

Fungal stress biology: a preface to the *Fungal Stress Responses* special edition

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Abstract There is currently an urgent need to increase global food security, reverse the trends of increasing cancer rates, protect environmental health, and mitigate climate change. Toward these ends, it is imperative to improve soil health and crop productivity, reduce food spoilage, reduce pesticide usage by increasing the use of biological control, optimize bioremediation of polluted sites, and generate energy from sustainable sources such as biofuels. This review focuses on fungi that can help provide solutions to such problems. We discuss key aspects of fungal stress biology in the context of the papers published in this Special Issue of Current Genetics. This area of biology has relevance to pure and applied research on fungal (and indeed other) systems, including biological control of insect pests, roles of saprotrophic fungi in agriculture and forestry, mycotoxin contamination

of the food-supply chain, optimization of microbial fermentations including those used for bioethanol production, plant pathology, the limits of life on Earth, and astrobiology.

Keywords Acid, alkali, chaotrope, ethanol, heat, hypoxic, osmotic, and salt stress · *Aspergillus wentii* · Astrobiology · *Beauveria bassiana* · Biofuels · *Cochliobolus heterostrophus* · Compatible solutes · *Cryomyces antarcticus* · Entomopathogenic fungi · Erythritol and mannitol · *Fusarium graminearum* · *Hortaea werneckii* · *Metarhizium robertsii* · *Neurospora crassa* · *Saccharomyces cerevisiae* · Trehalose · *Trichoderma atroviride* · UV-B radiation tolerance

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Introduction

This Special Issue *Fungal Stress Responses* is dedicated to understanding how fungi, important in natural and

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industrial systems, and for fields ranging from agriculture to astrobiology, can sense and cope with stress. Due to their ubiquitous nature and their extreme variation in growth phenotype, metabolite production, and response(s) to the environment, fungi have the potential to mitigate some of the world's most pressing problems. Fungi play central roles in agriculture, biotechnology, and basic research: they produce molecules used in the pharmaceutical, energy-producing, and food industries, and play important ecological roles. Because most of these applications impose complex and dynamic challenges and stresses upon the fungal cell, it is imperative to elucidate the stress biology of fungi. Furthermore, this can lead to knowledge-based approaches to manipulate and optimize processes driven by these microbes.

The papers in this Special Issue cover a wide range of organisms, both in their natural habitats and in industrial or other anthropogenic systems, such as agriculture. Collectively, these studies relate fungal ecology, cell biology, biophysical mechanisms, and molecular and physiological responses to stress. Here, we summarize the main outline of these articles.

Topics covered in this special issue

Insect-pathogenic fungi are used as model systems that not only have special significance for biological control, but are also pertinent to other aspects of fungal stress biology. Ortiz-Urquiza and Keyhani (2014) explain that the concept of stress has been rather poorly defined, and that related terminology may be used to refer to any/all condition(s) that differ from the optimum. This might imply that every change in condition can be interpreted as “stressful”, and as numerous parameters are in a constant state of flux, organisms are continuously exposed to stress. During infection of the insect host, several, more-profound stresses affect the fungal cells. The authors discuss both the fungi *Beauveria bassiana* and *Metarhizium robertsii*, and address the biochemical pathways during a number of stress responses including water loss, reactive oxygen species, and UV radiation. For both species, responses to these stresses include the accumulation of compatible solutes, enzymatic and non-enzymatic scavenging of reactive oxygen species, pigment synthesis, and the induction of DNA-damage repair systems. Many examples are given of molecules involved in signaling from membrane proteins and receptors (e.g., G-proteins and tetraspanins) toward downstream signaling pathways (such as MAP kinase cascades and cAMP-PKA pathways), ultimately leading to the transcription factors that activate genes. Regulation of the stress response during infection is a sensitive and intimate process, as demonstrated by the observation that an adenylate cyclase

deletion mutant of *M. robertsii* has only a slightly impaired virulence, while the gene disruption of the downstream PKA catalytic subunit results in a reduction of virulence of 90 %. In addition, cross talk of different signaling pathways is observed in *B. bassiana*, as deletion mutants of the Slt2 MAP kinase pathway (involved in cell wall sensing) resulted in reduced phosphorylation of the transcription factor of another pathway, namely Hog1 (involved in osmotic stress response). The authors conclude that the intricacies of signaling processes (e.g., the roles of epigenetic mechanisms) require more extensive study.

The genus *Metarhizium* includes remarkably versatile fungi that live as saprotrophs, in association with plants (e.g., as growth promoters), and as organisms that are pathogenic to insects. In their article, “Stress is the rule rather than the exception for *Metarhizium*”, Lovett and St. Leger (2014) also detail an example of transfer of nitrogen from insect cadavers to plants, a dramatic illustration of the intricate ecological networks that occur in soil. The authors follow the infection process and discuss the role of a large number of important molecular factors. For instance, the adhesin MAD1 and hydrophobins during adherence of a perilipin that regulates the turgor pressure of infection structures in the hemocoel is discussed. They highlight the stresses encountered during infection, including nutrient stresses experienced on the cuticle, oxidative stress within the cuticle, and osmotic stress within the hemocoel. Interestingly, it is upon emergence from the host that fungi face what is arguably the most formidable stress; i.e., UV exposure. This is also one of the key environmental factors which limit the effectiveness of these fungi as biological control agents. The authors state that many stress-related genes of *Metarhizium* have a pleiotropic nature, probably related to the battery of different environmental inputs that the fungus has to respond to. Genetic engineering has the potential, therefore, to increase the stress tolerance of this fungus.

Eleutherio et al. (2014) provide an authoritative review regarding the synthesis and breakdown of trehalose in *S. cerevisiae* and applications of trehalose metabolism in yeast and other organisms. They explain what we know and, importantly, what we might still need to discover by placing current knowledge in the context of scientific developments throughout the history of this field. The storyline explores the idiosyncratic character and behavior of this disaccharide and its roles in the protection against multiple stresses. A variety of stress-protection mechanisms are discussed, including water replacement during membrane desiccation, glass formation, and the preferential exclusion hypothesis. In a recent review focusing on biofuel fermentation (Cray et al. 2015), Eleutherio and collaborators also explore the role of kosmotropic activity, a key activity related to the modes-of-action of other compatible solutes (see below; Cray et al. 2013; Ball and Hallsworth

2015). The molecular biology of trehalose synthesis (common to many types of living system) and its regulation are examined in detail, with a focus on the TPS/TPP pathway in *S. cerevisiae*. As the authors explain, trehalose transport across the plasma membrane is key to effective stress protection, because trehalose must be located on both sides of the bilayer, and yet the mechanism(s) involved in the presumed re-assimilation of extracellular trehalose are yet to be elucidated. Hydrolysis of trehalose can provide the cell with the energy required to recover from stress. In addition, Eleutherio et al. (2014) provide intriguing insights into the role of trehalose metabolism in the biology of host infection by pathogenic microbes, and they allude to a variety of therapies to control infectious diseases.

It is likely that the capacity of fungal cells to sense and respond to visible light originated as a mechanism of defense against the consequences of harmful UV radiation and other damage that can be inflicted by excessive exposure. Biological clocks that run according to a daily cycle (circadian clocks) allow cells to anticipate the presence of light and prepare for daily changes in light and temperature. Fungi use light as a signal from the environment to regulate pigment biosynthesis, development, and entrain the circadian clock. The ascomycete *Neurospora crassa* has been used as a model for fungal photobiology and clock regulation. The key component of *N. crassa* photoreception is the white collar complex (WCC), a light-responsive transcription factor complex, but the genome contains genes for other types of photoreceptors. They include another type of blue light photoreceptor (cryptochrome), an opsin that is similar to the vertebrate photoreceptors, and two red light photoreceptors (phytochromes). The surge in fungal genome-sequencing projects has catalyzed the identification of fungal photoreceptors in many other species and their role in the photobiology of fungi is being actively investigated. Fuller et al. (2014) summarize in their review “Fungal photobiology: visible light as a signal for stress, space and time” our current knowledge on fungal photobiology with a detailed description of the role of the different types of photoreceptors in *N. crassa* and other fungi. The discovery that some pathogenic fungi use light as a signal during pathogenesis suggests new avenues of research to understand the mechanism of environmental sensing by fungal pathogens and new approaches to treat diseases using photoreceptors as antifungal targets.

Further insights into the stress biology of insect-pathogenic fungi are provided by Huarte-Bonnet et al. (2014), who home in on one stage of infection. “Oxidative stress in entomopathogenic fungi grown on insect-like hydrocarbons” studies the growth of *B. bassiana* on media containing hydrocarbons that feed the fungus when it is on the cuticle of insects. This imposes very specific stresses on the fungi, which now have to deal with reactive oxygen species

that must be degraded effectively within the cytoplasm as well as inside peroxisomes. Huarte-Bonnet et al. observe increases in superoxide dismutase and catalase levels when the fungus is inoculated onto hydrocarbon-supplemented media. This was confirmed by qRT-PCR measurements, which detected a substantial increase in expression levels for the *sod1*, *catA*, *catB*, and *catP* genes. Glutathione peroxidase was also induced, suggesting the removal of peroxides by cooperation between different enzymes. Huarte-Bonnet et al. provide a lucid, detailed discussion relating to the consequences of growth on cuticle hydrocarbons including the role of cytochrome P450 enzymes (CYP).

The cellular responses to osmotic stress in the yeast *S. cerevisiae* provide the focus for the review of the review by Solé et al. (2014). The key regulator of the response to osmotic stress is the protein kinase Hog1 (homologous to p38 in other organisms), and the authors review the role of this protein during the transcriptional changes that occur during the response to osmotic stress. One of the consequences of osmotic stress is a delay in the cell cycle, which provides time to adapt to the stress before resuming growth. Hog1 modulates the cell cycle arrest after osmotic stress by phosphorylation of several regulators of the cell cycle. A new layer of regulation to the cellular response to stress was introduced with the discovery of ~200 long non-coding RNAs (lncRNAs) that are strongly and rapidly induced upon osmotic stress. About 90 of these lncRNAs required Hog1, and the authors focused on the regulation of one of them, the lncRNA that is complementary to the *CDC28* gene, encoding the main cyclin-dependent kinase (CDK) of yeast. *Cdc28* regulates the cell cycle, and the authors found that the lncRNA participates in the induction of *CDC28* expression to facilitate the re-entry of the cell into the cell cycle after stress. The regulation occurs through a looping mechanism that allows the relocalization of Hog1 in the promoter of *CDC28* to promote additional protein interactions that result in the activation of transcription. Hog1 homologs may operate through similar mechanisms for transcriptional regulation in other fungi.

The accumulation of pigments may provide protection against excessive visible light, UV radiation, and oxidative stress. Carotenoids are terpenoids with antioxidant properties and have a wide absorption in the visible part of the light spectrum. The accumulation of various types of carotenoids, in many cases after exposure to light, suggests that these pigments may protect the fungal cell from damage caused by excessive illumination. The review by Avalos and Limón (2014) contains a comprehensive analysis of our current knowledge on the biosynthesis and roles of carotenoids and derivatives, in the context of fungal biology. The authors describe the chemical properties and roles of the carotenoids that accumulate in several fungal species, the enzymes that participate in their biosynthesis, and

their regulation. Carotenoid derivatives, such as trisporic acids and retinal, play relevant roles in certain fungi and act as sexual hormones or chromophores.

Medina et al. (2014) examined the effects of high solute concentrations (i.e., low water activity) and temperature on the accumulation of compatible solutes and expression of genes involved in sugar transport and mycotoxin production for xerotolerant/xerophilic fungi. Their paper reports a systems-inspired approach based on quantification of fungal growth rates, intracellular compatible solutes, mycotoxin concentrations, gene expression for key genes involved in sugar transport and mycotoxin production, and creation of a model that can be used to predict conditions under which production of mycotoxins occurs. The solute stressors studied were NaCl, which is an ionic osmotic stressor, and glycerol, which reduces water activity (and is chaotropic at high concentrations) and yet does not impose osmotic stress (see Alves et al. 2015 in this Special Issue). Medina et al. focus on interactions between temperature and stressor concentration as determinants for aspects of fungal growth phenotype and physiology in *Aspergillus*, *Penicillium*, and *Fusarium*. Interestingly, they report a link between up-regulation of sugar transport genes, stress tolerance, and mycotoxin production, which is consistent with both the high energy requirement for tolerance of extreme and multiple stresses, and studies suggesting that the robust stress biology of *Aspergillus* species is linked to an enhanced primary metabolism, i.e., increased flux in glycolysis and the TCA cycle (Flippin et al. 2009). The findings of Medina et al. provide key insights needed to understand the high competitive ability of fungi such as *Aspergillus* species, which can dominate their favored habitats (Cray et al. 2013) and can also be used by agriculturalists and the food industry to prevent mycotoxin contamination of foods and feeds. Furthermore, strains of *A. flavus* that have deletions in genes involved in the mycotoxin synthesis are being successfully used to competitively exclude toxigenic strains and reduce aflatoxin contamination of peanuts, maize, and cotton (Ehrlich et al. 2015).

In their article “Rock black fungi: excellence in the extremes, from Antarctic to space”, Selbmann et al. (2014) review the biology and phylogeny of rock-dwelling black meristematic fungi that can survive at the interface between biology and physics. Such organisms afford insights into early terrestrial life on Earth that was associated with mineral and saline environments. The focus is on diversity, taxonomy, and stress tolerance of black meristematic fungi in the Antarctic, a continent where life “more than on any other continent, is dominated by microbes”. These fungi, located mainly in two orders of the Ascomycota, are variously known as black meristematic fungi, black fungi, black yeasts (when inhabiting rocks), and microcolonial or rock-inhabiting fungi. As Selbmann et al. explain, black

meristematic fungi are typically polyextremotolerant, rather than extremophilic; their high melanin content gives rise to their exceptional resistance to UV. Selbmann et al. also discuss the link between high melanin levels in black meristematic fungi and efficient retention of the compatible solute glycerol; many other extremely stress-tolerant microbes also have other special adaptations of compatible solute metabolism which contribute to their robust biology. The authors predict a resurgence of research activity into the biology of black meristematic fungi, now that genome sequencing enables the use of various ‘-omics’ (and systems) approaches. This is indeed likely, given that the genome sequences of species such as *Hortaea werneckii* and *Cryomyces antarcticus* have recently been published. Furthermore, there is an urgent need to understand these charismatic microbes before climate change endangers their primary habitat.

The paper by Shalaby and Horwitz (2014) reviews the possible role of plant phenolic compounds as signals influencing fungal responses to oxidative stress during interactions with plants. The mode-of-action of some phenolic compounds is known to be mediated by their chaotropic activities (Cray et al. 2014, 2015). Fungi interacting with plants perceive a range of different plant compounds: phenolics and related compounds are ubiquitous in plant cell walls and likely to be encountered by invading pathogens. The authors review responses to different pre-formed and induced phenolics in an attempt to establish connections between studies of signaling and metabolism. Fungal pathogens may metabolize phenolic compounds or respond to them as signals, or both, and the authors suggest that fungal responses to phenolics and oxidants are integrated. Features of the molecular cross talk between plants and prokaryotic pathogens or symbionts are discussed including the possibility of specific recognition of different classes of phenolic compounds in interactions involving *Agrobacterium tumefaciens* VirA. Evidence from prokaryotic systems is discussed in relation to understanding of recognition of phenols by fungi, in particular in studies of the pathogens *Cochliobolus heterostrophus* and *Fusarium graminearum*. Phenolics may provide either antioxidant or pro-oxidant signals to modulate secondary metabolite production, and the authors suggest that better understanding of how fungal pathogens detect plant phenolic compounds as stress signals may facilitate the development of new strategies for control of fungal plant pathogens.

Mechanical damage to microbial cells can break the integrity of the cellular membrane and cause lethality. Whereas all living systems may have developed ways to cope with mechanical injuries, most research has focused on the mechanisms of response to injury in plants and animals. Hyphal breakage upon mechanical injury was previously characterized in fungi (Leonard and Dick 1973) and

the discovery that injuries promote the activation of asexual development in the ascomycete *Trichoderma atroviride* has enabled the elucidation of the molecular mechanism of this phenomenon using a combination of genetics and genomics. The review by Hernández-Oñate and Herrera-Estrella (2015) summarizes our current knowledge of the mechanisms of the response to injury in *T. atroviride* with the participation of calcium, the production of reactive oxygen species, the regulatory network of MAP kinases, and the lipid signaling pathways. The observations that several of the signaling molecules and the mechanisms that mediate the response to cellular damage are conserved across plant, animal, and fungal species suggest an ancient origin. The authors propose that fungi could be used as models to understand the mechanism of response to mechanical injuries in other types of eukaryotic cells.

The paper by Hohmann (2015) reviews recent progress in understanding osmoregulation in eukaryotes, concentrating in particular on the different roles of Hog1 in glycerol accumulation and volume recovery in yeast. Osmoregulation is critical for cell shape and turgor as well as intracellular dynamics. Glycerol at high concentrations can act as a stressor (Hallsworth et al. 1998; Williams and Hallsworth 2009; Alves et al. 2015) and is used as a compatible solute, playing diverse roles in yeast physiology. The author summarizes different aspects of the HOG MAPK signaling pathway, including the Sln1 branch and the Sho1 branch that appear to function independently and have different roles. The author reviews studies of how the HOG MAPK pathway communicates with other yeast MAPK pathways to control cell morphogenesis and how cross talk between the MAPK pathways has recently been used to re-wire osmostress-controlled expression of glycerol biosynthesis genes from Hog1 to Kss1-Fus3. The re-routed osmoregulation system offers opportunities to study osmoadaptation in yeast in the absence of the Hog1 kinase and may prove a useful tool to elucidate Hog1-dependent and independent mechanisms as well as redundancy and robustness of the MAPK system. However, the author also points out that we still lack a systems-level understanding of the interaction of the diverse MAPK signaling pathways in controlling homeostasis and morphogenesis, especially under non-stress conditions, and that many details of the Fps1 glycerol channel are still lacking.

The article entitled “Stress tolerance and virulence of insect-pathogenic fungi are determined by environmental conditions during conidial formation” by Rangel et al. (2015) focuses on the ways the conidial tolerance of entomopathogenic fungi to heat and UV-B radiation is influenced by environmental factors. The data demonstrates that physical, chemical, and nutritional conditions, which are present during mycelial growth, result in pronounced differences in the way the conidia subsequently survive stressful conditions.

The evidence comes from the investigation of the stress phenotypes of *Metarhizium robertsii*, which was grown on complex medium versus minimal medium. When conidia were produced on minimal medium, it was able to germinate more efficiently and was more resistant to heat and more virulent to insects than when grown on complex medium (see also Rangel et al. 2006a, 2008a, b). Among the conditions that induced higher tolerance to heat or UV-B radiation were the lack of water content and high alkalinity. However, this resistance and the associated robust phenotype come at a price of low conidial yield. Rangel et al. (2015) give insights into the physicochemical properties and ecophysiological roles of erythritol, trehalose, and mannitol in relation to fungal cell biology (see also Alves et al. 2015; Rangel et al. 2006a, b, 2008a, b). The authors have also shown that three levels of phenotypic plasticity occur for stress tolerance exhibited by *M. robertsii*, and this has profound consequences for its stress biology, virulence, and ecology. The authors concluded that physical and chemical parameters in combination with the nutritional factors can result in the significant difference in the conidial response to stress and can be exploited in the production of the entomopathogenic fungi for biological control.

The article by Braga et al. (2015) provides a clear explanation of the interactions between fungal conidia and solar radiation. Conidia are extremely important for the environmental persistence of the filamentous fungi, as well as for host recognition and infection of the pathogenic species of fungi. As both solar UV-A and UV-B can kill the conidia, as well as limit the proliferation and dispersion of fungi, it is important to summarize the available knowledge of the effects of solar radiation on conidia and on the major systems involved in the protection and repair of damage induced by solar UV radiation. The authors also assure the importance of the fungal pigmentation on conidial UV tolerance as published elsewhere (Braga et al. 2006; Rangel et al. 2006b). The review demonstrated that it is possible to manipulate fungi in laboratory conditions so that the resulting strains produce conidia that are more tolerant to solar radiation than wild type.

The article by Fernandes et al. (2015) covers aspects of UV radiation from sunlight, which is the most detrimental environmental factor that affects the viability of entomopathogenic fungi applied for pest control. The outcomes of studies on this topic can be affected by two compounding factors: the sensitivity of most entomopathogenic fungi to UV radiation and the variability of the laboratory methods that are used to study the UV sensitivity of entomopathogenic fungi. The review carefully analyzes several studies that have applied different methods for testing of natural and enhanced susceptibility to UV and makes inter- and intra-species comparisons. Both inter- and intra-species variability probably result from

the adaptation(s) of individual strains to diverse natural habitats/sets of conditions. Thus, the selection of strains with the best inherent tolerance to UV is an important step to select the most promising entomopathogenic fungi as biological control agents. Isolate screening for better tolerance to UV radiation as documented by Fernandes et al. (2015) as well as screening for superior tolerance to heat and higher virulence as documented elsewhere (Alston et al. 2005; Rangel et al. 2005, 2010; Fernandes et al. 2008, 2009, 2010, 2011) are important for the successful biological control of insects in agriculture. Although the use of UV lamps in the laboratory does not represent the complexity of the field tests, it does provide a useful technique to help find ways to increase the resistance to UV radiation of entomopathogenic fungi, which will eventually undergo the ultimate tests under field conditions.

The paper by (Hillmann et al. 2015) reviews recent studies of metabolic changes in filamentous fungi during adaptation to hypoxia. A better understanding of these changes and how they are regulated is important, because recent research suggests that adaptation to hypoxia is an important virulence trait of pathogenic fungi. The authors discuss studies of model organisms in the genus *Aspergillus* and suggest that most species have the capacity to grow in atmospheres with sparse amounts of oxygen, but none grows in the complete absence of oxygen. Recent ‘-omics’ studies designed to elucidate the metabolic and energetic consequences of oxygen limitation are discussed with regard to their relevance in clinical and biotechnological applications. Hypoxic conditions can frequently be found in flooded or waterlogged natural environments or in necrotic tissue with oxygen supply disrupted via the blood stream. Transcriptomic and proteomic studies have facilitated the study of fungal responses to low oxygen levels, but due to the high diversity in the hypoxic stress response of filamentous fungi, it is not easy to obtain a common picture of low oxygen responses in all filamentous fungi. In general, genes involved in glycolysis, steroid, and cell wall biosynthesis, as well as secondary metabolite metabolism, seem to be up-regulated, whereas transcript levels of ribosomal and purine/pyrimidine biosynthesis genes are down-regulated. This suggests that glycolysis contributes to a larger proportion of ATP generation and that the cell wall undergoes a significant restructuring under hypoxia. The authors conclude that, although we have only just begun to understand which measures filamentous fungi take to thrive in less oxygenated areas, and there are several species-specific aspects in hypoxia adaptation, nitric oxide (NO), and reactive oxygen species, mitochondrial signaling marks at least one common ground among fungal species in the genus *Aspergillus*.

The article by Alves et al. (2015) examines the biology of solute-induced stresses in the mycotoxin-producing, xerophilic fungus *Aspergillus wentii* via a series of experiments that includes characterization of growth and compatible solute responses to solute concentration, water activity, and chao-/kosmotropicity for 12 solute stressors. Additional, complementary studies of solute-induced perturbations of macromolecular model systems were carried out, and *S. cerevisiae* strains/mutants were used to determine chaotropic and osmotic activities of solute stressors. Alves et al. thereby disentangle the various stress parameters by which diverse solutes impact the cellular system, including biologically and biotechnologically pertinent substances such as salts, glucose, polyols, ethanol, and urea. According to the solute interactions with the fungal cell, and their primary modes-of-inhibitory action, these stressors partitioned into a number of natural categories: osmotically active (NaCl, KCl, glucose, sorbitol), non-osmotic and weakly to moderately chaotropic (ethanol, urea, ethylene glycol), both highly chaotropic and osmotically active (NH₄NO₃, MgCl₂, guanidine hydrochloride, CaCl₂), and inhibitory primarily due to low water activity (glycerol). This study thereby revealed that some stressors, including MgCl₂, can inhibit metabolism and cell multiplication via their chaotropic activity and by simultaneously imposing osmotic stress; a finding that is unprecedented for any type of living system. While not an osmotic stressor, it seems likely that ethanol can (at high concentrations) impose simultaneous chaotropicity and low water activity-induced stresses in *S. cerevisiae* (Hallsworth 1998; Cray et al. 2015). Conversely, high concentrations of MgCl₂ may ultimately inhibit the multiplication of extremely halophilic bacteria and Archaea due to chaotropicity rather than water activity or osmotic stress (Hallsworth et al. 2007; Yakimov et al. 2015). Based on their findings, Alves et al. justifiably question the validity of the ‘polyextremophile’ concept as it is currently applied. Their study also reveals that compatible solutes define the biotic window for fungal growth and metabolism under chaotropic osmotic conditions as well as other solute-induced stresses, and that kosmotropicity activities of compatible solutes can mitigate chaotropicity. The authors also discuss implications for preventing contamination of both the food-supply chain with mycotoxins and life-support systems used during space exploration missions.

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