Senescence in Fungi

Anthony Deepak D'souza and Ramesh Maheshwari

Anthony Deepak D'souza is a PhD student under Ramesh Maheshwari working on senescence in *Neurospora*.

Ramesh Maheshwari is a Professor at Department of Biochemistry, Indian Institute of Science, Bangalore. His research interests are fungal biology and genetics.

Fungi are non-photosynthetic, filamentous organisms (*Box* 1). The filaments or the hyphae are branched and divided into segments by transverse walls or septa. The growth of the hypha is restricted to its tip, which grows linearly by the apical addition of new cell wall material. The hyphal tip perpetuates itself as the mycelium spreads over the substrate. Consequently, a fungal mycelium is a system of hyphae designed for unlimited growth. This is best exemplified in a mushroom fungus whose mycelium spreads in the soil and produces fruiting bodies along the periphery of the subterranean mycelium. Such development of fruit bodies has been called a 'fairy ring' as it was thought that the 'ring' of mushrooms (see *Figure* 1) represented the area inside which the fairies danced! The diameter of the fairy ring enlarges as the mycelium extends radially and produces a new crop of fruit bodies (mushrooms) along the periphery. In some cases, the subterranean mycelium can occupy a very large area and can be several hundred years old. In North America, a colony of a basidiomycetes fungus, *Armillaria bulbosa*, which had spread to some ten acres in the forest soil was discovered. This colony was estimated to be some 1500 years old and can claim the record for the oldest and largest organism! Fungi can therefore be considered to be very long-lived organisms.

The immortal nature of a fungus is reflected in its ability to be continuously propagated by serial subcultures in the laboratory. However, there are strains, either produced in a laboratory or isolated from nature, that show the property of finite growth, that is, they show a progressive loss of growth culminating in death, a degenerative process known as *senescence* (*Box* 2). For example, in a survey of some 150 isolates of the fungus, *Neurospora intermedia* isolated in South India, the majority of the cultures remained healthy, but 26 cultures senesced in 10-50 subcultures [1]. These senescent isolates showed a progressive

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Box 1. Kingdom Fungi

The Fungal kingdom is divided into five divisions: Zygomycetes, Myxomycetes, Ascomycetes, Basidiomycetes and Deuteromycetes. The first two divisions constitute the 'lower fungi' whereas the rest come under 'higher fungi'.

Basidiomycetes include members characterized by the production of sexual spores, termed basidiospores. These are produced on specialized, microscopic, spore producing structure called basidium. For example, the mushrooms, rusts and smut fungi.

Ascomycetes include all fungi that produce sexual spores, ascospores, in a sac-like cell, ascus. For example, Yeast, *Podospora*, *Neurospora*, etc.

Figure 1. A 'fairy ring' of a mushroom fungus, Armillaria bulbosa. The centripetal growth of the subterranean mycelium has produced a ring of fruit bodies.

decline in growth rate and conidiation and ultimately the mycelium ceased to grow altogether (*Figure* 2).

Genetic studies revealed that senescence in fungal strains can be either paternally or maternally inherited. In the ascomycetous fungus *Podospora anserina*, the senescent trait is maternally inherited: the ascospores from a cross, non-senescent female x senescent male yielded mostly non-senescent progeny whereas the reciprocal cross, senescent female x non-senescent male yielded mostly senescent progeny. The senescent phenomenon was found to be associated with the accumulation of high copy numbers of circular plasmid (sen DNAs) elements in the mitochondria, which affected mitochondrial respiration resulting in death of the fungus. The circular plasmid elements were a result of excision and amplification of part of the mitochondrial genome and they could also act as insertion mutagens. A number

Box 2. Senescence

Senescence is an inherent degenerative program in multicellular organisms, that is manifested by a progressive decline in cellular energy production culminating with the death of a part or the whole organism. Fungi are eukaryotic organisms that can be considered immortal due to the fact that they can be indefinitely propagated. Therefore fungal strains that senesce as indicated by the progressive decline in growth vigor and conidiation culminating with death provide excellent model systems to investigate probable mechanisms of senescence. Fungi are also well suited for experimentation because they are easy to grow, have a short generation time and provide variants that can be analyzed genetically and biochemically.

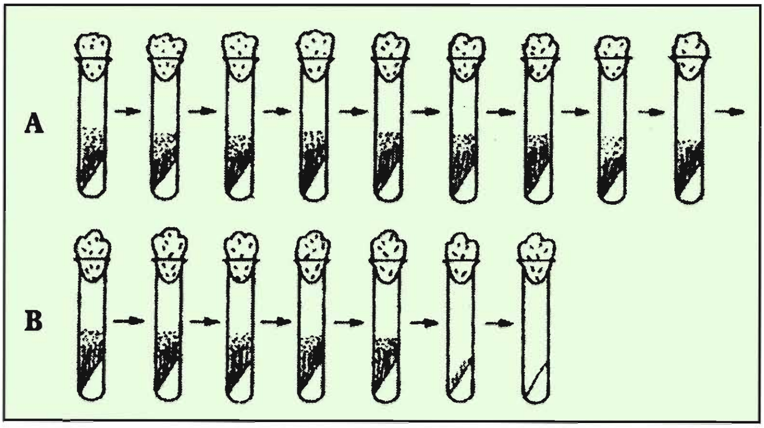

Figure 2. Identification of a senescent strain of Neurospora by serial subculturing.
A. A normal strain can be propagated indefinitely by transfer of conidia or vegetative mycelium.
B. A senescent strain dies after a specific number of subcultures.

of nuclear genes (for eg. *GRISEA*) were found to influence the accumulation of sen DNAs and the death of the fungus.

In addition to the circular plasmids, a few mitochondrial-based linear plasmids also were found to be responsible for death of the strains harboring them. Well-known examples are the Kalilo and the Maranhar plasmids in *Neurospora*.These plasmids are autonomous and self-replicating elements that initiate senescence by integrating into the mitochondrial genome, thus acting as insertional mutagens.

The paternally inherited senescent trait brings to light the importance of interactions of the nuclear and the mitochondrial genomes (*Figure* 3) for the normal functioning of the mitochondria. The mitochondrial genome encodes for about 15% of mitochondrial-based proteins. A nuclear mutation that affects a protein involved in a crucial function of mitochondrial metabolism would therefore be potentially lethal. A well-documented example is that of the natural death (*nd*) mutant of *Neurospora crassa*. In this mutant, the mutation in the '*nd*' gene leads to deletion of large chunk of the mitochondrial genome by hyper-recombinational events.

Large-scale rearrangements of the nuclear genome by DNA elements, for example, the *Ty* retrotransposon in yeast, can lead to aging. In yeast, a number of nuclear genes have been identified that play a role in aging. For example, the *LAG*1 (longevity

Box 3. Glossary of terms

Plasmid: An autonomously replicating extrachromosomal DNA.

Mutagen: An agent that induces a genetic mutation.

Retrotransposon: A translocating chromosomal segment that bears homology to a retrovirus.

Recombination: A process of rearrangement of genetic material by crossing over between two homologous segments of DNA.

Senescence in Fungi	
Nuclear based	**Mitochondrial based**
A. Transposon induced rearrangements of nuclear genome. Example: *Ty* retrotransposon of yeast	A. Mitochondrial plasmid induced rearrangement of mitochondrial genome Example: Kalilo and Maranhar plasmids of *Neurospora*
B. Mutation in nuclear genes Example: 'natural death' mutant of *Neurospora crassa*	B. Excision-amplification of mitochondrial genome Example: α, β sen-DNA elements in *Podospora anserina*

Figure 3. A broad classification of mechanisms of senescence in fungi.

assurance gene) and the *SIR* (silent information regulator) have been found to influence longevity and aging.

Parallels with Plants and Animals

The senescence phenomenon observed in fungi has a number of parallels in plants and animals. For example, in some higher plants, a degenerative disorder called cytoplasmic male sterility, results in abortion of pollen. This has been attributed to structural alterations induced in the mitochondrial genome. The introduction of certain nuclear genes, called 'restorer of fertility', restores the pollen fertility, again showing the interactions of the mitochondrial and the nuclear genomes. A number of restorer genes have been found to suppress cytoplasmic fertility. For example, in maize, three types of *CMS* (*CMS-T*, *CMS-C*, and *CMS-S*) have been recognized. This suggests that the restorer genes could be a rich source of nuclear genes involved in the maintenance of mitochondrial genome structure and function.

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In humans too several major disease causing mutations that affect longevity have been mapped to mitochondrial DNA and are therefore maternally inherited. In cells harboring the mutant and normal mitochondrial population (heteroplasmy), the phenotype is a reflection of the proportion of the two types of mitochondrial genomes in the cell.

In summary, the phenomenon of senescence in fungi shows the interaction of the nuclear and the mitochondrial genomes with extra-chromosomal elements (plasmids) as in plasmid based senescence. Furthermore, the examples of senescence in fungi emphasize the importance of the interactions between the nuclear and the mitochondrial genomes for the maintenance of the stability and the integrity of the mitochondrial genome. The senescence phenomenon in fungi opens up avenues for use of fungi as simple model systems to dissect and understand the molecular genetics of the senescence phenomenon in eukaryotes.

The examples of senescence in fungi emphasize the importance of the interactions between the nuclear and the mitochondrial genomes for the maintenance of the stability and the integrity of the mitochondrial genome.

Suggested Reading

[1] R Maheshwari, A Pandit and B Kannan, Senescence in strains of *Neurospora* from southern India, *Fungal Genet. Newsl.*, Vol. 41, p. 60, 1994.

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[3] A J F Griffiths, Fungal senescence - A review, *Ann. Rev Genet.*, Vol. 26, pp. 351-72, 1992.

[4] H D Osiewacz and A Hamann, DNA Reorganization and Biological Aging – A review, *Biochemistry* (Moscow), Vol. 62, pp. 1275-1284, 1997.

Address for Correspondence
Anthony Deepak D'souza and Ramesh Maheshwari
Department of Biochemistry
Indian Institute of Science
Bangalore 560012, India.

PLEASE NOTE

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Back Cover:
Date of birth of Claude Elwood Shannon should be 1916.

Pages 49 and 50:
Photograph on page 49 is Tim Hunt and on page 50 is Paul Nurse, but the text remains the same.