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Review 综述

丝状真菌衰老的研究进展

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摘 要：丝状真菌的衰老是一个涉及多种生理生化变化的复杂过程，受外部环境和遗传的共同影响，且伴随细胞功能退化与生理损伤。丝状真菌因其遗传操作容易、生命周期短、便于量化的衰老特征等优势被广泛用于衰老机制研究。本研究对丝状真菌的衰老特征进行综述，并归纳环境因素、线粒体稳定性、氧化应激和代谢水平等影响衰老的因素，解析衰老过程的调控机制，进一步挖掘丝状真菌在工业应用中的应用价值，期望能为人类衰老的研究提供新的研究思路。

关键词：丝状真菌；衰老；线粒体 DNA (mtDNA)稳定性；自噬；遗传；调控机制

Research progress in senescence of filamentous fungi

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Abstract: Senescence, a complex process involving multiple physiological and biochemical processes accompanied by degradation of cellular and organ functions and physiological damage, is influenced by both environmental and genetic factors. Filamentous fungi have been widely used in the study of senescence mechanism because of the easy genetic manipulation, short life cycle, and easy qualification of senescence characteristics. In this paper, we reviewed the senescence characteristics of filamentous fungi and summarized the factors influencing aging, such as environmental factors, mitochondrial stability, oxidative stress, and metabolic level. This review is expected to give new

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insights into the industrial application of filamentous fungi and the research on human senescence.
Keywords: filamentous fungi; senescence; mitochondrial DNA (mtDNA) stability; autophagy; heredity; regulatory mechanism

衰老一种是受环境和遗传调控相互作用的复杂生物学现象，涉及多种细胞功能的慢性衰退，并且引发疾病，是当前医学领域科学研究的重要方向之一[1-2]。通过酵母、线虫、果蝇、斑马鱼、鼠以及恒河猴等不同模式生物的研究[3]，大量关于衰老成因与机制的研究成果得以发表。丝状真菌是抗生素、生物酶类、有机酸和酿酒等多种制药和食品发酵工业的基础，在自然界中扮演着各种复杂有机物分解者的角色；然而，在丝状真菌工业化大规模发酵生产中，菌种衰老是一个无法回避的问题，菌种的衰老会直接导致菌体生长繁殖能力下降、发酵周期延长、抗不良环境条件的性能减弱等；因此，选育高产、高稳、高抗的优良菌株，可以缩短发酵周期、提高转化效率、降低生产成本[3]。丝状真菌因其遗传操作容易、生命周期短、有便于量化的衰老特征等优势被广泛用于衰老机制研究[4]。本文系统地归纳了多年来丝状真菌衰老的相关研究，总结了丝状真菌的衰老特征、影响因素，并探讨了其衰老研究的方向和应用前景，期望为提高丝状真菌工业生产效益及治疗人类衰老疾病提供新的研究思路。

1 丝状真菌衰老的特征

丝状真菌衰老是指随时间推移，其生长、代谢、分化和遗传等方面出现不可逆的功能退化现象；对于绝大多数丝状真菌而言，菌丝生长阶段是可以无限顶端极化生长的，然而，有些物种的丝状真菌生长发育到特定阶段会表现出独特的衰老特征[5]，主要表现为菌丝生长不规则、生长停滞、色素沉着增加等，还会影响某些丝状真菌产孢能力与配子生育力等有性生殖过程[6-7]。丝状真菌孢子在适宜条件下萌发形成菌丝，通过营养生长扩展为菌丝体，经历有性或者无性生殖产生孢子并释放，并启动新的生长周期。法国科学家 Rizet[4]于 1953 年发现木解霉(*Podospora anserina*)在短期内会出现不可逆转的自然衰老死亡现象。自此，研究人员发现木解霉在衰老研究中表现出极强的优势，因其生命周期短、线粒体 DNA (mitochondrial DNA, mtDNA)不稳定、衰老症状直观等特征成为衰老研究的明星[8-10]。木解霉野生型菌株以 7 mm/d 的线性速度生长，直至进入衰老阶段，此时其菌丝生长速度减慢，气生菌丝生长减少，菌丝最外圈褐绿色色素沉着明显[11]。此外，丝状真菌在细胞水平的衰老特征主要包括线粒体形态和超微结构的变化、质粒(plasmid) DNA 积累与 mtDNA 重组改变，例如在木解霉中，衰老菌株的线粒体形态从幼年的丝状网络转变成碎片化网络，线粒体发生融合与裂变[12]。在粗糙脉孢菌(*Neurospora crassa*)衰老过程中也发现了线粒体形态变化与 mtDNA 重组的衰老特征[13]。Orgel[14]研究表明，*P. anserina* 衰老还会引发核糖体分解，大分子生物合成的错误频率呈指数级增加，蛋白水平急剧下降。丝状真菌在衰老过程中，液泡在形态学上发生改变，细胞壁变得粗糙且不规则，并附着密集颗粒状物质，细胞整体形态变得粗大，细胞壁呈现肿胀状态[15]。在特定条件下，液泡的自噬活动可能会影响次级代谢产物的生产与分泌，在工业应用中具有潜在价值[16]。因此，丝状真菌衰老会涉及生长形态、线粒体和液泡的形态与结构、蛋白质合成与降解等方面的变化，这可能受多种因素的调控作用。

2　丝状真菌衰老的影响因素

丝状真菌衰老是一个涉及多因素、多阶段的过程。丝状真菌生长环境的变化会引起真菌压力应激，改变代谢过程，影响次级代谢产物合成，甚至导致真菌衰老或死亡[17-18]。然而，丝状真菌的衰老不仅受到温度、光照和 pH 等外部环境条件的影响，还受到线粒体稳态、代谢水平、衰老基因以及调控细胞周期的信号通路等内在机制的调控[4-8]。因此，理解这些因素的相互作用对于揭示衰老成因与机制至关重要。

2.1　环境因素影响丝状真菌衰老

2.1.1　温度

温度是一种关键的环境信号，影响丝状真菌孢子萌发、菌丝生长以及生存情况；外界环境温度的波动能引起丝状真菌压力应激，代谢水平改变，不仅会影响丝状真菌生长，严重时还会导致其衰老与死亡[18]。当丝状真菌处于极端温度环境时，其细胞壁或细胞膜是首要的温度感应器[19-20]，例如黄曲霉菌(*Aspergillus flavus*)菌丝在≥40 ℃高温胁迫下超微结构发生变化，菌丝体出现皱缩、塌陷现象，伴随着细胞壁变薄、膜通透性发生改变等特点，导致其细胞器受损，从而影响霉菌正常生长，促进真菌衰老[18]。在低温环境(<16 ℃)下，黄曲霉菌通过降低代谢的能量需求来减少自由基含量与氧化损伤，从而延缓衰老[21]。皱褶青霉(*Penicillium rugulosum*)在极低温时活性氧(reactive oxygen species, ROS)显著增加，从而诱发氧化应激，引发衰老[22]。温度对衰老的调控作用不仅限于直接影响细胞的结构和代谢，还可通过环磷酸腺苷依赖蛋白激酶 (cyclic adenosine monophosphate-dependent protein kinase A, cAMP/PKA)信号通路和全局调控因子 LaeA 等机制进行调控，例如黄曲霉在最适温度(37 ℃)下表达更高水平的正调控因子 acyA 和 pkaR，导致 cAMP/PKA 信号转导被激活，cAMP 水平显著增加[23]，而 cAMP 水平的提升可改善细胞的代谢状态和抗氧化能力，减少细胞的氧化应激，从而有助于延缓衰老[24]。研究发现温度影响黄曲霉和烟曲霉(*Aspergillus fumigatus*)等丝状真菌全局调控因子 *LaeA* 基因的调控网络，会破坏次级代谢产物的生物合成过程，从而影响其形态分化和寿命[25-26]，LaeA 是一种甲基转移酶，影响组蛋白修饰，温度变化影响该酶活性，导致染色体结构的改变，进而调控一系列基因的表达[27-28]，例如与衰老相关的基因 *Acatg*1 以及与次级代谢产物相关的球毛壳菌素和环匹阿黄曲霉菌基因表达过程发生变化，从而引起真菌衰老(图 1)。

2.1.2　光照

光照作为外部信号，影响丝状真菌的生理过程与形态变化[29]。例如红光能够促进红曲霉菌(*Monascus* sp.)的性发育，包括子囊孢子形成与菌丝体生长，同时促进 γ-氨基丁酸(gamma-aminobutyric acid, GABA)和柑橘素等次级代谢物的生成以抑制衰老[30]。白光和蓝光能够抑制黄曲霉菌(*Aspergillus flavus*)、寄生曲霉(*Aspergillus parasiticus*)和链格孢(*Alternaria alternata*)中霉菌毒素的产生，影响丝状真菌某些已知的次级代谢产物合成[31-32]，从而减缓菌丝生长，延缓衰老。丝状真菌对光信号的感知依赖于其多种光感受器和相关级联信号，丝状真菌的光感受器由一系列光敏受体组成，包括白领蛋白(white collar, WC)、隐花色素、视蛋白、感应(远)红光的光敏色素，这些光受体保证了丝状真菌对广泛光谱的感知与响应，适应多变的环境[33]。在 *N. crassa* 中，受红光和白光诱导表达的无性分生孢子调节蛋白(Ve-1)缺失时，无性分生孢子发育受阻，气生菌丝缩短，出现衰老特征[34]。在木解霉中，光敏色素蛋白基因(PaPhy1 和 PaPhy2)的缺失会引起活性氧增加，抑制子实体

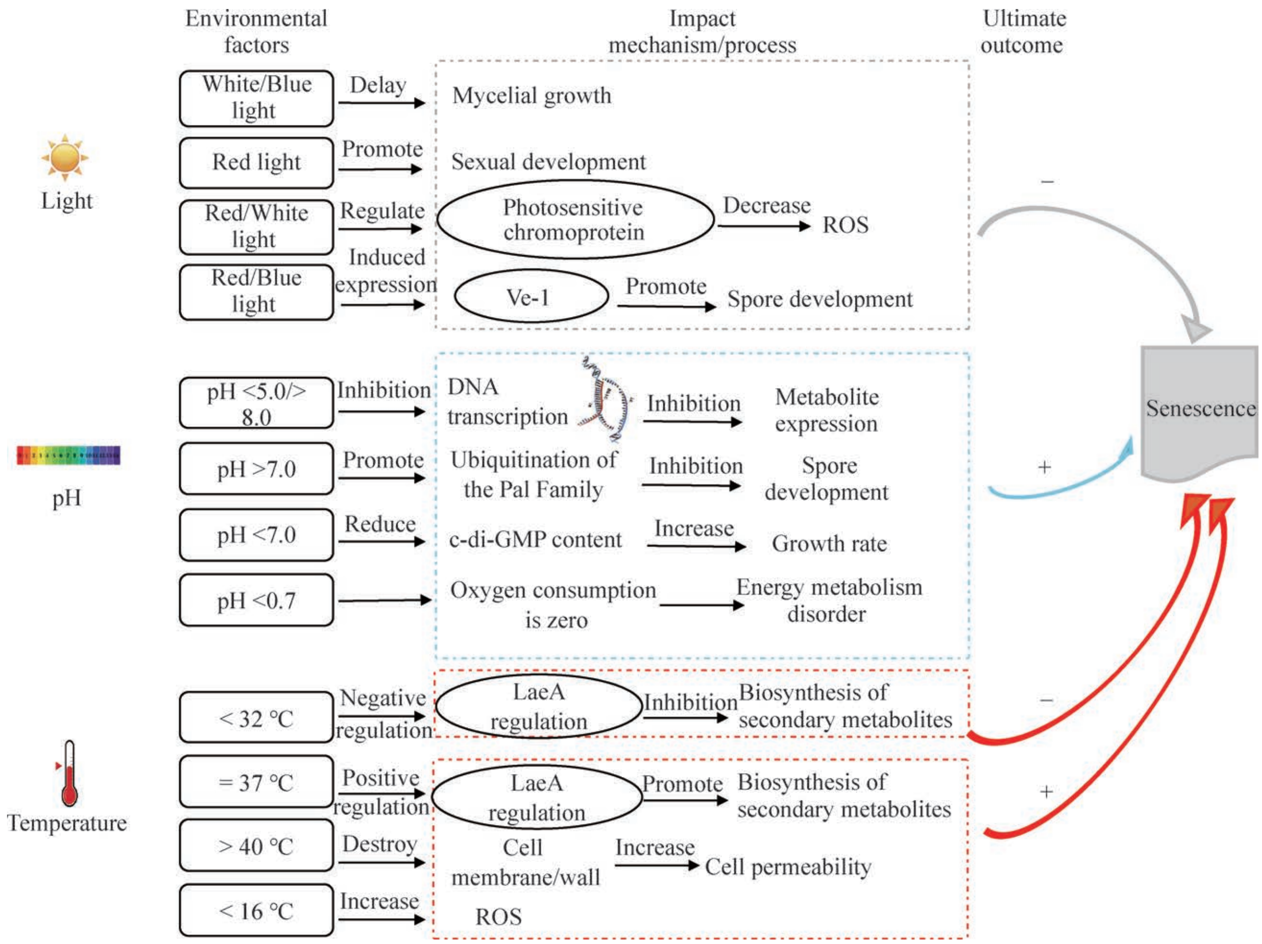

图1　影响丝状真菌衰老的环境因素及其调控

Figure 1　The environmental factors affecting the senescence of filamentous fungi and their regulation. +: Denotes promotion; −: Denotes inhibition.

发育，衰老延缓[35]。由此可知，光照与丝状真菌的形态发育有关，能够通过增加丝状真菌代谢通量或蛋白质分泌的酶的表达来调控衰老过程[36] (图 1)。

2.1.3　pH

在丝状真菌中，引起氧化应激的羟胺和氢氧根离子的解离和生成与 pH 值相关，丝状真菌生长环境 pH 的变化会改变相关基因的转录表达来维持细胞稳态，比如某些分泌酶和代谢物等，进一步影响丝状真菌的生长发育与衰老[37]。在 pH 值降至 5.80 以下或者增至 7.58 以上时，黑曲霉的耗氧量急剧下降，pH 值到达 0.7 时，耗氧量几乎为 0，能量代谢过程彻底紊乱[38] (表 1)，进而引发衰老；酸性 pH 值环境会导致桂花地霉(*Geotrichum fragrans*)细胞内环状二鸟苷酸 (cyclic diguanylate monophosphate, c-di-GMP)的含量下降，从而增加其在葡萄糖或乙酸盐上的生长速率，最终共同导致真菌的衰老[17]。在粉红单端孢(*Trichothecium roseum*)中，感受 pH 值的相关转录因子 *PacC* 缺失时，酸性 pH 值环境会导致孢子萌发减少，孢子变小，菌丝稀疏等衰老特征[38]。在构巢曲霉中，感受碱性 pH 值的蛋白(plasma membrane alkaline pH receptor H, PalH)家族通过泛素化影响下游转导信号通

路，发生与自噬类似的能量补给相反的作用，从而诱导衰老[41]。总之，丝状真菌体内存在 pH 值感受器，pH 值会影响丝状真菌代谢途径和某些信号通路，最终引起真菌衰老[29]。

2.2 遗传调控丝状真菌衰老

2.2.1 mtDNA 稳定性

mtDNA 稳定性在丝状真菌衰老和寿命控制中具有重要意义[42-43]。线粒体功能障碍或一些其他因素所引起的真菌衰老，都能追寻到mtDNA 稳定性改变的踪迹，mtDNA 的大规模重组是丝状真菌老化的重要标志[44-45] (图 1，表 2)。在丝状真菌衰老过程中，mtDNA 内含子会形成质粒样 DNA 并重新整合进 mtDNA 中，这种重组会导致 mtDNA 和部分基因丢失，进而影响衰老过程[46-48]。在木解霉中，质粒样 DNA 被释放和扩增，伴随着 mtDNA 重组增加，导线粒体基因减少，从而引起衰老[45-46,49]。木解霉在其他营养充足的前提下，减少葡萄糖的摄入，过氧化

表1 不同真菌中衰老的环境影响因素

Table 1 The environmental factors influencing senescence in different fungi

真菌 Fungi	影响因素 Factors	对衰老的调控 Regulation of aging	涉及功能 Functions	参考文献 References
Aspergillus flavus	高温 High temperature	+	细胞膜破坏、细胞壁变薄 Cell membrane disruption, cell wall thinning	[12]
Penicillium rugulosum	极低温 Extremely low temperature	+	活性氧 ROS	[13]
Geotrichum fragrans	酸性pH值 Acidic pH	+	鸟苷酸 GMP	[17]
Aspergillus flavus	低温 Low temperature	−	能量代谢 Energy metabolism	[21]
Alternaria alternata	红光 Red light	−	性发育、次级代谢 Sexual development, secondary metabolism	[22]
Aspergillus flavus, Aspergillus parasiticus	白光、蓝光 White light, blue light	−	次级代谢 Secondary metabolism	[25]
Neurospora crassa	白光、红光 White light, red light	受*Ve*-1调控 Regulated by *Ve-1*	无性生殖 Asexual reproduction	[34]
Podospora anserina	光照 Illumination	受*PaPhy*1、*PaPhy*2调控 Regulated by *PaPhy1* and *PaPhy2*	子实体发育 Fruiting body development	[35]
Aspergillus niger	高/低pH值 High/Low pH	+	能量代谢 Energy metabolism	[38]
Aspergillus fumigatus	酸性pH值 Acidic pH	受*PacC*调控 Regulated by *PacC*	无性生殖 Asexual reproduction	[39]
Aspergillus nidulans	pH值变化 Changes in pH	受*PalH*调控 Regulated by *PalH*	泛素化 Ubiquitination	[40]

+：促进；−：抑制。

+: Promotion; −: Inhibition.

氢水平降低，并且 mtDNA 稳定性增加，导致衰老延缓[50]。在木解霉中引入 ADP/ATP 易位基因(adenine nucleotide translocator, *PaAnt*)，同样发现了 mtDNA 稳定性大幅度下降，伴随着碎片化的线粒体超微结构、ROS 含量增加以及线粒体膜电位降低，这些变化共同导致真菌衰老[51]。在 *N. crassa* 中，参与 DNA 错配修复的(DNA mismatch binding protein, MutS)家族蛋白同源物基因(MutS homolog 1, *msh1*)的缺失会导致 mtDNA 大规模缺失和重排，从而加速衰老[52]。综上所述，mtDNA 的稳定性是影响衰老的关键因素。

2.2.2 自噬

自噬是一种细胞内部物质循环和降解的重要途径，在丝状真菌生长发育以及无性或有性生殖过程中发挥重要作用[73-74]。在丝状真菌中，错误折叠或损伤的线粒体蛋白优先通过自噬降解，维持蛋白质含量，这可能是延缓真菌衰老的重要途径[68]。在木解霉中，线粒体超氧化物清除酶(mitochondrial superoxide dismutase, MnSOD)缺失会诱导自噬发生，一些损伤的线粒体蛋白被选择性降解，这可能是该菌株延缓衰老的关键原因[69]。在球孢白僵菌(*Beauveria bassiana*)中，自噬相关蛋白 11 (autophagy related gene 11, ATG11)基因的缺失导致饥饿胁迫下的分生孢子显著减少(表 2)，表现出对氧化应激的敏感性增强和无性繁殖受损，影响自噬过程，可能导致衰老[75-76]。在顶头孢霉(*Acremonium chrysogenum*)中，自噬基因(*Acremonium chrysogenum* autophagy gene, *MoAtg*) *Acatg*1、*Acatg*8 和 *Acatg*11 的破坏会改变头孢菌素等次级代谢合成机制，分生孢子萌发延迟，从而影响衰老[77]。在稻巨座壳菌(*Magnaporthe grisea*)中，由饥饿、伤害等外界胁迫会抑制自噬负调节因子(mammalian target of rapamycin, mTOR)激酶活性，降低代谢需求，诱导自噬的发生，引起真菌衰老[78]。在稻瘟菌(*Magnaporthe oryzae*)中，自噬基因(*Magnaporthe oryzae* autophagy gene, *MoAtg*) *MoAtg*8、*MoAtg*4、*MoAtg*1、*MoAtg*6 和 *MoAtg*14 的敲除均会影响稻瘟菌菌丝的生长、产孢以及孢子的萌发，出现气生菌丝减少，分生孢子产生减少等衰老特征[79]。在禾谷镰孢菌(*Fusarium graminearum*)中，若与自噬相关基因(autophagy gene, *Atg*)缺失时，禾谷镰孢菌的气生菌发育与菌丝生长都会受到影响，同时影响其在孢子形成过程中孢子内部脂质的储存、利用和降解[70]。这些结果提示或许可以通过自噬来调节真菌生长发育或生殖过程以调控衰老。在自噬过程中，液泡参与降解衰老或受损的细胞器和蛋白质，这些细胞成分通过自噬小体的形式被运送到液泡中，增加细胞营养，从而抑制衰老[80]。

2.2.3 ROS 稳态

氧化应激是另一个影响丝状真菌衰老的重要因素。在有氧代谢过程中，ROS 的生成不可避免，ROS 也是导致真菌衰老的主要原因[81]。它们在低浓度时作为信号分子调节基因表达和细胞功能，但在高浓度时则引发氧化应激，损害细胞结构和功能，加速真菌衰老，氧化还原电位的波动和 ROS 是真菌细胞信号传导过程中的重要介质，包括分化和发育[53]。黑曲霉在 1 mmol/L 过氧化氢的氧化应激下，葡萄糖和氨摄取率显著降低，营养吸收减少，影响真菌生长并可能会引起衰老[54]。在木解霉中，O-甲基转移酶基因 *PaMth1* 缺失导致氧化应激增加，伴随抗氧化应激能力下降，导致衰老，其寿命平均减少 18%[82-83]。另外，线粒体复合物功能受损、线粒体蛋白稳定性下降同样会引起真菌因 ROS 含量积累而衰老[84-85]。然而 ROS 含量过低也会导致真菌衰老[86]。超氧化物歧化酶、过氧

表2　不同真菌中衰老的遗传调控

Table 2　Genetic regulation of senescence in different fungi

真菌 Fungi	涉及功能 Factors	基因/蛋白 Gene/Protein	参考文献 References
Podospora anserina	ADP/ATP	*PaAnt*	[37]
Podospora anserina	自噬 Autophagy	MnSOD	[45]
Beauveria bassiana	无性生殖 Asexual reproduction	Atg11	[46-47]
Acremonium chrysogenum	次级代谢合成 Secondary metabolite synthesis	*Acatg1*, *Acatg8*, *Acatg11*	[48]
Magnaporthe oryzae	自噬调节 Autophagy regulation	TOR	[49]
Magnaporthe grisea	无性生殖 Asexual reproduction	*MoAtg8*, *MoAtg4*, *MoAtg1*, *MoAtg6*, *MoAtg14*	[50]
Fusarium graminearum	脂质合成 Lipid synthesis	*Atg* family	[51]
Neurospora crassa	DNA错配修复 DNA mismatch repair	*msh*1	[52]
Aspergillus sp.	氧化应激 Oxidative stress	Nox complex	[53-54]
Aspergillus niger	氧化应激 Oxidative stress	SODA, *CcsA*	[55-56]
Aspergillus niger	合成代谢 Anabolism	*GcnE*	[57]
Metarhizium robertsii	能量代谢 Energy metabolism	*MAA_06480 MAA_02043*	[58]
Podospora anserina	细胞呼吸补偿机制 Cellular respiratory compensation mechanism	*PaCox1*	[59]
		PaCox17	[60]
	线粒体蛋白稳态 Mitochondrial protein homeostasis	*PaLon*	[61]
		PaClpP	[62]
		PaIap	[63]
	磷脂代谢 Phospholipid metabolism	*PaCrd1*	[63]
	线粒体基因稳态 Mitochondrial genetic homeostasis	*PaDnm1*	[64]
		PaAtpe, *PaAtpg*, *PaMic10*, *PaMic26*	[65]
	凋亡 Apoptosis	*PaAif2*	[66]
		PaAmid1	[67]
	氧化应激 Oxidative stress	*PaMth1*	[68-69]
		PaSod2, *PaSod3*	[70]
	自噬 Autophagy	*PaAtg1*	[71]
		PaAtg24	[72]

化氢酶、谷胱甘肽以及硫氧还原蛋白是丝状真菌 ROS 解毒系统[87]。在竹黄菌(*Shiraia bambusicola*)中，外源性氧化应激提高了真菌 ROS 解毒酶活性，刺激了真菌次生代谢，因而菌株在高浓度过氧化氢下仍不衰老。在丝状真菌糙皮侧耳菌(*Pleurotus ostreatus*)中，重金属 Pb 会引起氧化损伤，但在过氧化氢酶和谷胱甘肽帮助下，真菌仍可以继续生长而不衰老[88]。在木解霉转录组分析中，发现超氧化物歧化酶 3 (*Podospora anserina* superoxide dismutas 3, PaSod 3)的丰度在衰老过程中下降[89]。类似地，在黑曲霉中，缺铁会引起氧化应激，而超氧化物歧化酶基因(superoxide dismutas A gene, *SODA*)能与铜伴侣蛋白基因耦联，保护真菌并延缓衰老[55-56]。还原型烟酰胺腺嘌呤二核苷酸(nicotinamide adenine dinucleotide, NADH)脱氢酶是线粒体呼吸链最重要的蛋白之一，它不仅作为 ROS 的主要来源，还是氧自由基代谢调控相关途径的关键因子，NADH 脱氢酶的缺乏，可以削弱线粒体呼吸链，减少 ROS 的释放，而自由基的减少可抑制菌体的衰老；在孙悦的研究中，当木解霉中 NADH 脱氢酶基因(NADH dehydrogenase 3 gene, *Pandh3*)缺乏时，生命周期延长了 2 倍以上，说明 NADH 脱氢酶的存在会促进衰老[90]。因此，无论是线粒体功能障碍，还是环境胁迫，都会引起真菌氧化应激。在氧化应激条件下，ROS 解毒系统所介导的 ROS 稳态或许是调控丝状真菌衰老的关键。

2.2.4 代谢

丝状真菌的代谢水平决定了其生长速度和生物合成能力，其代谢失衡或降低可能导致细胞功能下降，最终促进衰老。在粗糙脉孢菌(*N. crassa*)中，生物钟相关基因 *lag-1* 和 *ras-1* 缺失会影响脂类代谢，同时脂质的缺乏会改变真菌昼夜节律性(表 2)，导致真菌衰老[91-93]。在木解霉中，参与磷脂稳态控制的基因 *PaIap* 缺失会影响真菌磷脂代谢过程，菌丝生长缓慢，衰老延缓[63]。在丝状真菌高山被孢霉(*Mortierella alpina*)中，KNO_3 处理会促进花生四烯酸(arachidonic acid, ARA)的合成代谢从而抑制衰老，而尿素处理则会加速脂质代谢，同时增加 ROS 含量，刺激菌丝体分解，导致衰老[94]。因此，维持代谢水平稳态对于调控真菌衰老具有重要意义。

2.2.5 其他

丝状真菌在不同的环境条件下，会发生 DNA 的甲基化水平、组蛋白的乙酰化/去乙酰化、小干扰 RNA 或长非编码 RNA 表达等表观遗传修饰改变[95]，导致基因的转录和翻译水平的变化。这些变化可能会影响丝状真菌的代谢途径和产物的合成[96]，引起丝状真菌的衰老和退化[97-98]。Kritsky 等研究表明，在 *N. crassa* 中，DNA 甲基化抑制剂 5-氮杂胞苷抑制光照对 *N. crassa* 孢子产生减少的影响，证明了 DNA 甲基化可抑制该真菌的基因 *dim-1* 的表达，影响分生孢子以及有性生殖结构发育并促进其衰老过程[99]。在罗伯茨绿僵菌(*Metarhizium robertsii*)中，对能量合成至关重要的基因(乙酰辅酶 A 乙酰转移酶 MAA_06480 和果糖-1,6-二磷酸酶 MAA_02043)在菌丝生长阶段被适度甲基化和高表达，引发能量代谢失衡，细胞功能下降，最终促进衰老[58]。由此可知，DNA 甲基化等表观遗传修饰在调控丝状真菌衰老中起着重要作用，这些修饰能够影响基因表达和代谢水平，从而引发衰老。

3 总结与展望

丝状真菌的衰老是一个复杂且多维度的过程，这一过程主要受到环境因素和内在遗传因素的影响。在与真菌衰老所有的影响因素中，

线粒体不稳定性(功能障碍和 mtDNA 不稳定)相关的研究最多，也是导致丝状真菌衰老的主要因素[81]。无论是温度、光照和 pH 等环境因素，或者是 DNA 甲基化、代谢改变等内在遗传因素，似乎都会引起线粒体不稳定性，特别是在木解霉中[18,38,41]。线粒体不仅负责细胞的能量供应，其功能障碍还会增加 ROS 含量并损伤 mtDNA，导致 mtDNA 重组和代谢水平变化，从而促进衰老；为了应对这些损伤，丝状真菌通过自噬与 ROS 解毒机制来修复受损蛋白，维持细胞稳态，延缓衰老[50,80,88]。综上所述，丝状真菌衰老是一个涉及外部环境与细胞内部机制相互作用的过程。

在以往衰老的研究中，端粒作为染色体末端的保护结构，其长度与细胞分裂次数和衰老密切相关。然而，丝状真菌的端粒长度并未显示与衰老直接关联。虽然端粒缩短与细胞衰老或凋亡有关[100-101]，但 Chakravarti 等在木解霉衰老过程中并未发现端粒缩短的结果[101]。目前，丝状真菌的研究涵盖了多个方面的内容，并且借助了多种先进的技术手段。随着高通量测序、蛋白质组学、代谢组学和生物信息学的发展，系统生物学方法为研究丝状真菌衰老提供了强大的工具[102-103]。通过整合多组学数据，构建动态的衰老网络模型，可以更全面地揭示衰老过程中的分子事件和调控网络。另外，丝状真菌的多样性提供了丰富的模型系统，用于探索不同环境适应性和衰老模式。许多丝状真菌的菌体衰老会导致工业化生产效率下降，影响生产效益。因此，深入研究丝状真菌衰老的机制对于工业应用领域，如提高抗生素和生物酶的生产效益具有重大意义。同时，揭示衰老的基本生物学原理，有利于为人类衰老疾病的预防和治疗提供新思路。

总之，丝状真菌衰老机制的研究正迎来一个充满希望的时代。借助跨学科合作与技术创新，有望在未来加深对衰老的认识，为增进人类福祉与推动可持续发展作出贡献。

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