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Review

Using evolutionary genomics, transcriptomics, and systems biology to reveal gene networks underlying fungal development

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ABSTRACT

Fungal model species have contributed to many aspects of modern biology, from biochemistry and cell biology to molecular genetics. Nevertheless, only a few genes associated with morphological development in fungi have been functionally characterized in terms of their genetic or molecular interactions. Evolutionary developmental biology in fungi faces challenges from a lack of fossil records and unresolved species phylogeny, to homoplasy associated with simple morphology. Traditionally, reductive approaches use genetic screens to reveal phenotypes from a large number of mutants; the efficiency of these approaches relies on profound prior knowledge of the genetics and biology of the designated development trait—knowledge which is often not available for even well-studied fungal model species. Reductive approaches become less efficient for the study of developmental traits that are regulated quantitatively by more than one gene via networks. Recent advances in genome-wide analysis performed in representative multicellular fungal models and non-models have greatly improved upon the traditional reductive approaches in fungal evo-devo research by providing clues for focused knockout strategies. In particular, genome-wide gene expression data across developmental processes of interest in multiple species can expedite the advancement of integrative synthetic and systems biology strategies to reveal regulatory networks underlying fungal development.

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1. Introduction

"Morphology was studied because it was the material believed to be the most favorable for the elucidation of the problems of evolution…" (Bateson, 1922)

Developmental biology, one of the most longstanding and deeply examined subdisciplines in biology, reveals how complex life forms are constructed by the growth, repositioning, structure, and identity of cells and tissues. Examination of morphological development has been vigorous in almost every major organismal group, and knowledge of developmental biology has accumulated along with advances in cell biology, developmental genetics, and the systems biology. Nevertheless, we remain ignorant of some of the basic elements of how a body shape is planned and formed in response to genetic and environmental signals—even in well studied models.

Evolutionary biology and developmental biology have long been considered complementary disciplines, and their synthesis has recently been boosted by their merger into the exciting field of evolutionary developmental biology (a.k.a. Evo-Devo)—research that investigates the developmental processes and the evolution of those processes among different organisms (Hall, 2012). Among the oldest models in cell biology, fungi have contributed significantly to evolutionary developmental biology and in recent times continue to serve as highly tractable workhorses for genetics and genomics, and now systems biology revolution (Bennett and Arnold, 2001).

Fungal diversity and fungal development

Fungi represent one of the most diverse organismal groups on earth in terms of their ecology, their ubiquity, and their manifold morphological forms. Among eukaryotes, fungi are relatively simple in terms of their cell and tissue types, along with high genome diversity accompanying their wide ecological distribution (Alexopoulos, 2007; Blackwell, 2011; Mohanta and Bae, 2015; Stajich *et al.*, 2009; Taylor *et al.*, 2017; Zeng *et al.*, 2017). Fungal development encompasses a very wide range of complexity, ranging from unicellular yeasts that can be found in flowers and guts of beetles and wasps (Lachance *et al.*, 2013; Stefanini *et al.*, 2012), to the largest known fruiting body of a wood decaying fungus—weighing nearly 500 kg (Dai and Cui, 2011), to postfire fungi that blossom quickly and transiently after forest fires (Glassman *et al.*, 2016), to the oldest known mycelium—over 1500 years in age and 15 ha in occupied area (Smith *et al.*, 1992). In addition, morphological divergence, which in fungi commonly includes the evolution of morphologies of highly reduced complexity, can make it challenging to identify orthologous structures among even closely related lineages (Wang *et al.*, 2016). Many higher fungi produce elaborate sexual reproductive structures predominantly for survival during their sexual life cycles, but during their asexual cycle these same fungi produce simple but vigorous structures that generate myriad, short lived asexual spores for rapid dispersal. Convergent and divergent evolution of phenotypes are not rare in fungi (Alexopoulos, 2007; Nagy *et al.*, 2014; Shang *et al.*, 2016; Torruella *et al.*, 2015), often resulting from diverse ecological pressures on a limited set of available simple reduced morphologies. For example, many leaf endophytic fungi produce dark-colored, covered, small fruiting bodies, while their saprotrophic relatives produce bright-colored, exposed, large fruiting bodies (Ruibal *et al.*, 2008; Wang *et al.*, 2009). Like plants and animals, some fungi—despite their more limited palette of cell and tissue types—have evolved structures for specific functions that are not common to other fungi. Remarkable examples of these innovative morphologies include the specialized and diverse penetration structures (appressoria) present in many plant pathogenic fungi (Ames, 2017; Geoghegan *et al.*, 2017; Mendgen *et al.*, 1996), the mycorrhizal nutrient bridges that develop between mushroom-forming fungi and their associated plants (Bravo *et al.*, 2017; Iwaniuk and Błaszkowski, 2014; Jiang *et al.*, 2017; Marks, 2012), differentiation of wood decay models among higher fungi (Floudas *et al.*, 2012; Hibbett and Donoghue, 2001; Nagy *et al.*, 2016), and the trapping rings, nets and adhesive hyphae unique to the nematode-trapping fungi in the Orbilliomycetes (Hyde *et al.*, 2014).

Fungal models for developmental biology

Fungal species have supplied model systems that have advanced multiple disciplines. Many of the fungi selected and developed as model systems share similar features: fast growth, short life cycle, manipulability in a laboratory setting, and distinctive morphology facilitating identification. Because these traits are not unusual in fungal species, the model species are often also of direct economic importance. The best-known and most well-studied experimental fungal model species are the yeasts *Saccharomyces cerevisiae* (bread and wine yeast) and *Schizosaccharomyces pombe* (Egel, 2013; Rose, 1981), which are important tools in molecular genetics, as well as human associated *Candida* species (Ene *et al.*, 2016; Prasad, 2017). As single-celled eukaryotes, these yeasts serve as powerful model systems for the investigation of numerous fundamental principles and mechanisms, including but not limited to cell-cycle control, mitosis and meiosis tool kits, genome organization, epigenetics and epigenomics, DNA recombination and repair, signal transduction, population genetics, and the aging process (Boynton *et al.*, 2017; Caudy *et al.*, 2017; Egel, 2013; Fuchs and Quasem, 2014; Salehzadeh-Yazdi *et al.*, 2014; Tsubouchi, 2006). A global genetic interaction network based on *S. cerevisiae* provides a wiring diagram of cellular function (Costanzo *et al.*, 2016). Yeasts also are models for developmental biology, especially for cell-to-cell communication, cell polarity, and budding and mating processes, although the scope of their contributions has been restricted to cellular development (Drubin, 1991; Liti, 2014; Tomičić and Raspor, 2017; Winters and Chiang, 2016). Representatives of long-time multicellular fungal models for developmental biology include the ascomycetous species *Aspergillus nidulans* (Braus *et al.*, 2002; Croft, 1966; Seo, 2005; Timberlake, 1993) and *Neurospora crassa* (Aramayo and Selker, 2013; Davis, 2000; Davis and Perkins, 2002; Mitchell, 1955; Selker, 2017) and their closely related species, and basidiomycetous species including *Schizophellum commune* (Casselton and Kües, 2007; Essig, 1922; Wessels, 1989), *Coprinopsis cinerea* (Plaza *et al.*, 2014), and *Coprinus comatus*

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