RESEARCH ARTICLE

First Report of *Hamigera ingelheimensis* Isolated from Cheoltan Mountain in Korea

Tae-Gyeong Kim[1], Leonid N. Ten[2], Soo-Min Hong[1], Seong-Keun Lim[1], Seung-Yeol Lee[1,2], and Hee-Young Jung[1,2,*]

[1]College of Agriculture and Life Sciences, Kyungpook National University, Daegu 41566, Korea
[2]Institute of Plant Medicine, Kyungpook National University, Daegu 41566, Korea

[*]Corresponding author: heeyoung@knu.ac.kr

ABSTRACT

A fungal strain designated KNUF-22-016 was isolated from a soil sample collected in Cheoltan Mountain in Yeongju, Korea. The cultural and morphological characteristics of this strain closely resembled those of *Hamigera ingelheimensis*. The colonies formed by the isolate appeared light orange to dark orange on Czapek yeast extract agar, its conidiophores were rarely branched, smooth-walled, measuring 109.9–864.8 × 4.1–7.4 µm, with its smooth-walled conidia being 2.3–4.6 × 1.9–3.5 µm in size. Phylogenetic analysis using concatenated sequences of the internal transcribed spacer (ITS) regions and the *Mcm7*, *RPB2* and *Tsr1* genes confirmed the affiliation of strain KNUF-22-016 with *H. ingelheimensis.* To the best of our knowledge, this fungus has not been previously documented in Korea.

Keywords: *Hamigera*, Multilocus sequence analysis, Soil-inhabiting fungi, Unreported fungi

pISSN : 0253-651X
eISSN : 2383-5249

Kor. J. Mycol. 2024 September, 52(3):155–163
https://doi.org/10.4489/kjm.520301

Received: June 09, 2024
Revised: July 10, 2024
Accepted: August 09, 2024

INTRODUCTION

The genus *Hamigera* was first established to accommodate two species that were formerly classified under the genus *Talaromyces* (*T. avellaneus* and *T. striatus*). These two species could be distinguished from other members of the genus because they formed individual asci rather than in chains. This distinctive trait led Stolk and Samson in 1971 to propose the genus *Hamigera* through the reclassification of *T. avellaneum* and *T. striatus* as *Hamigera avellanea* (the type species) and *H. striata*, respectively [1]. Since then, the taxonomic classification of *H. striata* has changed a few times and is currently recognized as *Pseudohamigera striata* [2]. In 2010, the taxonomic affiliations of several fungal isolates from the Agricultural Research Service Culture Collection (NRRL) were examined, and a multilocus sequence analysis (MLSA) using the *Mcm7*, *RPB2*, and *Tsr1* genes was conducted [3]. From the analyzed isolates, six strains were identified as new species within the genus *Hamigera*, namely *H. fusca*, *H. inflata*, *H. insecticola*, *H. pallida*, *H. paravellanea*, and *H. terricola* [3]. Another member of the genus *Hamigera*, *H. ingelheimensis*, underwent a series of reclassifications prior to being assigned its current taxonomic affiliation. Initially, it was classified as *Penicillium ingelheimensis*, after which it was reclassified as

Merimbla ingelheimensis based on a phylogenetic analysis distinguishing it from closely related species such as *H. avellanea* [4]. Following the Melbourne Code [5], which allows only a single name for a fungus, and to reflect the phylogenetic position of the species, *M. ingelheimensis* was later reclassified as *H. ingelheimensis* [6]. Recently, Houbraken et al. (2020) proposed the reclassification of *Talaromyces brevicompactus* to *Hamigera brevicompacta* based on phylogenetic analysis using concatenated sequences of the *BenA*, *CaM*, and *RPB2* genes [2]. As a result, the genus *Hamigera* currently encompasses nine species: *H. avellanea, H. fusca, H. inflata, H. ingelheimensis, H. insecticola, H. pallida, H. paravellanea, H. terricola*, and *H. brevicompacta*.

This study sought to identify previously unreported *Hamigera* species in Korea, isolated from a soil sample collected in Cheoltan mountain, Yeongju. This investigation was conducted as part of our research initiative focused on discovering indigenous Korean fungal species. The isolated strain KNUF-22-016 was characterized through both morphological and molecular analyses, and its taxonomic placement within the genus was confirmed utilizing an MLSA approach.

MATERIALS AND METHODS

Sample collection and fungal isolation

In 2023, soil samples were collected from Cheoltan Mountain in Yeongju, Gyeongsangbuk-do, Korea (36° 49'52.3"N, 128°37'46.1"E) and transported to the laboratory for further analysis. Fungi were isolated using the dilution plating method. Each soil sample was mixed with 10 mL of sterile distilled water, vortexed, serially diluted, and spread onto potato dextrose agar (PDA; Difco, Detroit, MI, USA) plates. The PDA plates were then incubated at 25°C for one week. Afterward, single fungal colonies were transferred to new plates and incubated under the same conditions. Several fungal strains were isolated and preliminarily identified by sequencing the internal transcribed spacer (ITS) regions. Among them, strain KNUF-22-016 was recognized as a fungal species that had not been previously identified in Korea. Therefore, this strain was selected for comprehensive analysis, including morphological and molecular phylogenetic analyses. Stock culture of the strain, namely, KNUF-22-016 (NIBRFGC000509833) was deposited in the National Institute of Biological Resources (NIBR) as metabolically inactive cultures.

Morphological and Cultural characterization

After one week of incubation at 25°C on Czapek yeast extract agar (CYA; MBcell, Seoul, Korea), malt extract agar (MEA; Difco, Detroit, MI, USA), and glycerol nitrate agar (G25N), the morphological features of isolate KNUF-22-016, including color, shape, and size, were recorded [3]. Additionally, cultures on CYA were incubated at 5°C and 37°C for one week [3]. The fungal characteristics were examined using a light microscope (BX-50, Olympus, Tokyo, Japan).

DNA extraction, PCR amplification, and sequencing

Genomic DNA was extracted from the mycelia using the HiGene Genomic DNA Prep Kit (Biofact, Daejeon, Korea) according to the manufacturer's instructions. For molecular analysis, the ITS regions, minichromosome maintenance complex component 7 (*Mcm7*), the second largest subunit of RNA polymerase II (*RPB2*), and ribosome biogenesis protein (*Tsr1*) genes were amplified via PCR [3]. Specifically, the ITS regions, the partial *Mcm7* gene, the partial *RPB2* gene, and the partial *Tsr1* gene were respectively amplified using primers ITS1F/ITS4 [7,8], 709F/1447R [9], 5F/7CR [10], and 1459F/2308R [9]. Subsequently, the sequences of the amplified ITS regions, as well as those of the *Mcm7*, *RPB2*, and *Tsr1* genes, were deposited in the GenBank database under accession numbers LC799815, LC800019, LC800020, and LC800021, respectively.

Molecular phylogenetic analyses

The sequences of our isolates were compared with reference sequences from the GenBank database of the National Center for Biotechnology Information (NCBI) using the Basic Local Alignment Search Tool (BLAST). The sequences of the ITS regions, the *Mcm7*, *RPB2*, and *Tsr1* genes were concatenated and phylogenetic trees were constructed using the maximum likelihood (ML), neighbor-joining (NJ), and maximum parsimony (MP) algorithms based on the Kimura model [11]. Phylogenetic analysis was conducted using the MEGA 7 (https://www.megasoftware.net/) software utilizing bootstrap values from 1,000 replications [12]. The reference sequences from the NCBI GenBank database are listed in Table 1.

Table 1. List of species used in phylogenetic analysis along with their GenBank accession numbers.

Species	Strain	GenBank accession numbers			
		ITS	*Mcm7*	*RPB2*	*Tsr1*
Hamigera avellanea	NRRL 1938^{T}	AF454075	GU092852	EU021627	GU092726
Hamigera avellanea	NRRL 58017	GU092954	GU092896	GU092917	GU092727
Hamigera brevicompacta	CBS 102661^{T}	NR_160208	–	MN969203	–
Hamigera fusca	NRRL 35721	GU092939	GU092888	GU111760	GU092717
Hamigera fusca	NRRL 35601^{T}	NR_137734	GU092879	GU111755	GU092715
Hamigera inflata	NRRL 58014^{T}	NR_137736	GU092895	GU092908	GU092725
Hamigera ingelheimensis	NRRL 3522	GU092960	GU092871	GU092911	GU092730
Hamigera ingelheimensis	NRRL 2110^{T}	MH856108	GU092856	GU092912	GU092728
Hamigera ingelheimensis	**KNUF-22-016**	**LC799815**	**LC800019**	**LC800020**	**LC800021**
Hamigera insecticola	NRRL 35386^{T}	NR_137684	GU092872	GU111754	GU092718
Hamigera insecticola	NRRL 35442	EF634416	GU092873	GU092907	GU092722
Hamigera pallida	NRRL 35718^{T}	NR_137737	GU092885	GU111758	GU092710
Hamigera paravellanea	NRRL 35714	GU092953	GU092882	GU092918	GU092737
Hamigera paravellanea	NRRL 35720^{T}	NR_137738	GU092887	GU092919	GU092738
Hamigera terricola	NRRL 29055^{T}	NR_137735	GU092860	GU111751	GU092712
Hamigera terricola	NRRL 35717	GU092945	GU092884	GU111757	GU092708
Hamigera brevicompacta	CBS 102661^{T}	NR_160208	–	MN969203	–
Pseudohamigera striata	NRRL 717^{T}	NR_145139	GU092901	GU092928	GU092697

ITS: internal transcribed spacer regions; *Mcm7*: minichromosome maintenance complex component 7; *RPB2*: the second largest subunit of RNA polymerase II; *Tsr1*: Tsr1 ribosome maturation factor. ^{T}Type strain. The strain isolated in this study is indicated in boldface.

RESULTS AND DISCUSSION

Cultural and morphology characteristics

After 7 days of incubation at 25°C on CYA, the colony size of strain KNUF-22-016 reached 67.1–69.8 mm. The colony exhibited a variety of colors ranging from light orange to dark orange, with a pale pink reverse side (Fig. 1A and 1B). In contrast, at 37°C, colony size decreased to 37.8–39.1 mm, indicating a suboptimal temperature for growth (Fig. 1C and 1D). After 7 days of incubation at 25°C on MEA, the colonies measured 61.2–62.9 mm, displaying a light pinkish cinnamon color with a pale pinkish reverse side (Fig. 1E and 1F). No growth was observed on G25N medium under the same culture conditions or on CYA after 7 days of incubation at 5°C. Conidiophores, arising from the colony surface, ranged in size from 109.9–864.8 × 4.1–7.4 µm (Fig. 1G and 1H). Apical whorls of metulae typically varied in size from 4.6–14.2 × 2.4–5.7 µm, each bearing five or more phialides measuring 6.5–10.6 × 1.6–3.3 µm (Fig. 1G and 1H). The conidia were observed to be 2.3–4.6 × 1.9–3.5 µm in size, with smooth walls (Fig. 1I). Based on both its cultural and morphological traits, the isolated strain KNUF-22-016 appears to be closely affiliated with *H. ingelheimensis* [3]. In contrast, KNUF-22-016 differed from its close relative, *H. avellanea*, in several aspects, including colony color, colony size (61.2–62.9 mm vs. 45–70 mm on MEA), conidiophore size (109.9–864.8 × 4.1–7.4 µm vs. 200–500 × 3–5 µm), and larger metulae (4.6–14.2 × 2.4–5.7 µm vs. 5–12 × 3–5 µm) (Table 2).

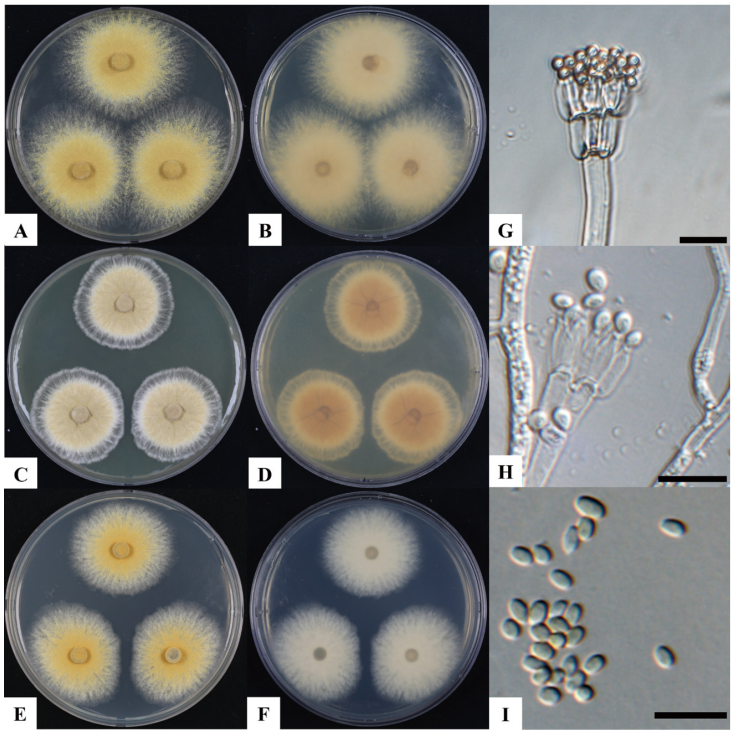

Fig. 1. Cultural and morphological characteristics of *Hamigera ingelheimensis* KNUF-22-016. A, B: colony on Czapek yeast extract agar (CYA) after 7 days at 25°C; C, D: colony on CYA after 7 days at 37°C; E, F: colony on malt extract agar (MEA) after 7 days at 25°C; G, H: conidiophores; I: conidia. Scale bars G-I = 10 µm.

Table 2. Comparison of morphological characteristics of KNUF-22-016 with reference species *Hamigera ingelheimensis* and *H. avellanea.*

Characteristics		*Hamigera ingelheimensis* KNUF-22-016[a]	*H. ingelheimensis*[b]	*H. avellanea*[c]
Colony	Color	CYA: light orange to dark orange and pink in reverse; MEA: light pinkish cinnamon	CYA: light salmon orange to capucine orange, pale pink near safrano pink in reverse; MEA: light pinkish cinnamon to cinnamon buff	CYA: conidial areas pinkish, deep red shades near Indian red in reverse; MEA: pale yellow to pinkish, vinaceous purple in reverse; G25N: light buff in reverse
	Size (diam.)	CYA: 67.1–69.8 mm; MEA: 61.2–62.9 mm in 7 days at 25°C	CYA: 55–65 mm; MEA: 70 mm in 7 days at 25°C	CYA: 50–70 mm; MEA: 45–70 mm; G25N: 23–24 mm in 7 days at 25°C
	Shape	CYA: plane, velutinous, no exudate; MEA: thin, plane, velutinous, low, heavy sporulation	CYA: plane, velutinous, no exudate; MEA: thin, plane, velutinous, low, heavy sporulation	CYA: lanose to velvety, low; MEA: thin, low, sporulating well; G25N: plane, low, thin
Conidiophores	Size (μm)	109.9–864.8 × 4.1–7.4	100–800 × 4–7	200–500 × 3–5
	Shape	rarely branched, smooth walls, arising from colony surface	rarely branched, smooth walls, arising from colony surface	rarely branched, arising from colony surface, smooth walls
Metulae	Size (μm)	4.6–14.2 × 2.4–5.7	3–14 × 3–6	5–12 × 3–5
Conidia	Size (μm)	2.3–4.6 × 1.9–3.5	3.5–5.0 × 2–3	3–5 × 2–3
	Shape	smooth walls	smooth walls	smooth walls
Philaides	Size (μm)	6.5–10.6 × 1.6–3.3	7–9 × 2–3	5–9 × 2.5–3.5
	Shape	acerose to ampulliform	acerose to ampulliform	ampulliform

CYA: Czapek yeast extract agar; MEA: malt extract agar; G25N: glycerol nitrate agar; Diam.: diameter.
[a] Fungal strain used in this study; [b] Source of description [3]; [c] Sources of description [1,3].

Molecular phylogeny analysis

The amplicons obtained from the ITS, *Mcm7*, *RPB2*, and *Tsr1* loci of strain KNUF-22-016 were 591, 681, 1020, and 781 bp long, respectively. The ITS sequence of the isolate exhibited 99.6–100% identity with several strains of *H. ingelheimensis*, including NRRL 29059 (GU092961), NRRL 3522 (GU092960), and CBS:163.42 (MH856108). Additionally, strain KNUF-22-016 exhibited a close relationship with *H. avellanea* NRRL 1938 (98.9% similarity, AF454075), *H. paravellanea* NRRL 35720 (98.9%, NR_137738), *H. brevicompacta* CBS 102661 (98.7%, NR_160208), and *H. fusca* NRRL 35601 (98.6%, NR_137734). Based on the similarity of the *Mcm7* gene sequence, *H. ingelheimensis* NRRL 2110 (100% similarity, GU092856), *H. paravellanea* NRRL 35720 (98.5%, GU092887), *H. avellanea* NRRL 58017 (98.3%, GU092896), and *H. inflata* NRRL 58014 (97.3%, GU092895) were the closest phylogenetic relatives of strain KNUF-22-016. The partial *RPB2* gene sequence of the isolate was 100, 99.2, 99.0, 98.9, and 97.4% similar to those of *H. ingelheimensis* NRRL 58707 (GU092909), *H. avellanea* NRRL 1938 (EU021627), *H. paravellanea* NRRL 35720 (GU092919), *H. brevicompacta* CBS 102661 (MN969203), and *H. terricola* NRRL 58014 (GU092908), respectively. The *Tsr1* sequence of strain KNUF-22-016 shared 100, 98.7, and 97.9% identity with *H. ingelheimensis* NRRL 2110 (GU092728), *H. avellanea* NRRL 1938 (GU092726), and *H. paravellanea* NRRL 35714 (GU092737), respectively. These findings demonstrated that several *Hamigera* species are closely related to strain KNUF-22-016. Although the isolate exhibited 100% similarity with various strains of *H. ingelheimensis* based on the sequences of the four molecular markers examined herein, it is evident that the strain could have not been precisely identified based on only

a single molecular marker. Therefore, multilocus sequence analysis was conducted using concatenated sequences of the ITS regions, as well as the *Mcm7*, *RPB2*, and *Tsr1* genes. This approach successfully allowed for the identification of the six members of the genus *Hamigera* from the current nine validated species [3]. The ML phylogenetic tree based on the concatenated sequences clearly demonstrated that the phylogenetic characteristics of KNUF-22-016 were consistent with those of *H. ingelheimensis* (Fig. 2). The same topology of the phylogenetic tree was also obtained using the NJ and MP algorithms, as indicated by the filled circles in Fig. 2, further supporting the affiliation of the isolate. Unfortunately, the sequences of the *Mcm7* and *Tsr1* genes for the recently described *H. brevicompacta* were unavailable in the GenBank database. However, the topology of the phylogenetic tree constructed using the concatenated sequences of only ITS regions and the *RPB2* gene (tree not shown) was similar to that of the abovementioned phylogenetic tree, confirming the differentiation of KNUF-22-016 from *H. brevicompacta* at the species level. The results of both morphological and phylogenetic analyses revealed that KNUF-22-016 is a strain belonging to *H. ingelheimensis*. To the best of our knowledge, this study represents the first report of this fungal species in Korea.

Various biologically active compounds have been identified in members of the genus *Hamigera.* Among the nine species mentioned above, the production of secondary metabolites has been more extensively studied in *H. avellanea*. The antifungal compounds hamigerone, dihydrohamigerone, and avellaneanone, the potential antimalarial compounds hamavellone B and hamigeromycins B, the bioactive alkaloid pseurotin A, and the anthraquinone pigments emodin, ω-hydroxyemodin, and emodic acid have been isolated from BCC 17816, KUFA 0732, and other strains of *H. avellanea* [13-16]. Among these, pseurotin A is known for its cytotoxic activity against mouse leukemia P388, human leukemia HL60, human lung carcinoma A-549, and human hepatic carcinoma BEL-7402 cell lines, as well as for its inhibition of the fungal chitin synthase and anti-inflammatory activity [17]. Emodin possesses a wide range of bioactive properties, including antibacterial, anticancer, cardioprotective, antioxidant, anti-fibrotic, and anti-inflammatory effects [18]. Eight species of the genus *Hamigera*, excluding *H. ingelheimensis*, produced avellanins A and B as the most common metabolites, exhibiting inhibitory activity against apolipoprotein B production [19]. Interestingly, *H. ingelheimensis* produced other structurally related compounds, including avellanin C and the cyclic hexapeptide PF1171C [20]. Avellanin C is known for its quorum-sensing (QS) inhibiting activity against *Staphylococcus aureus* [20]. The inhibition of QS in *S. aureus* can reduce bacterial virulence, thereby enhancing the host's innate immune response and limiting inflammation [21]. In contrast to *H. avellanea*, the production of bioactive compounds by *H. ingelheimensis* has not been thoroughly investigated. Therefore, isolate KNUF-22-016 can be considered a valuable strain for further study of this species in Korea.

This study provides the first record of the occurrence of *H. ingelheimensis* in Korea, contributing to the discovery of indigenous Korean fungal species. Additional research is needed to gain more comprehensive insights into the geographic distribution of *H. ingelheimensis* and its ecological and biological roles in Korean ecosystems, as well as to explore its potential therapeutic properties.

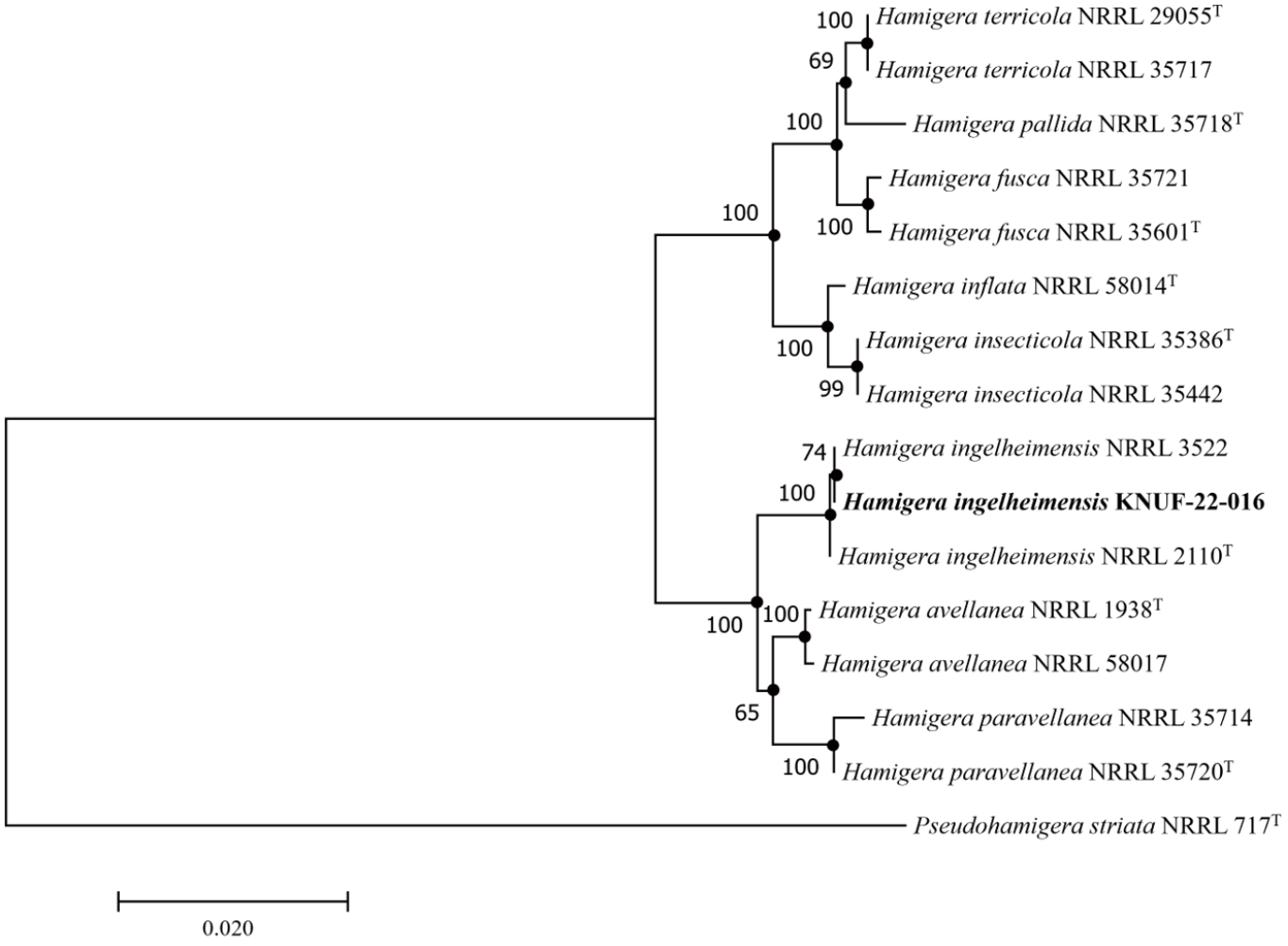

Fig. 2. Maximum-likelihood phylogenetic tree based on the combined sequences of internal transcribed spacer (ITS) regions, minichromosome maintenance complex component 7 (*Mcm7*), the second largest subunit of RNA polymerase II (*RPB2*), and Tsr1 ribosome maturation factor (*Tsr1*) showing the phylogenetic position of strain KNUF-22-016 among *Hamigera species*. Bootstrap values greater than 60% (based on 1,000 replications) are shown at branch points. The filled circles indicate that the corresponding nodes were also recovered in trees generated using the neighbor-joining and maximum parsimony algorithms. The isolated strain is indicated in bold. *Pseudohamigera striata* NRRL 717^T was used as an outgroup. Bar, 0.02 substitutions per nucleotide position.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

ACKNOWLEDGMENTS

This study was supported by the National Institute of Biological Resources, funded by the Ministry of Environment of the Republic of Korea [NIBR202203112].

REFERENCES

1. Stolk AC, Samson RA. Studies on *Talaromyces* and related genera I. *Hamigera* gen. nov. and *Byssochalmys*. Persoonia 1971;6:341–57.
2. Houbraken J, Kocsube S, Visagie CM, Yilmaz N, Wang XC, Meijer M, Kraak B, Hubka V, Besnch K, Samson RA, et al. Classification of *Aspergillus*, *Penicillium, Talaromyces* and related genera (*Eurotiales*): An overview of families, genera, subgenera, sections, series, and species. Stud Mycol 2020;165–9. doi: 10.1016/j.simyco.2020.05.002
3. Peterson SW, Jurjevic Z, Bills GF, Stchigel AM, Vega FE. Genus *Hamigera*, six new species and multilocus DNA sequence-based phylogeny. Mycologia 2010;102:847–64. doi: 10.3852/09-268
4. Pitt JI. The genus *Penicillium* and its teleomorphic states *Eupenicillium* and *Talaromyces*. London: Academic Press; 1979.
5. Mcneill J, Barrie FR, Buck WR, Demoulin V, Greuter W, Hawksworth DL, Herendeen PS, Knapp MSK, Prado J, Prud'homme Van Reine WF. International code of nomenclature for algae, fungi, and plants (Melbourne code). Regnum Vegetabile 154. Koenigstein: Koeltz Scientific Books; 2012.
6. Igarashi Y, Hanafusa T, Gohda F, Peterson S, Bills G. Species-level assessment of secondary metabolite diversity among *Hamigera* species and a taxonomic note on the genus. Mycologia 2014;5:102–9. doi: 10.1080/21501203.2014.917736
7. Gardes M, Bruns TD. ITS primers with enhanced specificity for basidiomycetes-application to the identification of mycorrhizae and rusts. Mol Ecol 1993;2:113–8. doi: 10.1111/j.1365-294X.1993.tb00005.x
8. White TJ, Bruns T, Lee S, Taylor J. Amplification, and direct sequencing of fungal ribosomal RNA genes for phylogenetics. PCR protocols: a guide to methods and applications. In: Innis MA, Gelfand DH, Sninsky JJ, White TJ, editors. New York AP 1990;18:315–22.
9. Schmitt I, Crespo A, Divakar PK, Fankhauser JD, HermanSackett E, Kalb K, Nelsen MP, Nelson NA, Rivas-Plata E, Shimp AD, Widhelm T, Lumbsch HT. New primers for promising single copy genes in fungal phylogenetics and systematics. Persoonia 2009;23:35–40. doi: 10.3767/003158509X470602
10. Peterson SW. Phylogenetic analysis of *Aspergillus* species using DNA sequences from four loci. Mycologia 2008;100:205–26. doi: 10.1080/15572536.2008.11832477
11. Kimura M. A simple method for estimating evolutionary rates of base substitutions through comparative studies of nucleotide sequences. J Mol Evol 1980;16:111–20.
12. Kumar S, Stecher G, Tamura K. MEGA7: Molecular Evolutionary Genetics Analysis Version 7.0 for Bigger Datasets. Mol Biol Evol 2016;33:1870–4. doi: 10.1093/molbev/msw054
13. Breinholt J, Kjaer A, Olsen CE, Rassing BR, Rosendahl CN. Hamigerone and dihydrohamigerone: two acetate-derived, antifungal metabolites from *Hamigera avellanea*. Acta Chem Scand 1997;51:1241–4.
14. Isaka M, Chinthanom P, Veeranondha S, Supothina S, Luangsa-ard JJ. Novel cyclopropyl diketones and 14-membered macrolides from the soil fungus *Hamigera avellanea* BCC 17816. Tetrahedron 2008;64:11028–33. doi: 10.1016/j.tet.2008.09.077
15. Isaka M, Chinthanom P, Kongthong, S, Supothina S, Ittiworapong S. Hamigeromycins C–G, 14-membered macrolides from the fungus *Hamigera avellanea* BCC 17816. Tetrahedron 2010;66:955–61. doi: 10.1016/j.tet.2009.11.101

16. Klaram R, Dethoup T, Machado FP, Gales L, Kumla D, Hafez Ghoran S, Sousa E, Mistry S, Silva AMS, Kijjoa A. Pentaketides and 5-p-hydroxyphenyl-2-pyridone derivative from the culture extract of a marine sponge-associated fungus *Hamigera avellanea* KUFA0732. Mar Drugs 2023;21:344. doi: 10.3390/md21060344
17. Abdelwahed KS, Siddique AB, Mohyeldin MM, Qusa MH, Goda AA, Singh SS, Ayoub NM, King JA, Jois SD, El Sayed KA. Pseurotin A as a novel suppressor of hormone dependent breast cancer progression and recurrence by inhibiting PCSK9 secretion and interaction with LDL receptor. Pharmacol Res. 2020;158:104847. doi: 10.1016/j.phrs.2020.104847
18. Luo N, Fang J, Wei L, Sahebkar A, Little PJ, Xu S, Luo C, Li G. Emodin in atherosclerosis prevention: pharmacological actions and therapeutic potential. Eur J Pharmacol. 2021;890:173617. doi: 10.1016/j.ejphar.2020.173617
19. Igarashi Y, Hanafusa T, Gohda F, Peterson S, Bills G. Species-level assessment of secondary metabolite diversity among *Hamigera* species and a taxonomic note on the genus, Mycology. 2014;5:102–9. doi: 10.1080/21501203.2014.917736
20. Igarashi Y, Gohda F, Kadoshima T, Fukuda T, Hanafusa T, Shojima A, Nakayama J, Bills G, Peterson S. Avellanin C, an inhibitor of quorumsensing signaling in *Staphylococcus aureus*, from *Hamigera ingelheimensis*. J Antibiot. 2015;68:707–10. doi: 10.1038/ja.2015.50
21. Daly SM, Elmore BO, Kavanaugh JS, Triplett KD, Figueroa M, Raja HA, El-Elimat T, Crosby HA, Femling JK, Cech NB, Horswill AR, Oberlies NH, Hall PR. Omega-Hydroxyemodin limits *Staphylococcus aureus* quorum sensing-mediated pathogenesis and inflammation. Antimicrob Agents Chemother 2015;59:2223–35. doi: 10.1128/AAC.04564-14