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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



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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

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(<https://www.ncbi.nlm.nih.gov/sra>), under BioProject ID number PRJNA528395.

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Specifications Table

Subject area	Biology
More specific subject area	Microbiology, Genomics
Type of data	Whole genomic sequence data
How data was acquired	Whole genome was sequenced with an Illumina NextSeq 500 machine
Data format	Raw
Experimental factors	Genomic DNA from pure culture
Experimental features	Whole genome sequencing
Data source location	The 13 <i>Aspergillus fumigatus</i> isolates sequenced in this article were cultured from an individual chronic granulomatous disease patient suffering from invasive aspergillosis over 2 years.
Data accessibility	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 accession 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).
Related research article	Ballard, E., Melchers, W.J.G., Zoll, J., Brown, A.J.P., Verweij, P.E., Warris, A., 2018. In-host microevolution of <i>Aspergillus fumigatus</i> : a phenotypic and genotypic analysis. <i>Fungal Genet. Biol.</i> 1–13. https://doi.org/10.1016/j.fgb.2018.02.003 [5].

Value of the data

- Genomic investigations of serial clinical isolates of *Aspergillus fumigatus* have potential to extend our insights into the molecular basis of novel azole antifungal drug resistance mechanisms.
- This dataset comprises whole genome sequences from 13 isogenic clinical isolates from an individual patient, a unique resource for molecular studies of in-host adaptation.
- The raw sequence data for these isolates will be useful to researchers investigating mechanisms of adaptation to a variety of stressors encountered in-host.

1. Data

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 and azole 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).

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Transparency document

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