

**Is it wrong if I use the word race?**  
Under freedom of speech, anybody is free to use any words. Even if they do not correspond to scientifically identifiable entities, races are a component of our psychological and social world (Figure 1), and as such their importance should not be dismissed. But mutual understanding requires some agreement between speakers and receivers, and so it is better to avoid terms of ambiguous or unclear meaning, especially in science.

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## Aspergillus

Antonis Rokas

**What is Aspergillus?** *Aspergillus* is a widely distributed genus of more than 250 species of largely saprophytic filamentous fungi belonging to the phylum Ascomycota. Originally described in 1729 by the botanist and priest Antonio Micheli, the genus got its name from the resemblance of its asexual spore-forming structure to the aspergillum, an instrument for sprinkling holy water, although some modern taxonomists profess that it more closely resembles a toilet bowl brush (Figure 1). To the dismay of amateur and professional systematists alike, *Aspergillus* species are morphologically very similar and hard to distinguish; however, their genomic diversity is on par with that of our own phylum, the Vertebrates.

#### How does Aspergillus reproduce?

It's complicated! The *Aspergillus* life cycle comprises asexual, parasexual, and sexual stages. Upon germination, haploid asexual spores grow into branched filaments or hyphae of interconnected cells, thus forming a web known as the mycelium. As the mycelium expands, hyphae from the same or from different spores intersect and occasionally fuse, a decision governed by a network of genes based on whether the hyphae are part of the same self or not. The onset of fusion marks the beginning of the parasexual stage — the haploid nuclei of the two mother hyphae will now be part of the same cell, continuing to divide mitotically and experience crossing over events between homologous chromosomes, until random chromosome loss eventually restores the haploid chromosome number. Alternatively, *Aspergillus* hyphae can enter the sexual stage. The specifics of entry to the sexual stage, which are determined by two mating types, differ between species that are obligate outcrossers (also known as heterothallic; individuals possess only one of the two mating types and can only mate with individuals of the opposite type) and species that also are capable of self-fertilization (homothallic; possess both mating types). Generally, the process begins with multiple divisions of a cell that contains two nuclei derived either from the same organism (in homothallic species) or

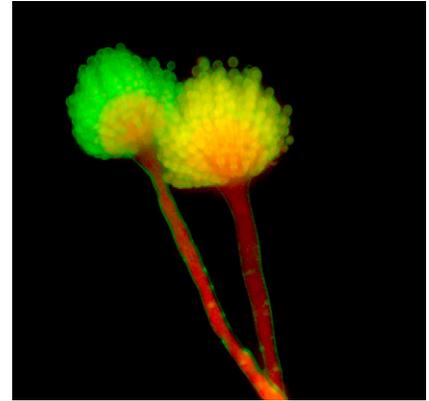


Figure 1. *Aspergillus*.

Two asexual fruiting bodies of the filamentous fungus *Aspergillus oryzae* after 3 days of growth on potato dextrose agar stained with Vybrant-DiO and Lysotracker Red dyes. The round cells at the tips are the asexual spores of the fungus (courtesy of Jonas King and John G. Gibbons).

from different ones (in homothallic and heterothallic species). These divisions eventually give rise to the ascus, the sexual spore-forming structure, in which the two nuclei in each cell fuse to form a diploid cell that undergoes meiosis and produces haploid ascospores. Although most *Aspergillus* species lack a known sexual stage, its recent discovery in a few species, coupled with the presence of intact mating and meiosis-related genes in several additional ones, suggest that many asexual species have cryptic sexual stages yet to be discovered.

#### What have we discovered from studying Aspergillus in the lab?

Research on *Aspergillus* has greatly contributed to our understanding of eukaryotic primary and secondary (or specialized) metabolism, the control of gene regulation by external environmental factors, the cell cycle, and fungal asexual and sexual development. The birth of *Aspergillus* as a model system dates back to Guido Pontecorvo's pioneering genetic work in the early 1950s on the nature of the gene, whose experiments laid the foundation of the concept of the gene as a unit of function rather than as one of mutation or recombination. One of the most beautiful recent examples of the importance and great value of *Aspergillus* concerns the identification of the genetic basis of the gene responsible for the human metabolic disease alkaptonuria — one of Garrod's classic "inborn errors of metabolism" — which results from

genetic errors in tyrosine/phenylalanine metabolism. Taking advantage of *Aspergillus*' ability to grow using any single amino acid as its sole carbon source, a Spanish research team was able not only to identify the fungal enzyme, but also to use its amino acid sequence as bait in sequence similarity searches against human transcript databases to isolate its human, disease-causing counterpart. Today, there are more than 50 laboratories around the world dedicated to *Aspergillus* research, and in the last decade, small international meetings that are affectionately known as 'Asperfests', have regularly taken place right before major fungal genetics conferences.

**Can you tell me something good about *Aspergillus*?** Because a great deal of the food eaten by *Aspergillus*, and more generally by fungi, is digested outside of their cells, these organisms possess astounding capabilities in exporting specialized enzymes that break it down, but also for synthesizing and secreting a variety of drugs to protect it from competitors. For example, *Aspergillus niger* is the near exclusive producer of citric acid, a preservative widely used in several different industries as well as a flavor enhancer of a variety of foods and beverages. The ability of *A. niger*, as well as of certain other *Aspergillus* species, to produce a wide variety of products safe for human use and consumption on an industrial scale has earned them the nickname 'cell factories'. Another well known example of an influential *Aspergillus* product is lovastatin, the cholesterol-reducing small molecule that Merck developed into the blockbuster drug Mevacor, which was originally isolated from *Aspergillus terreus*. But the most iconic and tasty *Aspergillus* products are courtesy of *Aspergillus oryzae*, Japan's 'national fungus' — the capacity of this organism to turn starch-rich grains, like rice and soy beans, into sugars makes it essential in the making of several different traditional Far-Eastern drinks and sauces, like the rice wine sake and soy sauce.

**How about something bad?** *Aspergillus*' penchant for making drugs, including disease-preventing ones, means that it can also produce some very potent toxins. Aflatoxin, a potent carcinogen and the causative agent of the mysterious Turkey X disease that killed tens of thousands of birds in England in the early 1960s,

is the most notorious one. Produced by *Aspergillus flavus*, aflatoxin frequently finds its way into human food and animal feeds thanks to the organism's ability to infect several major crops — to this day, consumption of aflatoxin-laced food around the globe results in a handful of human deaths per year as well as in billions of dollars in crop yield losses. In addition to *A. flavus*, several other *Aspergillus* species are opportunistic pathogens to a remarkably wide diversity of hosts. For example, *A. fumigatus* is the leading cause of human aspergillosis, a wide spectrum of diseases that results following inhalation of their highly abundant spores in individuals with compromised immune systems, and is one of the most common and deadly fungal opportunistic pathogens. *A. fumigatus* was also detected in many of the mold-contaminated steroid injections in the recent fungal meningitis epidemic that killed more than 3 dozen humans across the US. In contrast, in the 1990s an outbreak of infections caused by *Aspergillus sydowii* on sea fan corals resulted in dramatic coral die-offs, threatening the collapse of the entire ecosystem of gorgonian coral communities in the Caribbean. As biotic (e.g., the emergence of HIV altered the human disease landscape, dramatically increasing fungal infections) and abiotic (e.g., changes in climate are a major factor in emerging fungal-driven plant diseases) factors continue to shape the relationships between microbes and potential hosts, *Aspergillus*' proclivity toward opportunistic pathogenesis is something to watch out for.

#### Where can I find out more?

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## Primer

# Hibernation

Fritz Geiser

Hibernation (multiday torpor) and daily torpor in heterothermic mammals and birds are characterized by pronounced temporal reductions in body temperature, energy expenditure, water loss, and other physiological functions and are the most effective means for energy conservation available to endotherms. Hibernators express multiday torpor predominantly throughout winter, which substantially enhances winter survival. In contrast, daily heterotherms use daily torpor lasting for several hours during the rest phase. Although torpor is still widely considered to be a specific adaptation of cold-climate species, as we will see in this primer, it is used by many diverse species from all climate zones, including the tropics. While energy conservation during adverse conditions is an important function of torpor, it is also employed to permit energy-demanding processes such as reproduction and growth, especially when food supply is limited. Even migrating birds enter torpor to conserve energy for the next stage of migration. Although many heterothermic species will be challenged by anthropogenic influences such as habitat destruction, introduced species, novel pathogens and specifically global warming, not all are likely to be affected in the same way. In fact, as argued here, it is likely that opportunistic heterotherms may be better equipped to deal with these challenges than homeotherms because heterotherms have highly flexible energy requirements, can limit foraging and reduce the risk of predation, and often are also long-lived. In contrast, strongly seasonal hibernators, especially those restricted to mountain tops, and those that have to deal with new diseases that are difficult to combat at low body temperatures, are likely to be adversely affected.

#### A cool advantage

Living organisms are either ectothermic or endothermic.