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GENOME ANNOUNCEMENT

Genome Sequence of the Fungus *Glarea lozoyensis*: the First Genome Sequence of a Species from the *Helotiaceae* Family

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The anamorphic fungus *Glarea lozoyensis* mutant strain 74030 is an overproducer of pneumocandin B_0, which is chemically converted into Cancidas, a potent antibiotic against clinically important fungal pathogens. Pneumocandins are acylated, cyclic hexapeptides with unusual hydroxylated amino acids. With the *Glarea lozoyensis* genome, the first species from the large polyphyletic family *Helotiaceae* has been sequenced.

Glarea lozoyensis, formerly classified as *Zalerion arboricol*a (2), is an anamorphic fungus belonging to the Leotiales group. It produces lipopeptides with antifungal activities called pneumocandins which belong to the group of the echinocandin antibiotics. The wild-type strain (ATCC 20868) produces pneumocandin A_0 predominantly. In contrast, the strain sequenced here, 74030, which was obtained after two cycles of mutagenesis, is a pneumocandin B_0 overproducer (6). The acylated cyclic hexapeptide compound inhibits the synthesis of fungal cell wall glucan (9). It is chemically converted into caspofungin acetate (Cancidas), a potential therapeutic agent against fungal infections (7).

Here we present the whole-genome shotgun sequence of *Glarea lozoyenesis* ATCC 74030. The sequencing was performed using an Illumina HiSeq 2000 sequencer with a paired-end library and an additional mate pair library. The genome was assembled into 581 scaffolds (1 kb; N_{50}, 871 kb) containing 886 contigs with a total size of ~38.6 Mb. A total of 7,904 protein-coding genes were predicted by GlimmerHMM 3.0.1 (3), a coding capacity similar to that of other *Ascomycetes*. Out of these genes, 53.77% were assigned to putative functions based on similarity searches against Swiss-Prot (UniProtKB). The overall G+C content is 46.051. Additionally, 131 tRNA genes were predicted with tRNAscan-SE (5).

As pneumocandin B_0 is composed of six amino acids and a 10,12-dimethylmyristoyl side chain, it is hypothesized that a nonribosomal peptide synthetase (NRPS) and a polyketide synthase (PKS) are involved in its biosynthesis (1). A preliminary genome analysis using the gene cluster prediction tools antiSMASH (8) and SMURF (4) gave three hybrid PKS-NRPS clusters and six NRPS predicted clusters. In two of the putative NRPS clusters, six module domains were detected, as expected for pneumocandin biosynthesis.

Nucleotide sequence accession numbers. This Whole Genome Shotgun project has been deposited in DDBJ/EMBL/GenBank under accession no. GUE00000000. The version described in this article is the first version, AGUE01000000.

ACKNOWLEDGMENTS

We thank BaseClear (Leiden, Netherlands) for sequencing the *Glarea lozoyensis* genome, especially Walter Pirovano for helpful advice. We also thank Michael Müller for generous support and Gerald Bills for advice and contributions.

L.Y. was supported by an Alexander von Humboldt fellowship.

REFERENCES

1. **Adefarati AA, Giacobbe RA, Hensens OD, Tkacz JS.** 1991. Biosynthesis of L-671,329, an echinocandin-type antibiotic produced by *Zalerion arboricola*: origins of some of the unusual amino acids and the dimethylmyristic acid side chain. J. Am. Chem. Soc. **113**:3542–3545.
2. **Bills GF, Platas G, Fernando P, Masurekar P.** 1999. Reclassification of a pneumocandin-producing anamorph, *Glarea lozoyensis* gen. et sp. nov., previously identified as *Zalerion arboricola*. Mycol. Res. **103**:179–192.
3. **Delcher AL, Harmon D, Kasif S, White O, Salzberg SL.** 1999. Improved microbial gene identification with GLIMMER. Nucleic Acids Res. **27**:4636–4641.
4. **Khaldi N, et al.** 2010. SMURF: genomic mapping of fungal secondary metabolite clusters. Fungal Genet. Biol. **47**:736–741.
5. **Lowe TM, Eddy SR.** 1997. tRNAscan-SE: a program for improved detection of transfer RNA genes in genomic sequence. Nucleic Acids Res. **25**:955–964.
6. **Masurekar PS, Fountoulakis JM, Hallada TC, Sosa MS, Kaplan L.** 1992. Pneumocandins from *Zalerion arboricola*. II. Modification of product spectrum by mutation and medium manipulation. J. Antibiot. **45**:1867–1874.
7. **McCormack PL, Perry CM.** 2005. Caspofungin. A review of its use in the treatment of fungal infections. Drugs. **65**:2049–2068.
8. **Medema MH, et al.** 2011. antiSMASH: rapid identification, annotation and analysis of secondary metabolite biosynthesis gene clusters in bacterial and fungal genome sequences. Nucleic Acids Res. **39**(Suppl 2):W339–W346.
9. **Tkacz JS, DiDomenico B.** 2001. Antifungals: what's in the pipeline. Curr. Opin. Microbiol. **4**:540–545.

Received 20 December 2011 **Accepted** 20 December 2011

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doi:10.1128/EC.05302-11