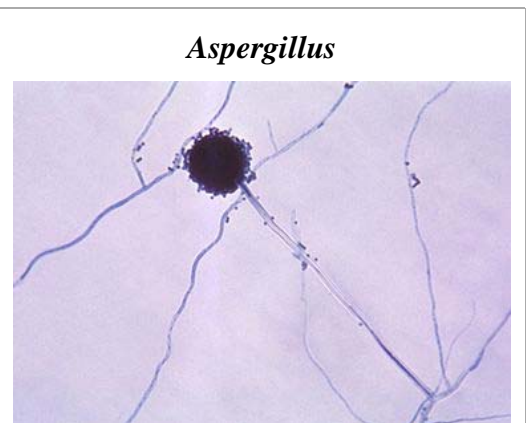


Aspergillus

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Aspergillus (/ˌæspərˈdʒɪləs/) is a genus consisting of a few hundred mold species found in various climates worldwide.

Aspergillus was first catalogued in 1729 by the Italian priest and biologist Pier Antonio Micheli. Viewing the fungi under a microscope, Micheli was reminded of the shape of an *aspergillum* (holy water sprinkler), from Latin *spargere* (to sprinkle), and named the genus accordingly.^[1] Today, *aspergillum* is also the name of an asexual spore-forming structure common to all *Aspergillus* species; around one-third of species are also known to have a sexual stage.^[2]



Conidial head of *Aspergillus niger*

Scientific classification

Kingdom:	Fungi
Division:	Ascomycota
Class:	Eurotiomycetes
Order:	Eurotiales
Family:	Trichocomaceae
Genus:	<i>Aspergillus</i>
	Micheli (1729)

Species

See List of *Aspergillus* species

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Taxonomy

Species

Aspergillus consists of a few hundred species.^[2]

Growth and distribution

Aspergillus is a member of the Deuteromycetes fungi, which is a group with no known sexual state. With DNA evidence forthcoming, all members of the genus *Aspergillus* likely are closely related and should be considered members of the Ascomycota. Members of the genus possess the ability to grow where a high osmotic concentration (high sugar, salt, etc.) exists. *Aspergillus* species are highly aerobic and are found in almost all oxygen-rich environments, where they commonly grow as molds on the surface of a substrate, as a result of the high oxygen tension. Commonly, fungi grow on carbon-rich substrates like monosaccharides (such as glucose) and polysaccharides (such as amylose). *Aspergillus* species are common contaminants of starchy foods (such as bread and potatoes), and grow in or on many plants and trees.

In addition to growth on carbon sources, many species of *Aspergillus* demonstrate oligotrophy where they



Aspergillus on a tomato in detail



Various *Penicillium*, *Aspergillus* spp. and other fungi growing in axenic culture



Historical model of *Aspergillus*, Botanical Museum Greifswald

are capable of growing in nutrient-depleted environments, or environments with a complete lack of key nutrients. *A. niger* is a prime example of this; it can be found growing on damp walls, as a major component of mildew.

Commercial importance

Species of *Aspergillus* are important medically and commercially. Some species can cause infection in humans and other animals. Some infections found in animals have been studied for years, while other species found in animals have been described as new and specific to the investigated disease, and others have been known as names already in use for organisms such as saprophytes. More than 60 *Aspergillus* species are medically relevant pathogens.^[3] For humans, a range of diseases such as infection to the external ear, skin lesions, and ulcers classed as mycetomas are found.

Other species are important in commercial microbial fermentations. For example, alcoholic beverages such as Japanese *sake* are often made from rice or other starchy ingredients (like manioc), rather than from grapes or malted barley. Typical microorganisms used to make alcohol, such as yeasts of the genus *Saccharomyces*, cannot ferment these starches. Therefore, *koji* mold such as *Aspergillus oryzae* is used to first break down the starches into simpler sugars.

Members of the genus are also sources of natural products that can be used in the development of medications to treat human disease.^[4]

Perhaps the largest application of *A. niger* is as the major source of citric acid; this organism accounts for over 99% of global citric acid production, or more than 1.4 million tonnes per year. *A. niger* is also commonly used for the production of native and foreign enzymes, including glucose oxidase and lysozyme. In these instances, the culture is rarely grown on a solid substrate, although this is still common practice in Japan, but is more often grown as a submerged culture in a bioreactor. In this way, the most important parameters can be strictly controlled, and maximal productivity can be achieved. This process also makes it far easier to separate the chemical or enzyme of importance from the medium, and is therefore far more cost-effective.

Research

A. nidulans (*Emericella nidulans*) has been used as a research organism for many years and was used by Guido Pontecorvo to demonstrate parasexuality in fungi. Recently, *A. nidulans* was one of the pioneering organisms to have its genome sequenced by researchers at the Broad Institute. As of 2008, a further seven *Aspergillus* species have had their genomes sequenced: the industrially useful *A. niger* (two strains), *A. oryzae*, and *A. terreus*, and the pathogens *A. clavatus*, *A. fischerianus* (*Neosartorya fischeri*), *A. flavus*, and *A. fumigatus* (two strains).^[5] *A. fischerianus* is hardly ever pathogenic, but is very closely related to the

common pathogen *A. fumigatus*; it was sequenced in part to better understand *A. fumigatus* pathogenicity.^[6]

Sexual reproduction

Of the 250 species of aspergilli, about 64% have no known sexual state.^[7] However, many of these species likely have an as yet unidentified sexual stage.^[7] Sexual reproduction occurs in two fundamentally different ways in fungi. These are outcrossing (in heterothallic fungi) in which two different individuals contribute nuclei, and self-fertilization or selfing (in homothallic fungi) in which both nuclei are derived from the same individual. In recent years, sexual cycles have been discovered in numerous species previously thought to be asexual. These discoveries reflect recent experimental focus on species of particular relevance to humans.

A. fumigatus is the most common species to cause disease in immunodeficient humans. In 2009, *A. fumigatus* was shown to have a heterothallic, fully functional sexual cycle.^[8] Isolates of complementary mating types are required for sex to occur.

A. flavus is the major producer of carcinogenic aflatoxins in crops worldwide. It is also an opportunistic human and animal pathogen, causing aspergillosis in immunocompromised individuals. In 2009, a sexual state of this heterothallic fungus was found to arise when strains of opposite mating types were cultured together under appropriate conditions.^[9]

A. lentulus is an opportunistic human pathogen that causes invasive aspergillosis with high mortality rates. In 2013, *A. lentulus* was found to have a heterothallic functional sexual breeding system.^[10]

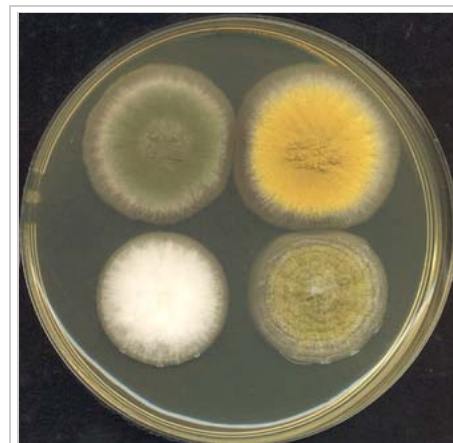
A. terreus is commonly used in industry to produce important organic acids and enzymes, and was the initial source for the cholesterol-lowering drug lovastatin. In 2013, *A. terreus* was found to be capable of sexual reproduction when strains of opposite mating types were crossed under appropriate culture conditions.^[11]

These findings with *Aspergillus* species are consistent with accumulating evidence, from studies of other eukaryotic species, that sex was likely present in the common ancestor of all eukaryotes.^{[12][13][14]}

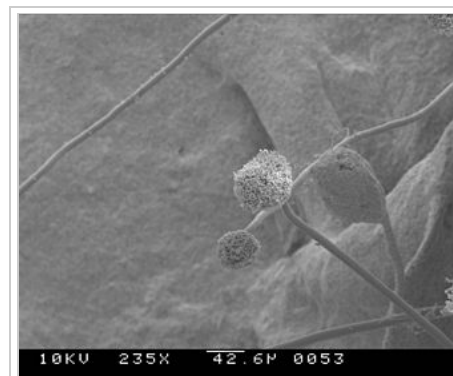
A. nidulans, a homothallic fungus, is capable of self-fertilization. Selfing involves activation of the same mating pathways characteristic of sex in outcrossing species, i.e. self-fertilization does not bypass required pathways for outcrossing sex, but instead requires activation of these pathways within a single individual.^[15]

Among those *Aspergillus* species that exhibit a sexual cycle, the overwhelming majority in nature are homothallic (self-fertilizing).^[16] This observation suggests *Aspergillus* species can generally maintain sex though little genetic variability is produced by homothallic self-fertilization. *A. fumigatus*, a heterothallic (outcrossing) fungus that occurs in areas with widely different climates and environments, also displays little genetic variability either within geographic regions or on a global scale,^[17] again suggesting sex, in this case outcrossing sex, can be maintained even when little genetic variability is produced.

Genomics



Four three-day-old *Aspergillus* colonies. Clockwise from top-left: an *A. nidulans* laboratory strain; a similar strain with a mutation in the *yA* marker gene involved in green pigmentation; an *A. oryzae* strain used in soy fermentation; *A. oryzae* RIB40



A scan of *Aspergillus* taken at 235 magnifications under a scanning electron microscope

The simultaneous publication of three *Aspergillus* genome manuscripts in *Nature* in December 2005 established the genus as the leading filamentous fungal genus for comparative genomic studies. Like most major genome projects, these efforts were collaborations between a large sequencing centre and the respective community of scientists. For example, the Institute for Genome Research (TIGR) worked with the *A. fumigatus* community. *A. nidulans* was sequenced at the Broad Institute. *A. oryzae* was sequenced in Japan at the National Institute of Advanced Industrial Science and Technology. The Joint Genome Institute of the Department of Energy has released sequence data for a citric acid-producing strain of *A. niger*. TIGR, now renamed the Venter Institute, is currently spearheading a project on the *A. flavus* genome.^[18]

Genome sizes for sequenced species of *Aspergillus* range from about 29.3 Mb for *A. fumigatus* to 37.1 Mb for *A. oryzae*, while the numbers of predicted genes vary from about 9926 for *A. fumigatus* to about 12,071 for *A. oryzae*. The genome size of an enzyme-producing strain of *A. niger* is of intermediate size at 33.9 Mb.^[1]

Pathogens

Some *Aspergillus* species cause serious disease in humans and animals. The most common pathogenic species are *A. fumigatus* and *A. flavus*, which produces aflatoxin which is both a toxin and a carcinogen, and which can contaminate foods such as nuts. The most common species causing allergic disease are *A. fumigatus* and *A. clavatus*. Other species are important as agricultural pathogens. *Aspergillus* spp. cause disease on many grain crops, especially maize, and some variants synthesize mycotoxins, including aflatoxin.

Aspergillosis

Aspergillosis is the group of diseases caused by *Aspergillus*. The most common subtype among paranasal sinus infections associated with aspergillosis is *A. fumigatus*.^[19] The symptoms include fever, cough, chest pain, or breathlessness, which also occur in many other illnesses, so diagnosis can be difficult. Usually, only patients with already weakened immune systems or who suffer other lung conditions are susceptible.

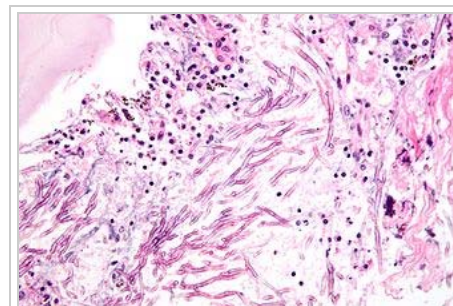
In humans, the major forms of disease are:^{[20][21]}

- Allergic bronchopulmonary aspergillosis, which affects patients with respiratory diseases such as asthma, cystic fibrosis, and sinusitis
- Acute invasive aspergillosis, a form that grows into surrounding tissue, more common in those with weakened immune systems such as AIDS or chemotherapy patients
- Disseminated invasive aspergillosis, an infection spread widely through the body
- Aspergilloma, a "fungus ball" that can form within cavities such as the lung

Aspergillosis of the air passages is also frequently reported in birds, and certain species of *Aspergillus* have been known to infect insects.^[3]

See also

- List of *Aspergillus* species
- Mold health issues
- New England Compounding Center meningitis outbreak
- Sick building syndrome



Pulmonary aspergillosis

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External links

- FungiDB: An integrated functional genomics database for fungi and oomycetes (<http://fungidb.org>)
- Aspergillus Genome Resources (NIH) (<http://www.ncbi.nlm.nih.gov/projects/genome/guide/aspergillus/>)
- Aspergillus Comparative Database (http://www.broad.mit.edu/annotation/genome/aspergillus_group/) Comparative genomic resource at the Broad Institute
- Central Aspergillus Data Repository (<http://www.cadre-genomes.org.uk/>)
- The Fungal Genetics Stock Center (<http://www.fgsc.net/>)
- The Aspergillus/Aspergillosis Website (<http://www.aspergillus.org.uk/>) An encyclopedia of *Aspergillus* for patients, doctors and scientists
- *Aspergillus* surveillance project at a large tertiary-care hospital. (<http://www.moldacrossamerica.org/ASPPAPER%20LC.pdf>) (PDF).
- The Aspergillus Genome Database (<http://www.aspgd.org/>)



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