



## Data Article

# Data of common and species-specific transcriptional host responses to pathogenic fungi



Mariolina Bruno<sup>a,\*</sup>, Robter Horst<sup>a</sup>, Marina Pekmezovic<sup>b</sup>,  
Vinod Kumar<sup>a,c</sup>, Yang Li<sup>a,d,e</sup>, Mihai G. Netea<sup>a,f</sup>, Jean-Paul Latgé<sup>g</sup>,  
Mark S. Gresnigt<sup>a,h,1,\*</sup>, Frank L. van de Veerdonk<sup>a,1,\*</sup>

<sup>a</sup> Department of Internal Medicine and Radboudumc Center for Infectious Diseases (RCI), Radboud University Medical Center, Nijmegen, The Netherlands

<sup>b</sup> Department of Microbial Pathogenicity Mechanisms, Leibniz Institute for Natural Product Research and Infection Biology – Hans Knöll Institute, Beutenbergstraße 11a 07745, Jena, Germany

<sup>c</sup> Department of Genetics, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands

<sup>d</sup> Centre for Individualised Infection Medicine (CiIM) and TWINCORE, joint ventures between the Helmholtz-Centre for Infection Research (HZI) and the Hannover Medical School (MHH), Hannover, Germany

<sup>e</sup> Department of Internal Medicine and Radboud Center for Infectious Diseases, Radboud University Medical Center, Nijmegen, the Netherlands

<sup>f</sup> Department for Genomics & Immunoregulation, Life and Medical Sciences Institute (LIMES), University of Bonn, 53115 Bonn, Germany




<sup>g</sup> Unité des Aspergillus, Institut Pasteur, Paris, France

<sup>h</sup> Junior Research Group Adaptive Pathogenicity Strategies, Leibniz Institute for Natural Product Research and Infection Biology – Hans Knöll Institute, Beutenbergstraße 11a 07745, Jena, Germany

DOI of original article: [10.1016/j.csbj.2020.12.036](https://doi.org/10.1016/j.csbj.2020.12.036)

\* Corresponding authors.

E-mail addresses: [mariolina.bruno@radboudumc.nl](mailto:mariolina.bruno@radboudumc.nl) (M. Bruno), [mark.gresnigt@leibniz-hki.de](mailto:mark.gresnigt@leibniz-hki.de) (M.S. Gresnigt), [frank.vandeveerdonk@radboudumc.nl](mailto:frank.vandeveerdonk@radboudumc.nl) (F.L. van de Veerdonk).

Social media:  (M. Bruno),  (M.S. Gresnigt),  (F.L. van de Veerdonk)

<sup>1</sup> shared senior authorship.

<https://doi.org/10.1016/j.dib.2021.106928>

2352-3409/© 2021 The Authors. 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/>)

ARTICLE INFO

Article history:  
 Received 9 February 2021  
 Revised 28 February 2021  
 Accepted 1 March 2021  
 Available online 4 March 2021

Dataset link: [Comparative host transcriptome in response to pathogenic fungi identifies common and species-specific transcriptional antifungal host response pathways \(Original data\)](#)

Keywords:  
 Immunology of fungal infections  
 Opportunistic pathogenic fungi  
*Candida albicans*  
*Aspergillus fumigatus*  
*Rhizopus. oryzae*  
 Coagulation  
 Type I interferon  
 Transcriptional immune response

ABSTRACT

Using a comparative RNA-Sequencing based transcriptional profiling approach, responses of primary human peripheral blood mononuclear cells (PBMCs) to common human pathogenic fungi have been characterized (Bruno et al. Computational and Structural Biology Journal). Primary human PBMCs were stimulated in vitro with the fungi *A. fumigatus*, *C. albicans*, and *R. oryzae* after which RNA was isolated and sequenced. From raw sequencing reads differential expressed genes in response to the different fungi were calculated by comparison with unstimulated cells. By overlapping differentially expressed genes in response to the pathogenic fungi *A. fumigatus*, *C. albicans*, and *R. oryzae* a dataset was generated that encompasses a common response to these three distinct fungi as well as species-specific responses. Here we present datasets on these common and species-specific responses that complement the original study (Bruno et al. Computational and Structural Biology Journal). These data serve to facilitate further fundamental research on the immune response to opportunistic pathogenic fungi such as *A. fumigatus*, *C. albicans*, and *R. oryzae*.

© 2021 The Authors. 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/>)

Specifications Table

Subject	Infectious Diseases
Specific subject area	Transcriptional responses of primary human immune cells to opportunistic pathogenic fungi
Type of data	Tables Figures
How data were acquired	Transcriptional data of peripheral blood mononuclear cells (PBMCs) stimulated with different fungal stimuli at different time points was acquired by RNA-Sequencing on a HiSeq 2500 sequencer (Illumina). Sequencing reads were mapped to the human genome using STAR (version 2.3.0) and differentially expressed genes were identified by statistics analysis using DESeq2 package from Bioconductor. Pathway enrichment analysis was performed using Cytoscape software with the ClueGO v2.5.5 and CluePedia v1.5.5 plugin. Pathway visualization have been implemented using the software Pathvisio (v. 3.3.0)
Data format	Raw Analysed Filtered
Parameters for data collection	Primary human PBMCs from healthy volunteers were stimulated with inactivated fungi of the species <i>A. fumigatus</i> (strain Ku80), <i>C. albicans</i> (strain UC820), <i>R. oryzae</i> (strain RA 99–880), or were left unstimulated for 4 h or 24 h at 37 °C with 5% CO <sub>2</sub> .
Description of data collection	After incubation, the supernatant was removed, and RNA was isolated using the mirVANA RNA isolation kit (Applied Biosystems) according to the protocol supplied by the manufacturer, and library preparation was performed using TruSeq RNA sample preparation kit v2 (Illumina).
Data source location	Laboratory of Experimental Internal Medicine – Radboudumc, Nijmegen, The Netherlands

(continued on next page)

Data accessibility	Repository name: GEO Data identification number: GSE162746 Direct URL to data: <a href="https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE162746">https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE162746</a>
Related research article	M. Bruno, I.M.W. Dewi, V. Matzaraki, R. ter Horst, M. Pekmezovic, B. Rösler, L. Groh, R.J. Röring, V. Kumar, Y. Li, A. Carvalho, M.G. Netea, J-P. Latgé, M.S. Gresnigt, and F.L. van de Veerdonk, Comparative host transcriptome in response to pathogenic fungi identifies common and species-specific transcriptional antifungal host response pathways, <i>Comput Struct Biotechnol J</i> , 2020 Dec 26;19:647–663. doi: <a href="https://doi.org/10.1016/j.csbj.2020.12.036">10.1016/j.csbj.2020.12.036</a> . eCollection 2021.

## Value of the Data

- This dataset represents a comparison of the transcriptional host response to three common opportunistic fungal pathogens that cause life-threatening infections such as candidiasis, aspergillosis, and mucormycosis in immunocompromised patients. The data can be used to obtain insights into responses commonly induced by opportunistic fungal pathogens as well as species-specific responses.
- Scientists from the fields immunology, mycology, and infection biology can benefit from this data.
- This dataset makes a plethora of data available to the scientific community allowing generation of hypotheses and validation of novel pathways. In particular, pathogen-specific and common changes in gene expression can aid in the generation of valuable hypotheses on the molecular mechanisms underlying the fungal-specific as well as common host responses to opportunistic fungal pathogens.
- Our data, presenting common and the fungal-specific host responses, can serve as a knowledge base for novel host-directed therapies, but also guide future projects, by providing directions of research for the fungal community.
- This dataset contains the common transcriptional response to opportunistic pathogenic fungi which includes the so far underexplored non-protein coding RNAs (lncRNAs).

## 1. Data Description

Phylogenetically different opportunistic pathogenic fungi, such as *Aspergillus fumigatus*, *Candida albicans*, and *Rhizopus oryzae* cause infections in immunocompromised patients with similar predisposing factors [1–3]. These include neutropenia, myeloablative, and immunosuppressive therapy [4]. This common patient cohort affected by these phylogenetically different fungi suggests the existence of also a common protective antifungal immunity that mediates resistance in healthy individuals. Nevertheless, there are also crucial differences in the pathogenesis of aspergillosis, candidiasis, and mucormycosis caused by *A. fumigatus*, *C. albicans*, and *R. oryzae* respectively [5–7], which highlights the need for species-specific immune responses.

Using comparative transcriptional profiling of the response of primary human immune cells we described the common “core” host response as well as species-specific responses to *A. fumigatus*, *C. albicans*, or *R. oryzae*. The key findings of this study are reported in [8], yet the specific data on the common and species-specific gene expression are available here as supporting information. An Overview of the data presented in this data article can be found in Fig. 1. RNA-Seq data of human PBMCs stimulated with *A. fumigatus*, *C. albicans*, or *R. oryzae* each compared to unstimulated cells ( $\text{Log}_2\text{FoldChange}$  and adjusted  $p$ -value) was analysed and filtered and presented in Table 1. In this table, genes that were differentially regulated for any of the fungi compared to unstimulated cells ( $\text{Log}_2\text{FC} > 1$  or  $< -1$  and adjusted  $p$ -value  $< 0.05$ ) were separated using a Venn analysis to identify shared and species-specific differentially regulated genes ( $\text{Log}_2\text{FC} > 0.9$  or  $< -0.9$  and adjusted  $p$ -value  $< 0.05$ ).

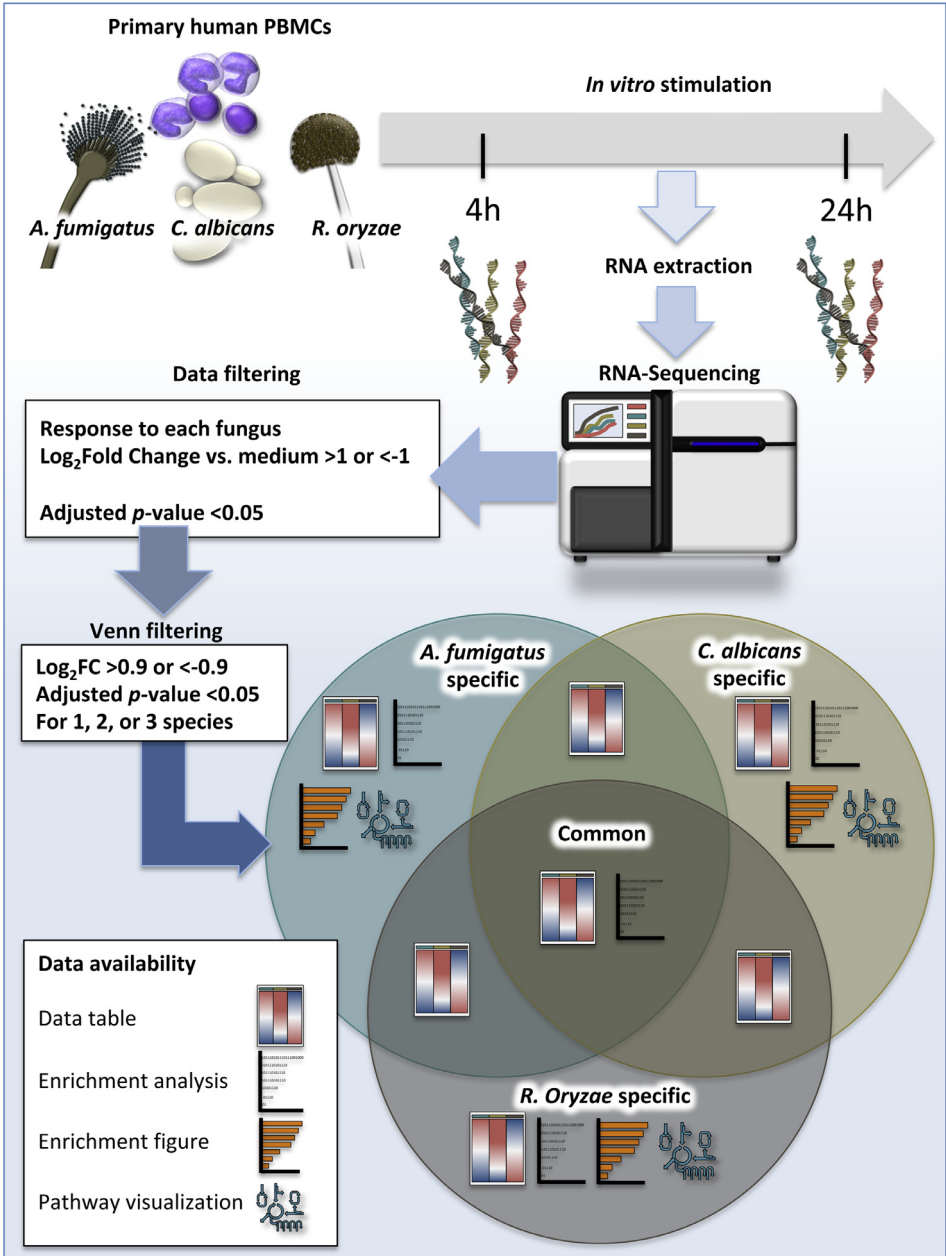
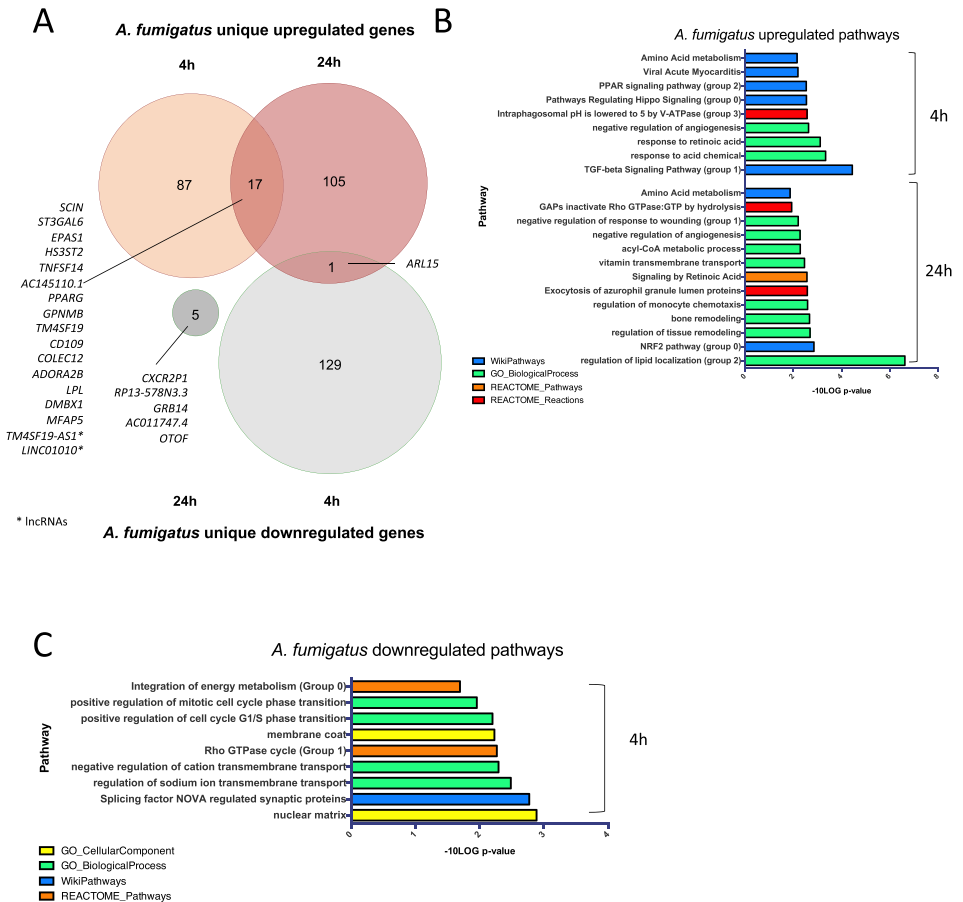


Fig. 1. Overview of the data presented in this data article.

Table 2 zooms in on the genes that are commonly differentially regulated in PBMCs responding to *A. fumigatus*, *C. albicans*, or *R. oryzae* and represent the “core response”. Among these common genes, 15 genes were up-regulated after both 4 h and 24 h stimulation (indicated in “##” in Table 2). Pathway enrichment analysis of these genes commonly differentially regulated in PBMCs responding to *A. fumigatus*, *C. albicans*, or *R. oryzae*, are presented in Table 3. Pathway



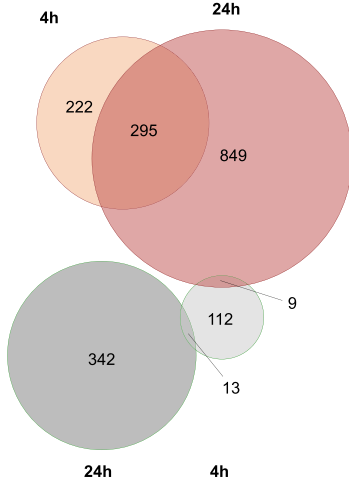
**Fig. 2.** *A. fumigatus*-specific transcriptional host response. (A) Venn diagram showing the differentially regulated genes in PBMCs from healthy volunteers that are uniquely up-regulated (up) and down-regulated (down) at different time points by *A. fumigatus* stimulation. (B) Enriched pathways within the set of *A. fumigatus*-uniquely upregulated genes after 4 h and 24 h plotted as the  $-\text{Log}_{10}$  of the  $p$ -value after Benjamini-Hochberg correction. (C) Enriched pathways within the set of *A. fumigatus*-uniquely downregulated genes after 4 h and 24 h plotted as the  $-\text{Log}_{10}$  of the  $p$ -value after Benjamini-Hochberg correction. No significantly enriched pathways could be identified in the *A. fumigatus*-specific differentially expressed downregulated genes at 24 h.

enrichment analysis of the species-specific differentially regulated genes in PBMCs responding to *A. fumigatus*, *C. albicans*, or *R. oryzae* are presented in Table 4. The number of species-specific genes and the enriched pathways are visualized for *A. fumigatus* (Fig. 2), *C. albicans* (Fig. 3), and *R. oryzae* (Fig. 4).

Differential expression analysis of *A. fumigatus* in PBMCs revealed 104 and 123 up-regulated and 5 and 130 down-regulated genes at 4 and 24 h respectively (Fig. 2A). Comparison over time showed that 17 of the early up-regulated genes were still up-regulated after 24 h, such as lipoprotein lipase (*LPL*), HIF2 $\alpha$  (*EPAS1*), and peroxisome proliferator-activated receptor- $\gamma$  (*PPARG*). No down-regulated genes at 4 h remained down-regulated after 24 h. Genes differentially expressed at 24 h were substantially different from those at 4 h (less than 20% overlap) (Fig. 2A). Pathway enrichment analysis showed that, among the others, *TGF $\beta$  signaling* ( $p = 3.55 \times 10^{-5}$  WIKI PATHWAYS), *Intraphagosomal pH is lowered to 5 by V-ATPase* ( $p = 2.68 \times 10^{-3}$  REACTOME), *Pathways Regulating Hippo Signaling* ( $p = 2.83 \times 10^{-3}$  WIKI PATHWAYS) and *PPAR $\gamma$  signaling*

A

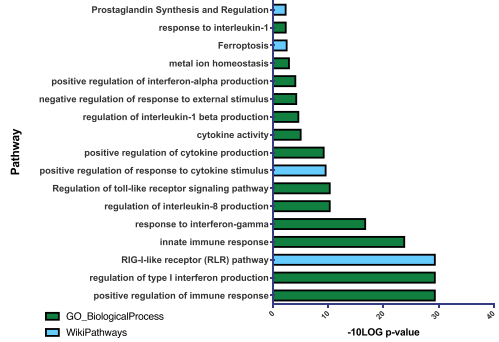
*C. albicans* unique upregulated genes



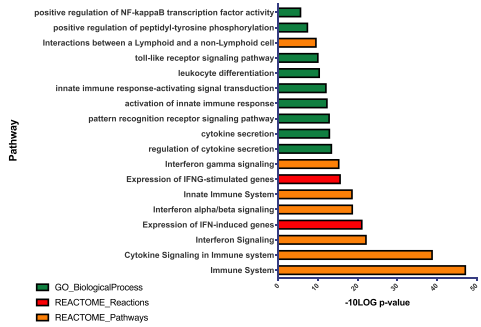
*C. albicans* unique downregulated genes

B

*C. albicans* upregulated pathways - 4h stimulation

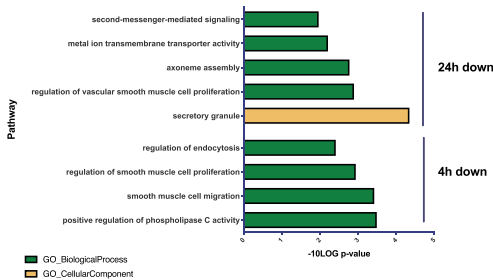


*C. albicans* upregulated pathways - 24h stimulation

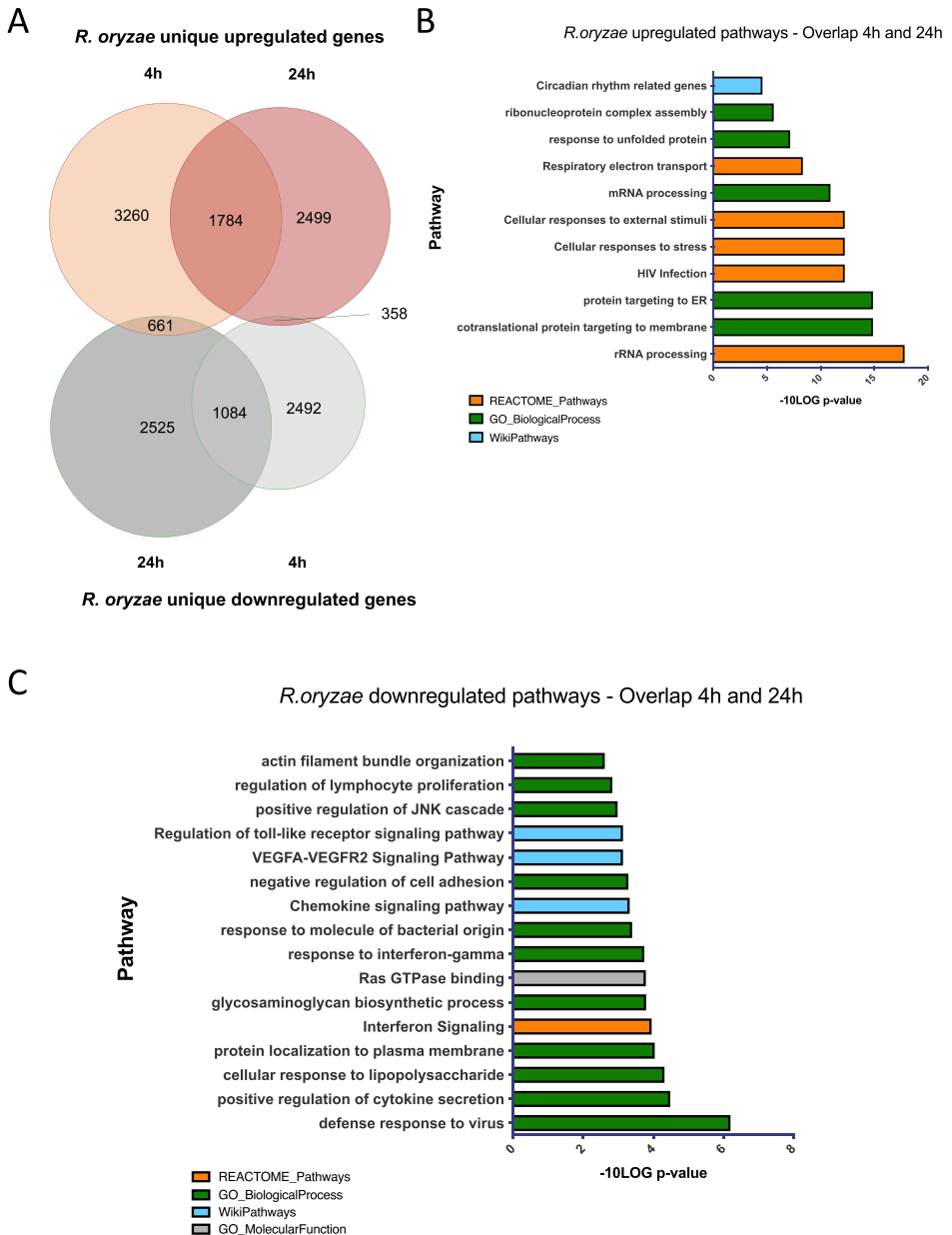


C

*C. albicans* downregulated pathways



**Fig. 3.** *C. albicans*-specific transcriptional host response. (A) Venn diagram showing the differentially regulated genes in PBMCs from healthy volunteers that are uniquely up-regulated (up) and down-regulated (down) at different time points by *C. albicans* stimulation. (B) Enriched pathways within the set of *C. albicans*-uniquely upregulated genes after 4 h and 24 h plotted as the  $-\log_{10}$  of the  $p$ -value after Benjamini-Hochberg correction. (C) Enriched pathways within the set of *C. albicans*-uniquely downregulated genes after 4 h and 24 h plotted as the  $-\log_{10}$  of the  $p$ -value after Benjamini-Hochberg correction.



**Fig. 4.** *R. oryzae*-specific transcriptional host response. (A) Venn diagram showing the differentially regulated genes in PBMCs from healthy volunteers that are uniquely up-regulated (up) and down-regulated (down) at different time points by *R. oryzae*-stimulation. (B) Enriched pathways within the set of *R. oryzae*-uniquely upregulated genes overlapping at 4 h and 24 h plotted as the  $-\text{Log}_{10}$  of the  $p$ -value after Benjamini-Hochberg correction. (C) Enriched pathways within the set of *R. oryzae*-uniquely downregulated genes overlapping at 4 h and 24 h plotted as the  $-\text{Log}_{10}$  of the  $p$ -value after Benjamini-Hochberg correction.

pathway ( $p = 2.89 \times 10^{-3}$  WIKI PATHWAYS) were significantly enriched after 4 h; after 24 h the most salient enriched pathways were *regulation of lipid localization* ( $p = 2.35 \times 10^{-7}$  GO), *NRF2 pathway* ( $p = 1.39 \times 10^{-3}$  WIKI PATHWAYS), and *Signaling by Retinoic Acid* ( $p = 2.7 \times 10^{-3}$  REACTOME) (Fig. 2B). The most relevant down-regulated pathway after 4 h were *regulation of sodium ion transmembrane transport* ( $p = 3.25 \times 10^{-3}$  GO), *Rho GTPase cycle* ( $p = 5.4 \times 10^{-3}$  REACTOME) and *Integration of energy metabolism* ( $p = 2 \times 10^{-2}$  REACTOME) (Fig. 2C). No significantly enriched pathways could be identified in the *A. fumigatus*-specific uniquely differentially expressed genes at 24 h. *C. albicans*-specific up-regulated 517 and 1153 genes and down-regulated 134 and 355 genes after 4 and 24 h respectively (Fig. 3A). Approximately half (295) of the up-regulated transcripts at 4 h remained up-regulated at 24 h. A minority (9 transcripts) shifted from down-regulation at 4 h to up-regulation at 24 h post-exposure. Only 13 transcripts down-regulated at 4 h remained down-regulated at 24 h and no transcripts shifted from up-regulation at 4 h to down-regulation at 24 h (Fig. 3A). A pathway enrichment analysis of the genes uniquely upregulated and downregulated in response to *C. albicans* stimulation is shown in Fig. 3B and Fig. 3C respectively. *R. oryzae*-stimulation specifically up-regulated 5705 and 4641 genes after 4 and 24 h respectively while 3934 and 4270 genes were down-regulated after 4 h and 24 h respectively (Fig. 4A). We observed 1784 genes that were up-regulated at both time points whereas 1084 were downregulated at both time points. Of those genes, 661 genes up-regulated at 4 h, but were down-regulated at 24 h, whereas 358 genes that were down-regulated at 4 h but induced at 24 h (Fig. 4A). Pathway enrichment analysis of the overlapping upregulated genes at both time points (4 and 24 h) showed a significant upregulation of *Ribonucleoprotein complex assembly* ( $p = 2.39 \times 10^{-6}$ , GO), *rRNA processing* ( $p = 1.41 \times 10^{-18}$ , REACTOME), *mRNA processing* ( $p = 1.20 \times 10^{-11}$ , GO), *Cellular responses to stress* (24h:  $p = 5.56 \times 10^{-13}$ , Reactome) pathways (Fig. 4B). In addition, there was a significant downregulation of TLR and cytokine-related signaling pathways (Fig. 4C).

In the following figures, we visualized the differential gene regulation in PBMCs responding to *A. fumigatus*, *C. albicans*, or *R. oryzae* in some specific pathways of interest emerged from the enrichment analysis. The coagulation pathway, presented in Fig. 5 is commonly significantly upregulated by all the three fungi. In Fig. 6 expression of genes in the pentose phosphate pathway (PPP) at both 4 and 24 h stimulation is visualized. It is possible to highlight that *R. oryzae* significantly up-regulated some PPP enzymes such as *G6PD*, *PGLS* and *RPIA* and *TKT*, the latter being significantly down-regulated by *C. albicans*. On the contrary, *A. fumigatus* and *C. albicans* significantly up-regulated *TALDO1*. Fig. 7 visualizes expression of genes in the type I IFN pathway gene upon stimulation of the three fungal species. A *C. albicans*-specific induction of key players in the type I IFN pathway can be appreciated. Fig. 8 visualizes the glycolysis and oxidative-phosphorylation pathways, which are differentially modulated by the three fungal species. While no drastic transcriptional changes can be observed in response to *A. fumigatus* and *C. albicans*, significant changes in glycolysis and oxidative-phosphorylation pathways are visible for *R. oryzae*, with a specific down regulation of rate-limiting glycolysis enzymes *HK1*, *HK2*, and *PKM2*.

## 2. Experimental Design, Materials and Methods

To obtain broad insights into the host response peripheral blood mononuclear cells were selected as these cells represent various types of innate and adaptive immune cells, predominantly monocytes, NK, B and T-cells. These cells were stimulated using fungal strains of each of the species *A. fumigatus*, *C. albicans*, and *R. oryzae*, which are well documented in literature [9–11]. RNA was isolated 4 and 24 h after stimulation to look at early as well as late responses.

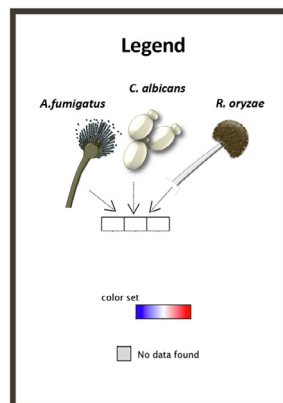
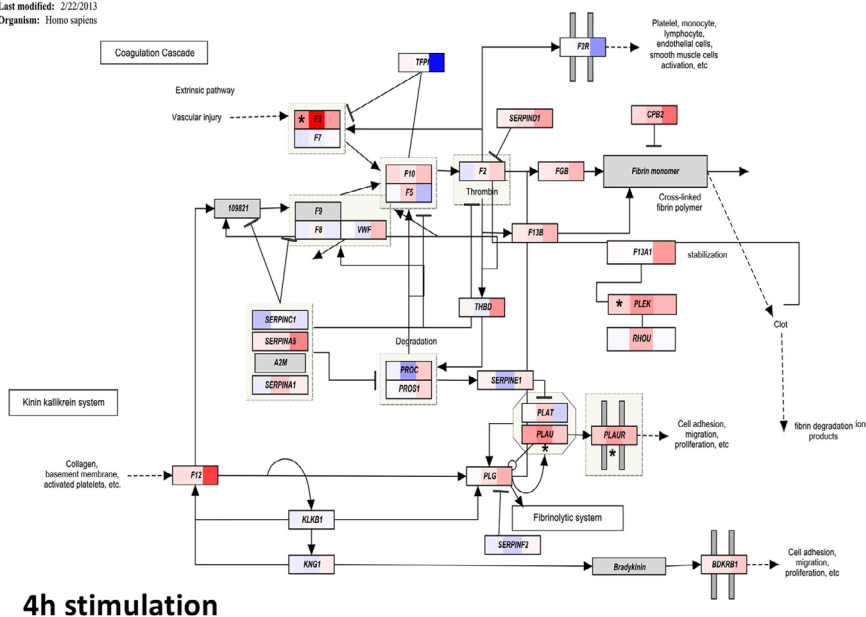
### 2.1. Cell stimulation, RNA isolation, sequencing and analysis

PBMCs ( $10^7$ ) were stimulated in 6 well plates with  $1 \times 10^7$ /mL *A. fumigatus* (Ku80, PFA fixed)  $1 \times 10^6$ /mL *C. albicans* (UC820, heat killed),  $1 \times 10^7$ /mL *R. oryzae* (RA 99–880, PFA fixed), or



A

Title: Complement and Coagulation  
Availability: CC BY 2.0  
Last modified: 2/22/2013  
Organism: Homo sapiens



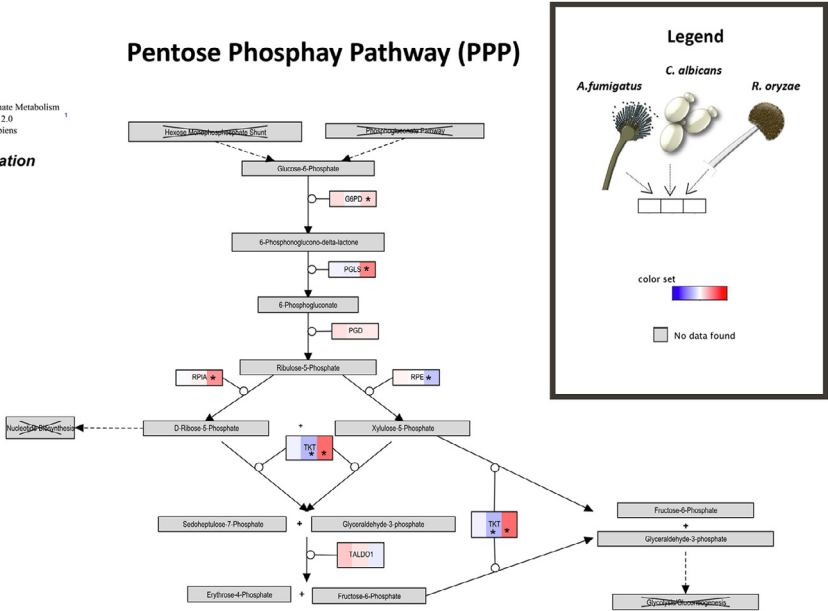
**Fig. 5.** The coagulation cascade is a core upregulated pathway. (A) Pathway visualization of coagulation cascade gene expression upon 4 h stimulation with *A. fumigatus* (left portion), *C. albicans* (central portion), and *R. oryzae* (right portion) extracted from the RNA-Seq dataset. Shades of red indicate upregulation, while shades of blue downregulation (see legend). Statistically significant upregulated genes are indicated with asterisks (\*). The original wikiPathways figure has been customized by the authors in order to include the gene *PLEK*.

were left unstimulated for 4 h or 24 h at 37 °C with 5% CO<sub>2</sub>. After incubation, the supernatant was removed and the cells were lysed. RNA was isolated using the mirVANA RNA isolation kit (Applied Biosystems) according to the protocol supplied by the manufacturer. RNA-Seq libraries were prepared from 1 µg RNA using the TruSeq RNA sample preparation kit v2 (Illumina) according to the manufacturer's instructions, and these libraries were subsequently sequenced on a HiSeq 2500 sequencer (Illumina) using paired-end sequencing of 2 × 50 bp, upon pooling of 10 samples per lane.

A

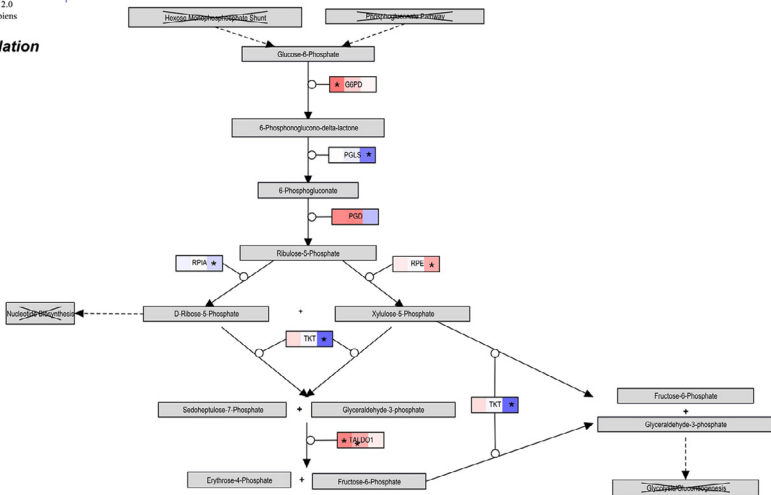
Title: Pentose Phosphate Metabolism  
 Availability: CC BY 2.0  
 Organism: Homo sapiens

4h stimulation



Title: Pentose Phosphate Metabolism  
 Availability: CC BY 2.0  
 Organism: Homo sapiens

24h stimulation

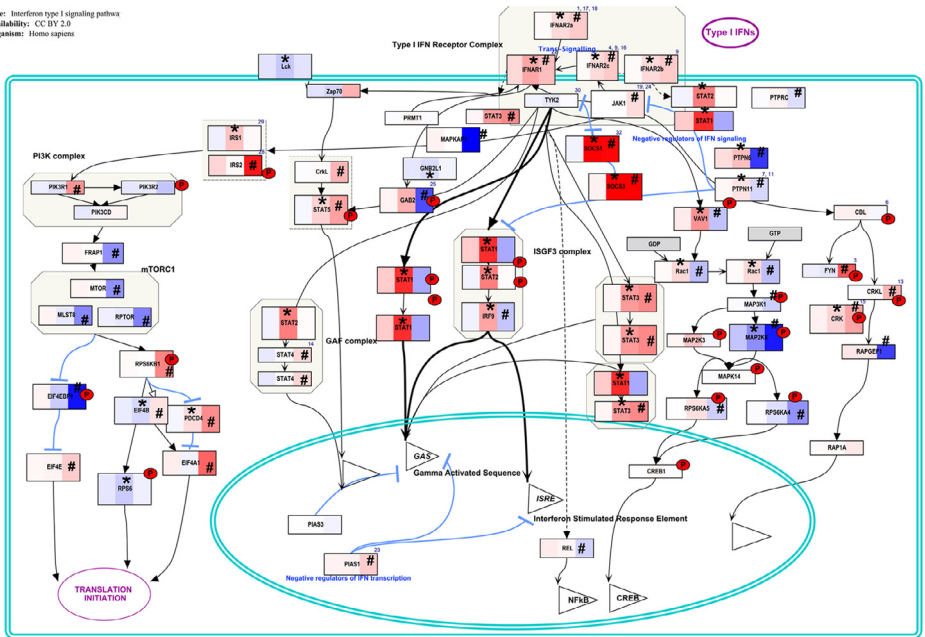


**Fig. 6.** visualization of the differential gene regulation in PBMCs responding to *A. fumigatus*, *C. albicans*, or *R. oryzae* in the Pentose Phosphate Pathway. (A) Pathway visualization of “Pentose Phosphate Pathway metabolism” genes expression upon 4 h and 24 h stimulation with *A. fumigatus*, *C. albicans*, and *R. oryzae* extracted from the RNA-Seq dataset. Shades of red indicate upregulation, while shades of blue downregulation (see legend). Statistically significant modulated genes are indicated with stars (\*).

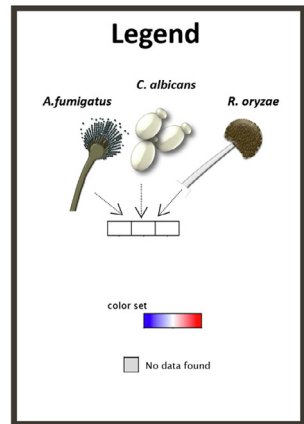
A

### Type I IFN visualization

Title: Interferon type I signaling pathway  
 Availability: CC BY 2.0  
 Organism: Homo sapiens



\* corrected p-value <0.05 for Candida  
 # corrected p-value <0.05 for Rhizopus

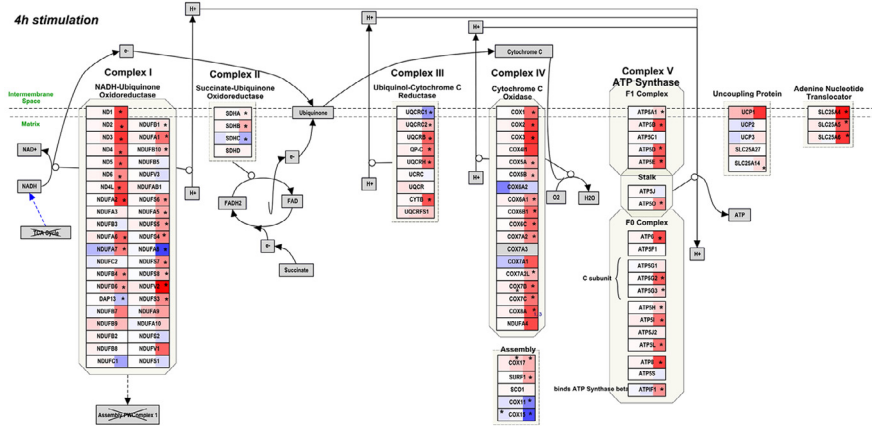


**Fig. 7.** Visualization of the differential gene regulation in PBMCs responding to *A. fumigatus*, *C. albicans*, or *R. oryzae* in type I IFN pathway. (A) Pathway visualization of “Interferon type I signaling pathways” genes expression upon 24 h stimulation with *A. fumigatus* (left portion), *C. albicans* (central portion), and *R. oryzae* (right portion). Shades of red indicate upregulation, while shades of blue downregulation (see legend). Statistically significant modulated genes are indicated with stars (\*) for *C. albicans* and hashes (#) for *R. oryzae* stimulation.

The RNA sequencing analysis of this dataset was performed as previously described (Li et al., 2016). Briefly, sequencing reads were mapped to the human genome using STAR (version 2.3.0) [12]. The aligner was provided with a file containing junctions from Ensembl GRCh37.71. Htseq-count of the Python package HTSeq (version 0.5.4p3) was used (the HTSeq package, <http://www-huber.embl.de/users/anders/HTSeq/doc/overview.html>) to quantify the read counts

A

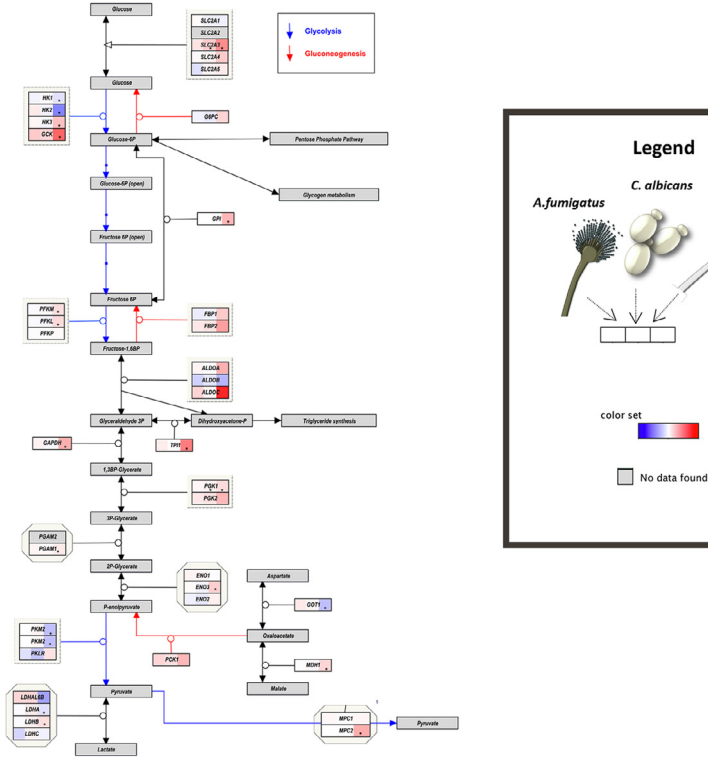
Title: Electron Transport Chain (OXPHOS)  
Organism: Homo sapiens



B

Title: Glycolysis and Gluconeogenesis 2  
Organism: Homo sapiens

4h stimulation



**Fig. 8.** Transcriptional modulation of Oxidative phosphorylation and glycolysis by *A. fumigatus*, *C. albicans* and *R. oryzae*. (A) Pathway visualization of “Electron Transport Chain (OXPHOS)” genes expression upon 4 h stimulation with *A. fumigatus* (left portion), *C. albicans* (central portion), and *R. oryzae* (right portion). Shades of red indicate upregulation, while shades of blue downregulation (see legend). Statistically significant modulated genes are indicated with stars (\*). (B) Pathway visualization of “Glycolysis and gluconeogenesis” genes expression upon 24 h stimulation with *A. fumigatus* (left portion), *C. albicans* (central portion), and *R. oryzae* (right portion). Shades of red indicate upregulation, while shades of blue downregulation (see legend). Statistically significant modulated genes are indicated with stars (\*).

per gene based on annotation version GRCh37.71, using the default union-counting mode. Raw count matrix was saved in a single raw\_counts\_collected.csv, which contains all the raw counts per sample of all the conditions and can be found at <https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE162746>.

Given the absence of sample replicates, PBMC donors were considered biological replicates. After quality control 2 donors stimulated for 4 h and three donors stimulated for 24 h with *R. oryzae* needed to be excluded from the analysis. Differentially expressed genes were identified by statistics analysis using DESeq2 package from Bioconductor [13]. The statistically significant threshold (FDR  $p \leq 0.05$  and Fold Change  $\geq 2$ ) was applied.

## 2.2. Pathway enrichment analysis

Pathway enrichment analysis was performed using Cytoscape software with the ClueGO v.2.5.5 and CluePedia v.1.5.5 plugin [14]. To interpret and visualize the functionally group terms in the form of gene networks and pathways we have used Reactome, Wikipathways, and Gene Ontology (GO) categories, by excluding the annotations with the IEA code (Inferred from Electronic Annotation, which are assigned automatically computationally inferred based in sequence similarity comparisons. Degree of functional enrichment was determined by sorting enriched terms based on a  $p$ -value threshold of  $<0.05$ . Unless otherwise specified, we used the following GEO settings: to reduce the redundancy of GO terms we applied the GO term fusion of related terms with similar associated genes. We used GO tree intervals between levels 3 and 8 and a GO Term/Pathway Connectivity (Kappa score) of 0.4 and a GO Term/Pathway Selection (% Genes) of 3%. The statistical test used for the enrichment was based on a right-sided hypergeometric option. The hypergeometric test  $p$ -values are further corrected for multiple testing using the Benjamini Hochberg multiple testing correction [15]. For *R. oryzae* modulated genes due to the high number of modulated genes, we performed pathway analysis on the list of overlapping genes between 4 h and 24 h. The complete pathways analysis results and settings for each specific fungal stimulation are available in Table 4.

## 2.3. Pathway visualization

Pathvisio (v. 3.3.0), the graphical editor for biological pathways [16, 17], was used to visualize the most relevant pathways involving genes with significant differences and pathways with significant enrichment. By using WikiPathways plugin for PathVisio to search homo sapiens pathways in the online pathway database the following pathways have been visualized: “Complement and Coagulation cascade”, “Interferon type I signaling pathway”, “Type II interferon signaling (IFNG)”, “Electron Transport Chain (OXPHOS)”, “Pentose Phosphate Metabolism” and “Glycolysis and Gluconeogenesis”. In the case of “Complement and Coagulation cascade” the pathway representation from WikiPathways have been edited for size and clarity and to include other relevant genes (e.g. *PLAU* and *SERPINF2*) The RNA-Seq dataset with all differentially expressed genes (DEGs) and their adjusted  $p$ -value was used; genes were coloured by  $\text{Log}_2\text{FC}$  values derived from each fungal stimulation versus RPM differential expression, performed as described in the RNA-Seq paragraph. The pathway involves up or down-regulating genes induced by *A. fumigatus* (left), *C. albicans* (center) and *R. oryzae* (right), indicating red for the up-regulating genes and blue for the down-regulating genes. The symbol “\*” have been used in some of the pathways to indicate a significant  $p$ -value. In Data in Brief Fig. 5-8, to distinguish *C. albicans* and *R. oryzae* DEGs, we used the symbols “\*” and “#” respectively.

## Ethics Statement

Buffy coats were obtained from anonymized healthy donors after written consent (Sanquin Blood Bank, Nijmegen, the Netherlands). For validation experiments blood was similarly obtained

from buffy coats or collected from healthy volunteers by venous blood puncture after informed consent was obtained. All experiments were performed and conducted in accordance to Good Clinical practice, the Declaration of Helsinki, and the approval of the Arnhem-Nijmegen Ethical Committee (nr.2010/104).

### **CRedit Author Statement**

**Mariolina Bruno:** Conceptualization, Methodology, Validation, Visualization, Data curation, Writing - Original Draft, Writing - Review & Editing; **Rob ter Horst:** Software, Formal analysis, Investigation, Data curation; **Marina Pekmezovic:** Formal analysis, Visualization, Writing - Review & Editing; **Vinod Kumar:** Software, Data curation, Resources; **Yang Li:** Software, Data curation, Resources; **Mihai G. Netea:** Conceptualization, Supervision, Project administration; **Jean-Paul Latgé:** Conceptualization, Supervision, Funding acquisition; **Mark S. Gresnigt:** Supervision, Conceptualization, Methodology, Validation, Visualization, Data curation, Writing - Original Draft, Writing - Review & Editing, Visualization; **Frank L. van de Veerdonk:** Supervision, Conceptualization, Methodology, Writing - Review & Editing, Visualization, Project administration, Funding acquisition.

### **Declaration of Competing Interest**

The authors declare that they have no known competing financial interests or personal relationships which have, or could be perceived to have, influenced the work reported in this article.

### **Data Availability**

[Comparative host transcriptome in response to pathogenic fungi identifies common and species-specific transcriptional antifungal host response pathways \(Original data\)](#) (NCBI).

### **Acknowledgments**

As also mentioned in the related research article, we thank all funding sources. We thank all healthy volunteers for donating blood. We thank Diletta Rosati for the help in the lab and Anton Nikolaev for the support with the raw data submission to the GEO database. M.S.G. was funded by the Deutsche Forschungsgemeinschaft (DFG) Emmy Noether Program (project no. [434385622 / GR 5617/1-1](#)). M.G.N. was supported by an ERC Advanced Grant ([#833247](#)), a Spinoza Grant of the Netherlands Organization for Scientific Research, and a Competitiveness Operational Program Grant of the Romanian Ministry of European Funds (FUSE), FLvdV was supported by aVidi grant of the Netherlands Association for Scientific Research, the Europeans Union's Horizon 2020 research and innovation pro-gramme under grant agreement no 847507, and the "La Caixa" foundation (ID 100010434).

### **Supplementary Materials**

Supplementary material associated with this article can be found in the online version at doi:[10.1016/j.dib.2021.106928](#).

### **References**

- [1] S. Bonnet, R. Duléry, K. Regany, M. Bouketouche, L. Magro, V. Coiteux, S. Alfandari, C. Berthon, B. Quesnel, I. Yakoub-Agha, Long-term follow up of invasive aspergillosis in allogeneic stem cell transplantation recipients and leukemia patients: differences in risk factors and outcomes, *Curr. Res. Transl. Med.* 65 (2017) 77–81, doi:[10.1016/j.retram.2017.05.003](#).

- [2] B.J. Kullberg, M.C. Arendrup, Invasive Candidiasis, *New Engl. J. Med.* 373 (2015) 1445–1456, doi:[10.1056/NEJMr1315399](https://doi.org/10.1056/NEJMr1315399).
- [3] R.E. Lewis, S.P. Georgiadou, F. Sampsonas, G. Chamilos, D.P. Kontoyiannis, Risk factors for early mortality in haematological malignancy patients with pulmonary mucormycosis, *Mycoses* 57 (2014) 49–55, doi:[10.1111/myc.12101](https://doi.org/10.1111/myc.12101).
- [4] F. Almeida, M.L. Rodrigues, C. Coelho, The still underestimated problem of fungal diseases worldwide, *Front. Microbiol.* 10 (2019), doi:[10.3389/fmicb.2019.00214](https://doi.org/10.3389/fmicb.2019.00214).
- [5] U. Binder, E. Maurer, C. Lass-Flörl, Mucormycosis – from the pathogens to the disease, *Clin. Microbiol. Infect.* 20 (2014) 60–66, doi:[10.1111/1469-0691.12566](https://doi.org/10.1111/1469-0691.12566).
- [6] M.G. Netea, L.A.B. Joosten, J.W.M. van der Meer, B.-J. Kullberg, F.L. van de Veerdonk, Immune defence against Candida fungal infections, *Nature Rev. Immunol.* 15 (2015) 630–642, doi:[10.1038/nri3897](https://doi.org/10.1038/nri3897).
- [7] F.L. van de Veerdonk, M.S. Gresnigt, L. Romani, M.G. Netea, J.-P. Latgé, *Aspergillus fumigatus* morphology and dynamic host interactions, *Nat. Rev. Microbiol.* 15 (2017) 661–674, doi:[10.1038/nrmicro.2017.90](https://doi.org/10.1038/nrmicro.2017.90).
- [8] M. Bruno, I.M.W. Dewi, V. Matzaraki, R. Ter Horst, M. Pekmezovic, B. Rösler, L. Groh, R.J. Röring, V. Kumar, Y. Li, A. Carvalho, M.G. Netea, J.P. Latgé, M.S. Gresnigt, F.L. van de Veerdonk, Comparative host transcriptome in response to pathogenic fungi identifies common and species-specific transcriptional antifungal host response pathways, *Comput. Struct. Biotechnol. J* (2021).
- [9] K.L. Becker, V. Aimanianda, X. Wang, M.S. Gresnigt, A. Ammerdorffer, C.W. Jacobs, R.P. Gazendam, L.A.B. Joosten, M.G. Netea, J.P. Latgé, F.L. van de Veerdonk, *Aspergillus* cell wall chitin induces anti- and proinflammatory cytokines in human PBMCs via the Fc- $\gamma$  receptor/Syk/PI3K pathway, *mBio* 7 (2016) e01823–15, doi:[10.1128/mBio.01823-15](https://doi.org/10.1128/mBio.01823-15).
- [10] R.I. Lehrer, M.J. Cline, Interaction of *Candida albicans* with human leukocytes and serum, *J. Bacteriol.* 98 (1969) 996–1004.
- [11] L.-J. Ma, A.S. Ibrahim, C. Skory, M.G. Grabherr, G. Burger, M. Butler, M. Elias, A. Idnurm, B.F. Lang, T. Sone, A. Abe, S.E. Calvo, L.M. Corrochano, R. Engels, J. Fu, W. Hansberg, J.-M. Kim, C.D. Kodira, M.J. Koehrsen, B. Liu, D. Miranda-Saavedra, S. O’Leary, L. Ortiz-Castellanos, R. Poulter, J. Rodriguez-Romero, J. Ruiz-Herrera, Y.-Q. Shen, Q. Zeng, J. Galagan, B.W. Birren, C.A. Cuomo, B.L. Wickes, Genomic analysis of the basal lineage fungus *Rhizopus oryzae* reveals a whole-genome duplication, *PLoS Genet* 5 (2009) e1000549, doi:[10.1371/journal.pgen.1000549](https://doi.org/10.1371/journal.pgen.1000549).
- [12] A. Dobin, C.A. Davis, F. Schlesinger, J. Drenkow, C. Zaleski, S. Jha, P. Batut, M. Chaisson, T.R. Gingeras, STAR: ultrafast universal RNA-seq aligner, *Bioinformatics* 29 (2013) 15–21, doi:[10.1093/bioinformatics/bts635](https://doi.org/10.1093/bioinformatics/bts635).
- [13] M.I. Love, W. Huber, S. Anders, Moderated estimation of fold change and dispersion for RNA-seq data with DESeq2, *Genome Biol.* 15 (2014) 550, doi:[10.1186/s13059-014-0550-8](https://doi.org/10.1186/s13059-014-0550-8).
- [14] G. Bindea, B. Mlecnik, H. Hackl, P. Charoentong, M. Tosolini, A. Kirilovsky, W.-H. Fridman, F. Pagès, Z. Trajanoski, J. Galon, ClueGO: a Cytoscape plug-in to decipher functionally grouped gene ontology and pathway annotation networks, *Bioinformatics* 25 (2009) 1091–1093, doi:[10.1093/bioinformatics/btp101](https://doi.org/10.1093/bioinformatics/btp101).
- [15] Y. Benjamini, Y. Hochberg, Controlling the false discovery rate: a practical and powerful approach to multiple testing, *J. R. Stat. Soc. Ser. B (Methodol.)* 57 (1995) 289–300.
- [16] M. Kutmon, M.P. van Iersel, A. Bohler, T. Kelder, N. Nunes, A.R. Pico, C.T. Evelo, PathVisio 3: an extendable pathway analysis toolbox, *PLoS Comput. Biol.* 11 (2015), doi:[10.1371/journal.pcbi.1004085](https://doi.org/10.1371/journal.pcbi.1004085).
- [17] M.P. van Iersel, T. Kelder, A.R. Pico, K. Hanspers, S. Coort, B.R. Conklin, C. Evelo, Presenting and exploring biological pathways with PathVisio, *BMC Bioinformatics* 9 (2008) 399, doi:[10.1186/1471-2105-9-399](https://doi.org/10.1186/1471-2105-9-399).