Data Article

Raw genome sequence data for 13 isogenic *Aspergillus fumigatus* strains isolated over a 2 year period from a patient with chronic granulomatous disease

Eloise Ballard, Jan Zoll, Willem J.G. Melchers, Alistair J.P. Brown, Adilia Warris, Paul E. Verweij

*Medical Research Council Centre for Medical Mycology at the University of Aberdeen, Aberdeen Fungal Group, Institute of Medical Sciences, Aberdeen, UK*

*Department of Medical Microbiology, Radboud University Medical Centre, Centre of Expertise in Mycology, Nijmegen, the Netherlands*

**Abstract**

Azole-resistance in *Aspergillus fumigatus* is an emerging worldwide threat as it precludes the use of one of the 3 major classes of antifungal drugs to treat chronic and invasive aspergillosis [1]. In addition to the well-known environmental emergence of azole-resistant *A. fumigatus* strains, associated with the use of fungicides in agriculture [2,3], the development of in-host resistance, facilitated by medical antifungal use, has been described [4]. Investigations involving linked sets of (isogenic) clinical isolates of *A. fumigatus* sequentially recovered from individual patients, are extremely important in order to improve our understanding of how azole resistance develops in-host. Here we present the whole genome sequences of 13 clinical isogenic *A. fumigatus* isolates. These isolates were cultured from a single patient suffering from invasive aspergillosis over a period of 2 years. This patient underwent a wide range of antifungal therapies and the resultant isolates acquired multiple azole resistance in-host during the course of infection. The data presented here is related to our research paper titled “In-host microevolution of *Aspergillus fumigatus*: a phenotypic and genotypic analysis” which describes the phenotypic characterisation of these clinical isolates [5]. The raw sequence data was deposited in the NCBI Sequence Read Archive.

*Corresponding author. E-mail address: Paul.Verweij@radboudumc.nl (P.E. Verweij).*

https://doi.org/10.1016/j.dib.2019.104021

2352-3409/© 2019 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
In this article, we present the raw whole genome sequences of 13 clinical isolates of *Aspergillus fumigatus*. These isolates were cultured from clinical specimens obtained from a single patient over a period of 2 years. This patient was diagnosed with chronic granulomatous disease as well as severe chronic obstructive pulmonary disease and allergic bronchopulmonary aspergillosis [6]. This patient suffered from various episodes of invasive aspergillosis. A wide range of therapies, including azole monotherapy andazole combination therapy with echinocandins, were administered over the 2 year period, but unfortunately the patient died from the infection. The 13 *A. fumigatus* isolates had acquired high levels of itraconazole and posaconazole resistance during the course of infection, as well as varying degrees of voriconazole resistance [5]. These 13 isolates were subjected to whole genome sequencing and the raw sequence data are presented in this article.
2. Experimental design, materials, and methods

2.1. Origin of fungal isolates

The 13 clinical isolates sequenced in this article were isolated from a male adult patient diagnosed with X-linked chronic granulomatous disease. The patient was also diagnosed with severe chronic obstructive pulmonary disease (Gold IV) and allergic bronchopulmonary aspergillosis. The patient suffered from 3 episodes of invasive aspergillosis and developed an aspergilloma which, due to their poor respiratory condition, could not be surgically removed. The patient was prophylactically treated with interferon-gamma, trimethoprim-sulphamethoxazole and itraconazole. Between June and December 2011, the patient was treated with itraconazole and subsequently voriconazole in combination with an echinocandin (caspofungin or anidulafungin). Isolate V130-15 was collected on 22/11/11 from fluid around the right shoulder and isolates V130-14, V130-18 and V130-54 were collected from pus in the right shoulder on 25/11/11. Between December 2011 and January 2013, the patient was treated with a variety of therapies consecutively, namely liposomal amphotericin B, itraconazole, and anidulafungin in combination with voriconazole. Between August and December 2013, the patient was treated with posaconazole, followed by posaconazole in combination therapy with micafungin. Isolates V157-39, V157-40, V157-47, V157-48 and V157-62 were collected from bronchoalveolar lavage fluid (BALf) on 9/12/13. Isolates V157-59, V157-60 and V157-61 were collected from BALf on 12/12/13; and isolate V157-80 was collected from BALf on 19/12/13. Unfortunately, fungal eradication was not achieved, and the patient died from his infection.

The isolates were cultured and morphologically identified as *A. fumigatus* at Radboud University Medical Centre, Nijmegen, the Netherlands [6].

2.2. Fungal culture

*A. fumigatus* conidia from glycerol stocks frozen at ~80 °C were spread onto Sabouraud dextrose agar in T75 culture flasks (Greiner Bio-One, Germany), and incubated at 37 °C. After 7 days, conidia were harvested via immersion in 30 mL phosphate buffered saline (PBS) (Thermo Fisher Scientific, UK) containing 0.05% Tween-80 (Thermo Fisher Scientific, UK). In specific cases, conidia were inoculated in liquid glucose minimal media and incubated overnight at 37 °C rotating at 200 rpm. Mycelial mass was subsequently harvested using vacuum filtration and used for DNA isolation.

2.3. Whole genome sequencing

DNA was extracted from either conidia or mycelia. Conidia or mycelia were suspended in TE buffer (pH 8, 1% SDS, 2% Triton X100, 100mM NaCl) and the resultant suspension was shaken for 30 min at 70 °C. DNA was extracted using phenol/chloroform extraction and purified using the QIAamp DNA Blood Mini kit (Qiagen, Germany). A fragmented genomic DNA library was prepared using a Nextera XT DNA sample preparation kit (Illumina, USA). Sequencing was performed in a paired end 2×150 bp mode using an Illumina NextSeq 500 machine (Illumina, USA).

2.4. Location of raw sequence data

The raw sequence data was deposited in the NCBI Sequence Read Archive (https://www.ncbi.nlm.nih.gov/sra), under BioProject ID number PRJNA528395. The BioSample numbers for each isolates whole genome sequence are as follows: SAMN11180820 (V130-15); SAMN11180821 (V130-14); SAMN11180822 (V130-18); SAMN11180823 (V130-54); SAMN11180824 (V157-39); SAMN11180825 (V157-40); SAMN11180826 (V157-47); SAMN11180827 (V157-48); SAMN11180828 (V157-62); SAMN11180829 (V157-59); SAMN11180830 (V157-60); SAMN11180831 (V157-61); SAMN11180832 (V157-80).
Acknowledgments

EB, AB and AW are supported by the Wellcome Trust Strategic Award (grant 097377), and the MRC Centre for Medical Mycology at the University of Aberdeen (grant MR/N006364/1). AB was also supported by the Biotechnology and Biological Research Council (BB/K017365/1) and the Medical Research Council (MR/M026663/1). The work in this paper is funded by a BBSRC EASTBIO grant (BB/M010996/1) awarded to AW. The funders had no role in study design, data interpretation, or the decision to submit the work for publication.

Transparency document

Transparency document associated with this article can be found in the online version at https://doi.org/10.1016/j.dib.2019.104021.

References

[1] A.J. Ullmann, J.M. Aguado, S. Arikan-Akdagli, D.W. Denning, A.H. Groll, K. Lagrou, C. Lass—Flörl, R.E. Lewis, P. Munoz, P.E. Verweij, A. Warris, F. Ader, M. Akova, M.C. Arendrup, R.A. Barnes, C. Beigelman-Aubry, S. Blot, E. Bouza, R.J.M. Brüggemann, D. Buchheidt, J. Cadzela, E. Castagnola, A. Chakrabarti, M. Cuenca-Estrella, G. Dimopoulos, J. Fortun, J.P. Gargueux, J. Garbino, W.J. Heinz, R. Herbrecht, C.P. Heussel, C.C. Klöbler, N. Klimko, B.J. Kullberg, C. Lange, T. Lehrnbecher, J. Löfler, O. Lortholary, J. Maertens, O. Marchetti, J.F. Meis, L. Pagano, P. Ribaud, M. Richardson, E. Rolides, M. Ruhike, M. Sanguinetti, D. C. Sheppard, J. Sinkó, A. Skia, M.J.G.T. Vehreschild, C. Viscoli, O.A. Cornely. Diagnosis and management of Aspergillus diseases: executive summary of the 2017 ESCMID-ECMM-ERS guideline, Clin. Microbiol. Infect. 24 (2018) e1—e38. https://doi.org/10.1016/j.cmi.2018.01.002.

[2] E. Snelders, H.A.L. Van Der Lee, J. Kuijpers, A.J.M.M. Rijs, J. Varga, R.A. Samson, E. Mellado, A.R.T. Donders, W.J.G. Melchers, P.E. Verweij, Emergence of azole resistance in Aspergillus fumigatus and spread of a single resistance mechanism, PLoS Med. 5 (2008) 1629—1637. https://doi.org/10.1371/journal.pmed.0050219.

[3] J. Zhang, E. Snelders, B.J. Zwaan, S.E. Schoustra, J.F. Meis, K. van Dijk, F. Hagen, M.T. van der Beek, G.A. Kampinga, J. Zoll, W.J. G. Melchers, P.E. Verweij, A.J.M. Debets, A novel environmental azole resistance mutation in Aspergillus fumigatus and a possible role of sexual reproduction in its emergence, mBio 8 (2017) 1—13. https://doi.org/10.1128/mBio.00791-17.

[4] S.M.T. Camps, B.E. Dutilh, M.C. Arendrup, A.J.M.M. Rijs, E. Snelders, M.A. Huynen, P.E. Verweij, W.J.G. Melchers, Discovery of a hapE mutation that causes azole resistance in Aspergillus fumigatus through whole genome sequencing and sexual crossing, PLoS One 7 (2012) e50034. https://doi.org/10.1371/journal.pone.0050034.

[5] E. Ballard, W.J.G. Melchers, J. Zoll, A.J.P. Brown, P.E. Verweij, A. Warris, In-host microevolution of Aspergillus fumigatus: a phenotypic and genotypic analysis, Fungal Genet. Biol. (2018) 1—13. https://doi.org/10.1016/j.fgb.2018.02.003.

[6] P.E. Verweij, J. Zhang, A.J.M. Debets, J.F. Meis, F.L. van de Veerendonk, S.E. Schoustra, B.J. Zwaan, W.J.G. Melchers, In-host adaptation and acquired triazole resistance in Aspergillus fumigatus: a dilemma for clinical management, Lancet Infect. Dis. 16 (2016) e251—e260. https://doi.org/10.1016/S1473-3099(16)30138-4.