, evolve in response to climatic changes, and how these adaptations may impact their resistance to antifungal treatments and other stressors and their immunological profile. By integrating physiological studies with advanced multi-omics approaches—genomics, transcriptomics, and proteomics—this project aims to delineate the complex physiological and molecular mechanisms underlying fungal thermal tolerance and pathogen emergence and the consequences of these changes to the virulence of the fungus. **Objectives:** 1. Characterise the thermal tolerance limits and physiological mechanisms in C. auris and related environmental Candida species: Determine the thermal performance curves, including optimal growth temperatures and lethal temperature thresholds across diverse Candida strains. Apply genomic sequencing, transcriptomic profiling, and proteomic analyses to identify the genetic and molecular determinants underpinning thermal tolerance. 2. Quantify the capacity for rapid evolution of increased thermal tolerance due to climate warming:

- Conduct laboratory-based experimental evolution studies (via serial passage experiments) to track adaptive changes in C. auris and environmental Candida species under increased temperatures.
- Employ genomic sequencing and comparative transcriptomic analyses to identify mutations and gene expression shifts associated with rapid thermal adaptation.

3. Assess cross-tolerance, including increased resistance to antifungal agents and environmental stressors:

- Investigate whether thermal-adapted Candida strains exhibit cross-resistance to antifungal drugs, thereby increasing their potential to become clinically significant pathogens.
- Use comprehensive proteomic and transcriptomic analyses coupled with antifungal susceptibility assays to evaluate the interplay between thermal adaptation, drug resistance, and broader environmental stress responses.

4. Assess whether thermal adaptation induces changes in the immune and pathogenicity profile of C. auris that has the impact to further affect its pathogenicity:

- Investigate how immune recognition by C-type lectins are altered by strains undergoing thermos-adaptation
- Determine whether the interaction of C. auris with human macrophages and neutrophils (ROS production, phagocytosis, fungal killing, cytokine secretions) are altered in high temperature adapted strains.
- Deterine whether high temperature adapted strains are altered in their virulence using a Galleria infection model.

Through an interdisciplinary approach combining microbiology, evolutionary biology, medical mycology, immunology and environmental sciences, this research will elucidate critical aspects of fungal adaptation in response to global climate change, particularly the potential emergence of novel pathogens. The integration of physiological and cutting-edge multi-omics techniques ensures robust and detailed insights into the adaptive mechanisms of C. auris, enabling better prediction and control strategies.

The project will benefit from the extensive expertise and state-of-the-art facilities available at the University of Exeter and University of Bristol, with supervision provided by Prof. Gabriel Yvon-Durocher, Prof. Neil Gow and Dr. Borko Amulic. Prof. Yvon-Durocher brings critical insights into microbial thermal ecology and evolutionary biology, Prof. Gow contributes significant expertise in medical mycology and fungal pathogenicity and Dr. Borko Amulic is an expert in host-pathogen interactions focusing on deciphering how innate immune cells respond to fungi. Collaboratively leveraging the resources of the Living Systems Institute and the Centre for Medical Mycology at the University of Exeter and the School of Cellular and Molecular Medicine at the University of Bristol, this project will position us to better understand, anticipate, and manage emerging fungal threats in a warming world.

Supervisory Team	
Lead Supervisor	
Name	Professor Gabriel Yvon-Durocher
Affiliation	Exeter
College/Faculty	Environment Science and Economy
Department/School	Geography
Email Address	g.yvon-durocher@exeter.ac.uk
Co-Supervisor 1	
Name	Professor Neil Gow
Affiliation	Exeter
College/Faculty	Health and Life Sciences
Department/School	Bioscience
Co-Supervisor 2	
Name	Dr Borko Amulic
Affiliation	Bristol
College/Faculty	
Department/School	School of Cellular and Molecular Medicine
Co-Supervisor 3	
Name	
Affiliation	
College/Faculty	
Department/School	