Preprints.org

Data Descriptor

Not peer-reviewed version

RNA-Seq Dataset of *Candida tropicalis* Under Antifungal Stress: Transcriptomic Profiles Supporting Studies on Adaptation and Resistance

Orfa Inés Contreras-Martínez , Katia Aviña-Padilla * , Alberto Angulo-Ortíz *

Posted Date: 28 November 2025

doi: 10.20944/preprints202511.2143.v1

Keywords: *Candida tropicalis*; RNA-Seq; antifungal stress; differential expression; transcriptomics; isoespintanol

Preprints.org is a free multidisciplinary platform providing preprint service that is dedicated to making early versions of research outputs permanently available and citable. Preprints posted at Preprints.org appear in Web of Science, Crossref, Google Scholar, Scilit, Europe PMC.

Copyright: This open access article is published under a Creative Commons CC BY 4.0 license, which permit the free download, distribution, and reuse, provided that the author and preprint are cited in any reuse.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 28 November 2025 doi:10.20944/preprints202511.2143.v1

Disclaimer/Publisher's Note: The statements, opinions, and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions, or products referred to in the content.

Data Descriptor

RNA-Seq Dataset of *Candida tropicalis* Under Antifungal Stress: Transcriptomic Profiles Supporting Studies on Adaptation and Resistance

Orfa Inés Contreras-Martínez [1], Katia Aviña-Padilla [2,*] and Alberto Angulo-Ortíz [3,*]

[1] Biology Department, Faculty of Basic Sciences, University of Córdoba, Monteria 230002, Colombia
[2] Cell Biology Department, CINVESTAV, Mexico
[3] Chemistry Department, Faculty of Basic Sciences, University of Córdoba, Monteria 230002, Colombia
* Correspondence: katia.avinap@cinvestav.mx (K.A.-P.); aaangulo@correo.unicordoba.edu.co (A.A.-O.)

Abstract

Candida tropicalis is one of the main causes of invasive candidiasis. Its ability to form powerful biofilms and its resistance to the antifungals used for its control make it a pathogen of great relevance and global concern. The purpose of this study is to show data on the changes in the transcriptome of *C. tropicalis* caused by the natural monoterpene isoespintanol (ISO). We present an RNA-Seq dataset profiling the transcriptomic response of *C. tropicalis* exposed to antifungal treatment ISO compared to untreated controls. RNA was extracted from six biological samples and sequenced using the Illumina NovaSeq platform, generating over 160 million paired end reads with an average mapping rate of 84% against the *C. tropicalis* reference genome (*GCA_000006335v3* The dataset includes the processed read-count table, normalized expression matrices and a list of differentially expressed transcripts, along with metadata describing experimental conditions, sequencing platform, mapping statistics, and treatment information. Together, these files enable downstream analyses of differential expression, functional enrichment, and comparative antifungal response. This dataset constitutes a valuable resource for exploring molecular mechanisms of antifungal response and adaptation in Candida species.

Keywords: *Candida tropicalis*; RNA-Seq; antifungal stress; differential expression; transcriptomics; isoespintanol

1. Summary

Candida tropicalis is an opportunistic fungal pathogen of great clinical relevance [1–3], it is considered the second most virulent Candida species after *Candida albicans*; the growing resistance to antifungals, especially to azoles, amphotericin B and echinocandins is of great concern. The World Health Organization (WHO) classifies *C. tropicalis* as a high-risk pathogen, considering it a threat to public health and highlighting the urgent need for research and surveillance [4–6]. Thus, the search for novel, effective and safe compounds with antifungal potential against these pathogens, using precise, and reproducible methodologies, is urgent. In this context, plant-based compounds represent an excellent alternative to investigate. To better understand transcriptional mechanisms underlying this adaptive response, RNA-Seq was performed on *C. tropicalis* cultures treated with the natural antifungal monoterpene, isoespintanol (ISO) and untreated controls (INO) [7]. The resulting dataset captures the genome wide transcriptional landscape associated with antifungal exposure and provides a foundation for comparative analyses across Candida species. This work complements existing resources for *Candida albicans* and *Candida glabrata* by extending transcriptomic knowledge to a less characterized yet clinically relevant species.

2. Data Description

© 2025 by the author(s). Distributed under a Creative Commons CC BY license.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 28 November 2025 doi:10.20944/preprints202511.2143.v1

2.1. Background and Summary

Candida tropicalis is a clinically relevant opportunistic yeast widely isolated from bloodstream, urogenital, and invasive infections, where it is particularly associated with high mortality in immunocompromised and critically ill patients [8,9]. Unlike other non-*albicans Candida* species, *C. tropicalis* exhibits increased adherence, biofilm formation, and metabolic plasticity, especially in environments enriched in hydrocarbons and lipids, which makes it both a pathogen and a biotechnologically useful organism. The growing emergence of antifungal resistance, especially to azoles and echinocandins has positioned this species as a priority pathogen for the discovery of alternative therapeutic molecules [10–13].

Isoespintanol (2-isopropyl-3,6-dimethoxy-5-methylphenol) is a natural monoterpene phenol isolated from *Oxandra cf. xylopioides*, a plant species from the Annonaceae family. It has been reported to exhibit antioxidant, membrane disruptive, and broad-spectrum antifungal properties, including activity against *Candida* spp., [14–16]. Nevertheless, the molecular pathways and stress response mechanisms triggered by ISO in fungal cells remain largely unexplored. Understanding these cellular responses is essential to decipher whether ISO acts by inducing oxidative imbalance, affecting membrane integrity, impairing metabolic pathways, or triggering programmed cell death.

To contribute to address this gap, we generated a comprehensive transcriptomic dataset based on high-throughput RNA sequencing (RNA-seq). *C. tropicalis* cultures were exposed to ISO at their minimum inhibitory concentration (MIC_{90} = 391.6 µg/mL) for four hours (Stage B), while control cells were grown under identical conditions without treatment (Stage A). For control condition, five independent biological replicates were included and one for treatment totaling six RNA-seq libraries, **Table 1**.

Table 1. Samples of *Candida tropicalis* treated with the antifungal (ISO) and untreated yeasts (INO).

No	Sample	Condition
1	RNAINO1	Control
2	RNAINO2	Control
3	RNAINO3	Control
4	RNAINO4	Control
5	RNAINO5	Control
6	RNAISO1	Treatment

Although the experimental design initially considered three biological replicates per group (six RNA-seq libraries in total), the treated yeast cells exhibited remarkably rapid loss of viability due to the fungicidal activity of ISO, resulting in severe cellular stress, and RNA degradation. This led to the successful recovery of only one high quality RNA sample from the treatment condition, in contrast to the five control samples that met RNA integrity and yield requirements (RIN ≥ 5.3; total RNA ≈ 0.5–1.5 µg), **Table 2**.

Table 2. RNA obtained from *C. tropicalis* with and without treatment. RNA was quantified by the ribogreen colorimetric method (Invitrogen), and its integrity (RNA integrity numbers = RIN) was evaluated by capillary electrophoresis.

No	Sample Code	RNA purified ng/µL	Volume µL	Total RNA µg	RIN
1	RNAINO1	29.51	27	0.797	7.2
2	RNAINO2	32.701	24	0.785	7.8
3	RNAINO3	62.576	25	1.564	5.6
4	RNAINO4	71.71	19	1.362	6.6
5	RNAINO5	80.251	19	1.525	6.5

© 2025 by the author(s). Distributed under a Creative Commons CC BY license.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 28 November 2025 doi:10.20944/preprints202511.2143.v1

6	RNAISO1	21.275	24	0.521	5.3

*Quality control of total RNA extracted from Zoea type larvae of *Callinectus sapidus*.

Rather than being a limitation, we considered that this biological constraint underscores the relevance of the dataset, as it captures a *rare transcriptional state* associated with early lethality and cell collapse under monoterpene induced stress. The dataset therefore provides a valuable resource for investigating rapid antifungal responses, oxidative damage, and cell death pathways in *C. tropicalis*, and supports future comparative analyses of antifungal mechanisms and resistance evolution.

Total RNA was extracted, verified for purity and integrity sequenced on the Illumina NovaSeq platform (150 bp paired end), and aligned against the *C. tropicalis* reference genome (Ensembl release GCA000006335v3). Gene expression was quantified and normalized using the TMM method implemented in EdgeR [17]. Differential expression analysis revealed 186 genes significantly altered between conditions ($|\log_2 FC| > 1$, FDR < 0.05), including 159 upregulated and 27 downregulated transcripts, **Figure 1**.

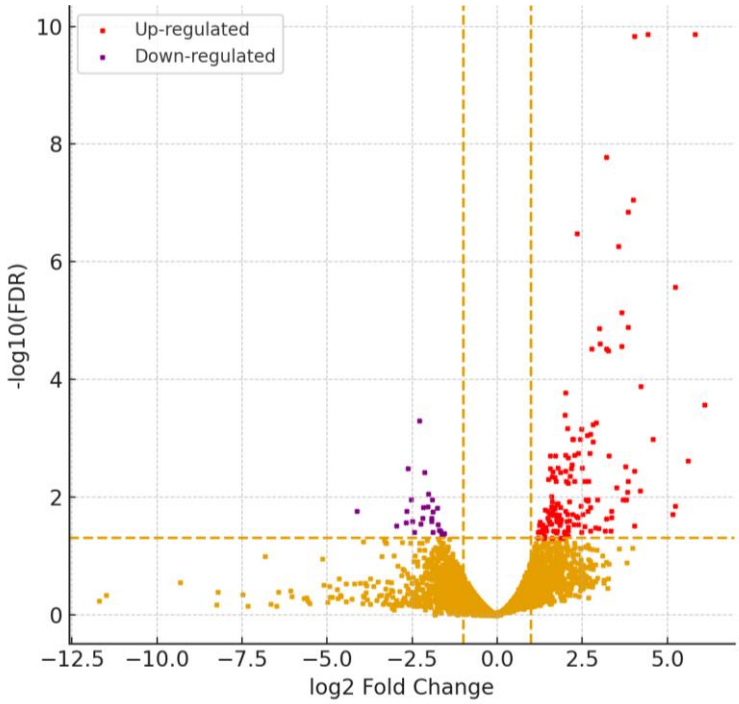


Figure 1. Volcano plot of differentially expressed genes in *Candida tropicalis* following ISO exposure. The volcano plot displays the relationship between transcriptional fold changes ($\log_2$ fold change) and statistical significance ($-\log_{10}$ FDR). Vertical dashed lines indicate the threshold for biologically relevant expression changes ($|\log_2 FC| \geq 1$), while the horizontal dashed line marks the significance cutoff (FDR ≤ 0.05). Significantly upregulated genes are shown in red, whereas downregulated genes are depicted in purple. Genes that do not meet significance thresholds are represented in ochre.

Functional annotation indicates activation of oxidative stress defense mechanisms, efflux transporters, mitochondrial responses, and lipid/membrane remodeling pathways consistent with a cellular adaptation to oxidative and membrane targeting stress induced by ISO, **Figure 2.**

© 2025 by the author(s). Distributed under a Creative Commons CC BY license.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 28 November 2025 doi:10.20944/preprints202511.2143.v1

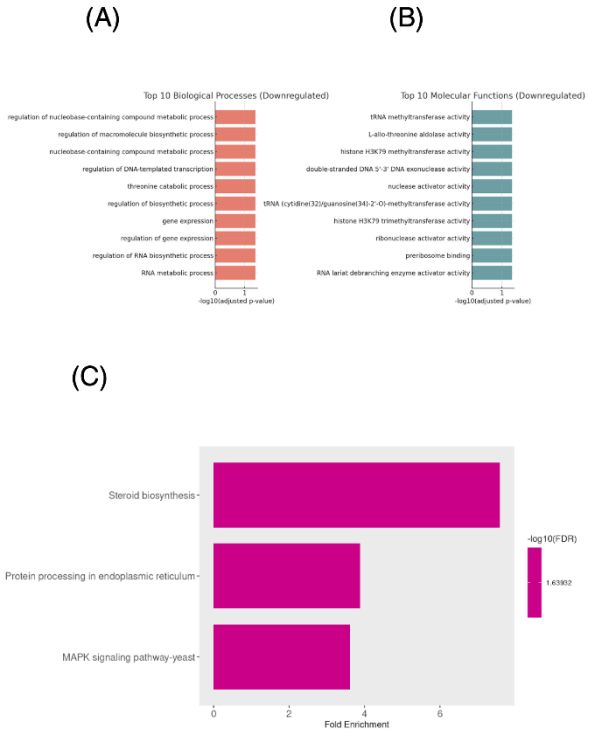


Figure 2. Functional enrichment of differentially expressed genes in *Candida tropicalis* exposed to ISO**.** Functional enrichment analysis revealed that ISO treatment significantly represses genes involved in RNA metabolism and macromolecule biosynthesis. The top enriched Gene Ontology Biological Processes (left) and Molecular Functions (right) among downregulated genes include regulation of nucleobase containing compound biosynthesis, RNA metabolic process, tRNA and histone methyltransferase activity, and ribonuclease activator function, indicating a global suppression of transcriptional activity and RNA processing. In contrast, KEGG pathway enrichment of upregulated genes (bottom) shows activation of stress responsive mechanisms, particularly steroid biosynthesis, protein processing in the endoplasmic reticulum, and the MAPK signaling pathway.

Data including raw counts, normalized count matrices, metadata describing sample conditions, and reproducible analysis scripts are freely available in the GitHub repository:https://github.com/kap8416/transcriptomicsofcandidatropicalis_isoespintanol. Additionally, the dataset is deposited in Mendeley Data https://data.mendeley.com/datasets/tr3rnz67jc/1 [18]. The dataset adheres to the FAIR data principles [19] and is distributed under the Creative Commons Attribution 4.0 (CC-BY 4.0) license to promote transparent reuse, reproducibility, and integration into future meta-analyses or comparative fungal transcriptomics.

2.2. Technical validation

To guarantee the reliability and reproducibility of this dataset, multiple layers of technical validation were applied across RNA extraction, sequencing, and bioinformatic processing. Total RNA from each biological replicate was isolated using TRIzol (Invitrogen), quantified via Ribogreen fluorometry, and assessed on an Agilent 2100 Bioanalyzer. Samples yielded RIN above 5.0 [20], and

© 2025 by the author(s). Distributed under a Creative Commons CC BY license.

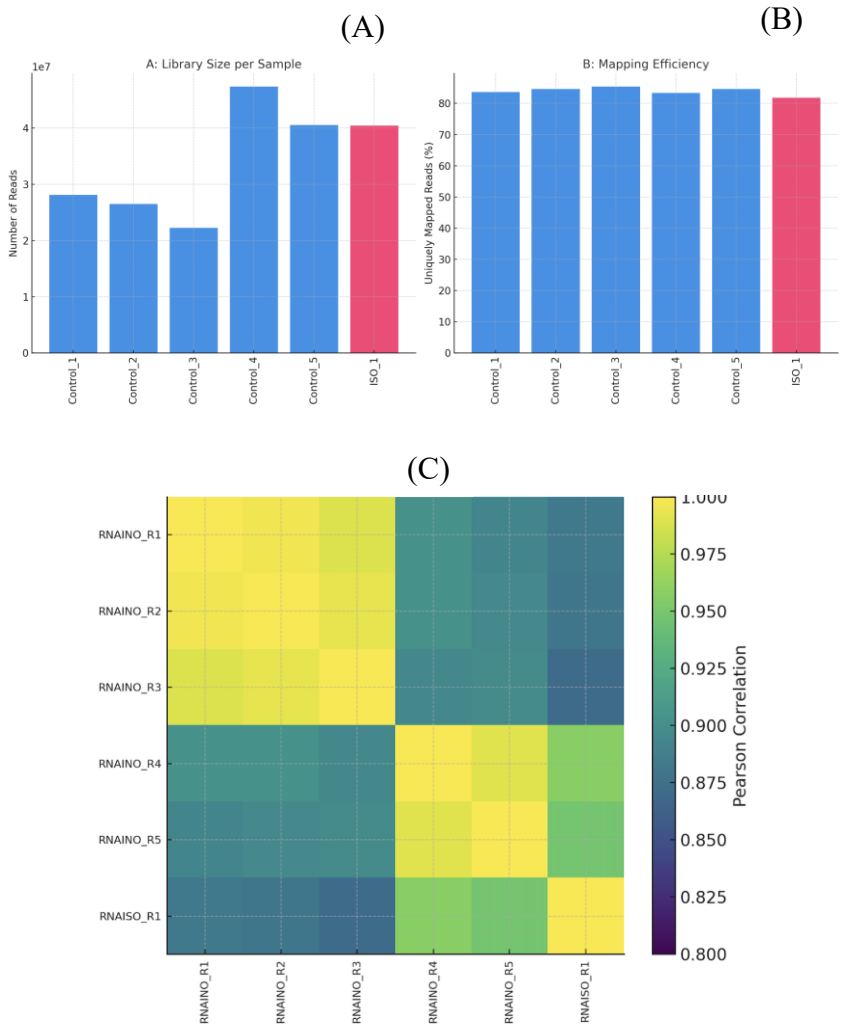
Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 28 November 2025 doi:10.20944/preprints202511.2143.v1

comparable yields between control (0.785 ± 0.02 µg) and ISO-treated samples (0.797 ± 0.03 µg), demonstrating no bias during extraction. RNA-seq libraries were prepared using the Illumina TruSeq Stranded mRNA protocol and sequenced on a NovaSeq 6000 platform, producing over 20 million paired-end reads (150 bp) per sample. FASTQC and MultiQC reports [21,22] showed Phred quality scores > Q30 for > 95% of bases, negligible adapter contamination, and stable GC content, confirming high sequencing performance, **Table 3.**

Table 3. NGS sequencing experiment by RNA-seq of *C. tropicalis*. General sequencing statistics for each sample/library.

Sample	Total reads	Clean reads percentage
RNAINO1	28105694	97.5
RNAINO2	26484468	97.6
RNAINO3	22254288	97.8
RNAINO4	47384824	92.4
RNAINO5	40520642	94.9
RNAISO1	40451606	94.9

Sequencing libraries generated between 22 and 47 million paired end reads per sample (**Figure 3A**), ensuring sufficient depth for transcriptome profiling. Reads were aligned to the *C. tropicalis* reference genome (Ensembl GCA000006335v3) using Bowtie2 [23], achieving mapping rates RNA-seq reads were aligned to the *C. tropicalis* reference genome (REF GCA_000006335.3).



© 2025 by the author(s). Distributed under a Creative Commons CC BY license.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 28 November 2025 doi:10.20944/preprints202511.2143.v1

Figure 3. Quality assessment of RNA-seq data from *C. tropicalis* under control and ISO treatment conditions. (A) Library size distribution across samples shows consistent sequencing depth between biological replicates, with comparable total read counts between control and ISO-treated libraries. (B) Mapping efficiency to the *C. tropicalis* reference genome (GCA_000006335v3) ranged from 81% to 85%, with no major differences between groups, indicating high alignment quality and low contamination. (C) Sample to sample Pearson correlation heatmap based on normalized gene expression values. Biological replicates clustered tightly by condition, with high intra group correlation ($r > 0.95$ for control and $r > 0.93$ for ISO), and clear separation between treated and untreated samples, confirming strong biological reproducibility and treatment dependent transcriptional divergence.

The distribution of reads mapped to annotated genes, together with the low proportion of rRNA derived sequences, confirmed that the RNA-seq libraries were highly enriched for mRNA and that library preparation was technically consistent (**Figures 3A-B**). Mapping efficiency ranged from 81.78% to 85.41% uniquely mapped reads, indicating high quality libraries and minimal contamination or ribosomal RNA interference. The average mapped read length remained consistent across samples (~280–294 bp), confirming the integrity of sequencing and alignment processes (**Table 4**), **Figure 3B.** The sample to-sample Pearson correlation heatmap (**Figure 3C)** shows strong clustering of biological replicates within each condition, indicating high reproducibility of the RNA-seq data. Control and ISO-treated sample form two well defined groups, with intra group correlation values above 0.93. In contrast, inter group correlations are lower, reflecting clear transcriptional differences driven by ISO exposure rather than technical variability.

Table 4. Mapping of RNA-seq transcriptomes. Mapping was performed against the C. tropicalis reference genome (REF GCA000006335v3).

Sample	Input reads	Avg. read length	Uniquely mapped reads	Uniquely mapped %	Avg. mapped length
RNAINO1	13919105	297	11644999	83.66	294.04
RNAINO2	13126552	297	11109083	84.63	294.30
RNAINO3	11031241	297	9421688	85.41	294.48
RNAINO4	23290325	284	19411950	83.35	280.33
RNAINO5	19912037	291	16856314	84.65	287.88
RNAISO1	19832040	292	16219548	81.78	288.70

Differential expression analysis was performed using EdgeR with TMM normalization [17]. Dispersion trends (common, trended, and tagwise) fell within previously reported ranges for yeast transcriptomes [24], confirming the suitability of our statistical model (**Figure 4A**). MA plots further demonstrated the symmetry of expression changes and highlighted significantly altered genes (FDR < 0.05) (**Figure 4B**). P-values were adjusted using the Benjamini–Hochberg false discovery rate method [25] to ensure statistical robustness. Biologically, the differentially expressed genes (DEGs) aligned with known antifungal response mechanisms. Up-regulated genes were enriched in pathways associated with oxidative stress mitigation, efflux transporter activation, and cell membrane adaptation, consistent with stress responses previously reported in *Candida* spp. under antifungal pressure [26,27]. Heatmap visualization of the top 50 DEGs confirmed a distinct transcriptional reprogramming pattern between treated and untreated groups (**Figure 4C**).

© 2025 by the author(s). Distributed under a Creative Commons CC BY license.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 28 November 2025 doi:10.20944/preprints202511.2143.v1

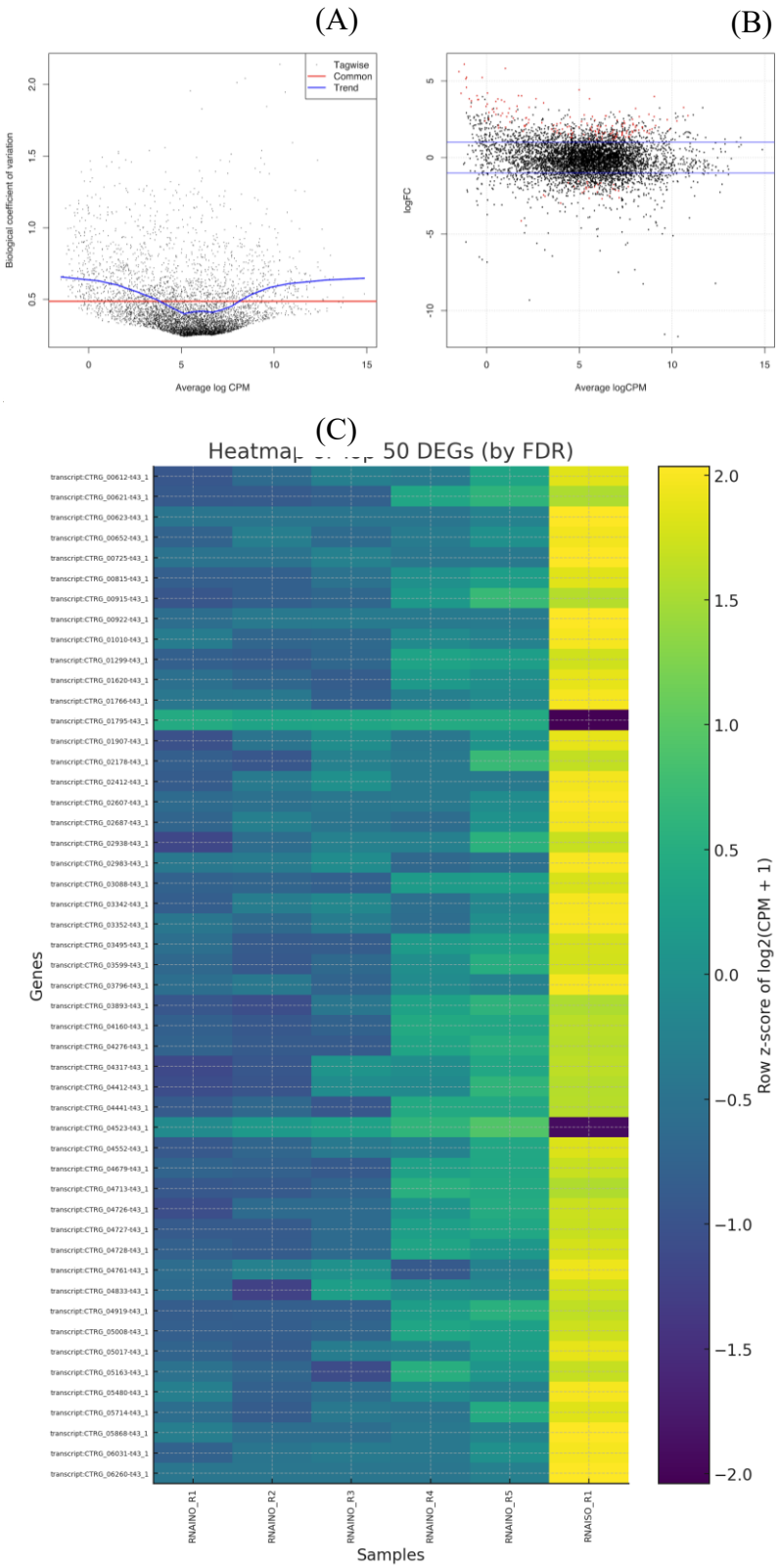


Figure 5. Differential expression validation and visualization of top DEGs. (A) Biological coefficient of variation (BCV) plot showing dispersion estimates across genes using tagwise, common, and trend estimates, confirming appropriate modeling of biological variability in *C. tropicalis*. (B) MA plot representing log2 fold changes versus average logCPM; red dots indicate significantly differentially expressed genes (FDR < 0.05). (C) Heatmap of the top 50 DEGs ranked by FDR, standardized by row z-scores of log2(CPM+1). A clear separation is observed between control (RNAINO) and ISO–treated (RNAISO) samples, demonstrating consistent transcriptional reprogramming in response to treatment.

© 2025 by the author(s). Distributed under a Creative Commons CC BY license.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 28 November 2025 doi:10.20944/preprints202511.2143.v1

Collectively, these results confirm that the dataset is technically sound, biologically consistent, and suitable for downstream applications such as antifungal mode of action studies, gene regulatory network modeling, or comparative fungal transcriptomics.

3. Methods

3.1. Fungal Strain, Growth Conditions, and Treatment

Candida tropicalis was cultured in Sabouraud Dextrose Broth (SDB) at 30 °C with shaking at 150 rpm until reaching mid-logarithmic phase (OD600 ≈ 0.8). ISO (2-isopropyl-3,6-dimethoxy-5-methylphenol), previously isolated and characterized from *Oxandra cf. xylopioides* [16], was dissolved in DMSO and applied at a final concentration corresponding to its minimum inhibitory concentration (MIC_{90} = 391.6 µg/mL). Cultures were incubated for 4 h under treatment (Stage B), while control cells received an equivalent volume of DMSO (Stage A). Three independent biological replicates were generated per condition.

3.2. RNA Extraction and Quality Assessment

Total RNA was extracted from 50 mg of fungal biomass using TRIzol reagent (Invitrogen) according to the manufacturer's instructions. The aqueous phase was recovered after chloroform separation, precipitated with isopropanol, washed with 75% ethanol, and resuspended in RNase-free water. RNA concentration was measured using the Quant-iT™ RiboGreen Assay (Thermo Fisher Scientific). RNA integrity was assessed on an Agilent 2100 Bioanalyzer using the RNA 6000 Nano Kit; only samples with RNA Integrity Number (RIN) > 7.0 were used for library preparation. Yield was consistent between conditions (0.785 ± 0.02 µg Control vs. 0.797 ± 0.03 µg ISO-treated).

3.3. Library Preparation and RNA Sequencing

RNA-seq libraries were generated using the Illumina TruSeq Stranded mRNA Sample Preparation Kit following poly-A selection. Library quality and insert size were validated using the Agilent Bioanalyzer. Libraries were pooled equimolarly and sequenced on the Illumina NovaSeq 6000 platform, producing paired-end reads of 150 bp. Each sample yielded > 20 million read pairs. Raw BCL files were converted to FASTQ using Illumina bcl2fastq.

3.4. Preprocessing and Alignment

Sequence quality was evaluated using FastQC [22], and summary metrics were compiled using MultiQC [21]. Adapter trimming and low-quality base removal were performed using Trimmomatic. High-quality reads were aligned to the *C. tropicalis* reference genome (Ensembl release GCA000006335v3) using Bowtie2 [23] with default sensitive parameters. Mapping statistics (alignment rate, uniquely mapped reads, rRNA contamination) were extracted using SAMtools and summarized per sample.

3.5. Quantification and Differential Expression Analysis

Aligned reads were quantified at the gene level using HTSeq-count in "union" mode. Gene expression values were normalized using the trimmed mean of M-values (TMM) method implemented in the EdgeR package. Genes with low counts (< 1 count per million in ≥ 3 samples) were excluded. Differential expression between Stage A (control) and Stage B (ISO-treated) was assessed using EdgeR's quasi-likelihood F-test. Genes with |log2 fold change| > 1 and FDR < 0.05 [25] were considered significantly differentially expressed. Functional enrichment was conducted using ShinyGO https://bioinformatics.sdstate.edu/go/ analysis.

© 2025 by the author(s). Distributed under a Creative Commons CC BY license.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 28 November 2025 doi:10.20944/preprints202511.2143.v1

3.6. Data Availability and Reproducibility

All raw FASTQ files, normalized count matrices, sample metadata, and scripts used for analysis are available in the GitHub repository: **https://github.com/kap8416/transcriptomicsofcandidatropicalis_isoespintanol**. A curated dataset will be deposited in **Mendeley Data** (doi: 10.17632/tr3rnz67jc.1), following FAIR data principles.

4. User Notes

This dataset is suitable for a wide range of downstream analyses in fungal biology, transcriptomics, and antifungal research. Beyond the differential expression analysis described here, users may employ the raw and processed data for Gene Ontology (GO) and KEGG pathway enrichment to identify biological processes, molecular functions, and cellular components affected by ISO exposure. The dataset is also well-suited for reconstructing co-expression networks, inferring regulatory modules, and identifying transcription factors or non-coding RNAs involved in antifungal stress responses.

Furthermore, because the dataset includes raw counts, metadata, and reproducible analysis scripts, it can be used to benchmark normalization strategies (e.g., TMM, TPM, DESeq2), evaluate statistical models for differential expression, or train machine learning models to predict drug susceptibility or resistance in Candida spp. Comparative transcriptomic studies across *Candida albicans*, *C. glabrata*, *C. auris*, and *C. tropicalis* may also benefit from this resource. All files are openly accessible through the linked repository and permanently archived in Mendeley Data. Users are encouraged to cite this dataset when incorporating it into secondary analyses, meta-analyses, or computational modeling. Any modifications or re-use of the data should comply with the CC-BY 4.0 license.

Supplementary Materials: The following supporting information can be downloaded at the website of this paper posted on Preprints.org: raw_counts.txt, count_per_million.txt and DE_transcripts.txt. Dataset: https://data.mendeley.com/datasets/tr3rnz67jc/1. Dataset License: CC-BY 4.0 Mendeley Dataset: doi: 10.17632/tr3rnz67jc.1.

Author Contributions: Conceptualization, K.A.P., O.I.C.-M. and A.A.-O.; Methodology, K.A.P., O.I.C.-M. and A.A.-O.; Data curation, K.A.P.; Writing—original draft preparation, K.A.P., O.I.C.-M. and A.A.-O.; Writing—review and editing, K.A.P., O.I.C.-M. and A.A.-O.

Funding: KAP acknowledges SECIHTI for a fellowship CVU (227919).

Data Availability Statement: All datasets supporting the findings of this study are available as Supplementary Files accompanying this article.

Acknowledgments: The authors thank the Office of the Vice Rector for Research and Outreach at the University of Córdoba for covering the publication costs and the National Center for Genomic Sequencing (Medellín, Colombia) for technical assistance and sequencing services. Thanks to Neifer Martínez and Vanessa Vega for their assistance in preparing the graphical abstract.

Conflicts of Interest: The author declares no conflict of interest.

References

1. Spruijtenburg, B.; De Carolis, E.; Magri, C.; Meis, J. F.; Sanguinetti, M.; de Groot, T.; Meijer, E. F. J. Genotyping of *Candida tropicalis* Isolates Uncovers Nosocomial Transmission of Two Lineages in Italian Tertiary Care Hospital. *Journal of Hospital Infection* **2025**, *155*, 115–122. https://doi.org/10.1016/j.jhin.2024.10.003.
2. Suto, Y.; Horiba, K.; Masuda, Y.; Tanaka, K.; Hashino, M.; Kuroda, M.; Fukuda, H. *Candida tropicalis* Brain Abscess Diagnosed by Metagenomic Next-Generation Sequencing: A Case Report. *Internal Medicine* **2025**, 5937–25. https://doi.org/10.2169/internalmedicine.5937-25.

© 2025 by the author(s). Distributed under a Creative Commons CC BY license.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 28 November 2025 doi:10.20944/preprints202511.2143.v1

3. Doan, H. T.; Chiu, Y. L.; Cheng, L. C.; Coad, R. A.; Chiang, H. Sen. *Candida tropicalis* Alters Barrier Permeability and Claudin-1 Organization in Intestinal Epithelial Cells. *Journal of Physiological Investigation* **2025**, *68* (1), 67–76. https://doi.org/10.4103/ejpi.EJPI-D-24-00090.
4. Delma, F. Z.; Spruijtenburg, B.; Meis, J. F.; de Jong, A. W.; Groot, J.; Rhodes, J.; Melchers, W. J. G.; Verweij, P. E.; de Groot, T.; Meijer, E. F. J.; Buil, J. B. Emergence of Flucytosine- Resistant *Candida tropicalis* Clade, the Netherlands. *Emerg Infect Dis* **2025**, *31* (7), 1354–1364. https://doi.org/10.3201/eid3107.241918.
5. Xiong, H.; Zhao, R.; Han, S.; Liu, Z.; Zhang, X.; Jia, Z.; Cui, J.; Zhang, Y.; Wang, X. Research Progress on the Drug Resistance Mechanisms of *Candida tropicalis* and Future Solutions. *Frontiers in Microbiology*. **2025**, 16, 1594226. https://doi.org/10.3389/fmicb.2025.1594226.
6. Tseng, K. Y.; Chen, Y. Z.; Zhou, Z. L.; Tsai, J. N.; Tseng, M. N.; Liu, H. L.; Wu, C. J.; Liao, Y. C.; Lin, C. C.; Tsai, D. J.; Chen, F. J.; Hsieh, L. Y.; Huang, K. C.; Huang, C. H.; Chen, K. T.; Chu, W. L.; Lin, C. M.; Shih, S. M.; Hsiung, C. A.; Chen, Y. C.; Sytwu, H. K.; Yang, Y. L.; Lo, H. J. Detection in Orchards of Predominant Azole-Resistant *Candida tropicalis* Genotype Causing Human Candidemia, Taiwan. *Emerg Infect Dis* **2024**, *30* (11), 2323–2332. https://doi.org/10.3201/eid3011.240545.
7. Contreras-Martínez, O. I.; Angulo-Ortíz, A.; Santafé-Patiño, G.; Aviña-Padilla, K.; Velasco-Pareja, M. C.; Yasnot, M. F. Transcriptional Reprogramming of *Candida tropicalis* in Response to Isoespintanol Treatment. *Journal of Fungi* **2023**, 9, 1199. https://doi.org/10.3390/jof9121199.
8. Papon, N.; Courdavault, V.; Clastre, M.; Bennett, R. J. Emerging and Emerged Pathogenic Candida Species: Beyond the *Candida albicans* Paradigm. *PLoS Pathog* **2013**, *9* (9). https://doi.org/10.1371/journal.ppat.1003550.
9. Zuza-Alves, D. L.; Sila-Rocha, W. P.; Chaves, G. An Update on *Candida tropicalis* Based on Basic and Clinical Approaches. *Front Microbiol* **2017**, *8*. https://doi.org/10.3389/fmicb.2017.01927.
10. Magill, S.-O. E. E. J. Changes in Prevalence of Health Care–Associated Infections. *New England Journal of Medicine* **2019**, *380* (11), 1085–1086. https://doi.org/10.1056/nejmc1817140.
11. Cornely, O. A.; Sprute, R.; Bassetti, M.; Chen, S. C. A.; Groll, A. H.; Kurzai, O.; Lass-Flörl, C.; Ostrosky-Zeichner, L.; Rautemaa-Richardson, R.; Revathi, G.; Santolaya, M. E.; White, P. L.; Alastruey-Izquierdo, A.; Arendrup, M. C.; Baddley, J.; Barac, A.; Ben-Ami, R.; Brink, A. J.; Grothe, J. H.; Guinea, J.; Hagen, F.; Hochhegger, B.; Hoenigl, M.; Husain, S.; Jabeen, K.; Jensen, H. E.; Kanj, S. S.; Koehler, P.; Lehrnbecher, T.; Lewis, R. E.; Meis, J. F.; Nguyen, M. H.; Pana, Z. D.; Rath, P. M.; Reinhold, I.; Seidel, D.; Takazono, T.; Vinh, D. C.; Zhang, S. X.; Afeltra, J.; Al-Hatmi, A. M. S.; Arastehfar, A.; Arikan-Akdagli, S.; Bongomin, F.; Carlesse, F.; Chayakulkeeree, M.; Chai, L. Y. A.; Chamani-Tabriz, L.; Chiller, T.; Chowdhary, A.; Clancy, C. J.; Colombo, A. L.; Cortegiani, A.; Corzo Leon, D. E.; Drgona, L.; Dudakova, A.; Farooqi, J.; Gago, S.; Ilkit, M.; Jenks, J. D.; Klimko, N.; Krause, R.; Kumar, A.; Lagrou, K.; Lionakis, M. S.; Lmimouni, B. E.; Mansour, M. K.; Meletiadis, J.; Mellinghoff, S. C.; Mer, M.; Mikulska, M.; Montravers, P.; Neoh, C. F.; Ozenci, V.; Pagano, L.; Pappas, P.; Patterson, T. F.; Puerta-Alcalde, P.; Rahimli, L.; Rahn, S.; Roilides, E.; Rotstein, C.; Ruegamer, T.; Sabino, R.; Salmanton-García, J.; Schwartz, I. S.; Segal, E.; Sidharthan, N.; Singhal, T.; Sinko, J.; Soman, R.; Spec, A.; Steinmann, J.; Stemler, J.; Taj-Aldeen, S. J.; Talento, A. F.; Thompson, G. R.; Toebben, C.; Villanueva-Lozano, H.; Wahyuningsih, R.; Weinbergerová, B.; Wiederhold, N.; Willinger, B.; Woo, P. C. Y.; Zhu, L. P. Global Guideline for the Diagnosis and Management of Candidiasis: An Initiative of the ECMM in Cooperation with ISHAM and ASM. *The Lancet Infectious Diseases*. Elsevier Ltd May 1, 2025, pp e280–e293. https://doi.org/10.1016/S1473-3099(24)00749-7.
12. Fakhri-Demeshghieh, A.; Yousefipour, A.; Bolouki, Y.; Bigdeli, M. S.; Zamani, E.; Farajkhoda, A.; Salmani, A.; Katiraee, F.; Bokaie, S. Antifungal Resistance of Candida Spp. Isolates From HIV/AIDS Patients in Iran 1999–2024: A Systematic Review and Meta-Analysis. *Journal of Clinical Laboratory Analysis*. **2025**. https://doi.org/10.1002/jcla.70101.
13. Kadariswantiningsih, I. N.; Empitu, M. A.; Santosa, T. I.; Alimu, Y. Antifungal Resistance: Emerging Mechanisms and Implications (Review). *Molecular Medicine Reports*. **2025**. https://doi.org/10.3892/mmr.2025.13612.
14. Rojano, B.; Saez, J.; Schinella, G.; Quijano, J.; Vélez, E.; Gil, A.; Notario, R. Experimental and Theoretical Determination of the Antioxidant Properties of Isoespintanol (2-Isopropyl-3,6-Dimethoxy-5-Methylphenol). *J Mol Struct* **2008**, *877*, 1–6.

© 2025 by the author(s). Distributed under a Creative Commons CC BY license.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 28 November 2025 doi:10.20944/preprints202511.2143.v1

15. Contreras, O.; Angulo, A.; Santafé, G. Mechanism of Antifungal Action of Monoterpene Isoespintanol against Clinical Isolates of *Candida tropicalis*. *Molecules* **2022**, *27*, 5808. https://doi.org/10.3390/molecules27185808.
16. Contreras Martínez, O. I.; Ortíz, A. A.; Patiño, G. S. Antifungal Potential of Isoespintanol Extracted from *Oxandra xylopioides* Diels (Annonaceae) against Intrahospital Isolations of Candida SPP. *Heliyon* **2022**, *8* (10). https://doi.org/10.1016/j.heliyon.2022.e11110.
17. Robinson, M. D.; McCarthy, D. J.; Smyth, G. K. EdgeR: A Bioconductor Package for Differential Expression Analysis of Digital Gene Expression Data. *Bioinformatics* **2009**, *26* (1), 139–140. https://doi.org/10.1093/bioinformatics/btp616.
18. Aviña Padilla, Katia; Angulo-Ortiz, Alberto; Contreras-Martinez, Orfa Ines. **2025**, "RNA-Seq dataset of *Candida tropicalis* under antifungal stress", Mendeley Data, V1, doi: 10.17632/tr3rnz67jc.1
19. Wilkinson, M. D.; Dumontier, M.; Aalbersberg, Ij. J.; Appleton, G.; Axton, M.; Baak, A.; Blomberg, N.; Boiten, J. W.; da Silva Santos, L. B.; Bourne, P. E.; Bouwman, J.; Brookes, A. J.; Clark, T.; Crosas, M.; Dillo, I.; Dumon, O.; Edmunds, S.; Evelo, C. T.; Finkers, R.; Gonzalez-Beltran, A.; Gray, A. J. G.; Groth, P.; Goble, C.; Grethe, J. S.; Heringa, J.; t Hoen, P. A. C.; Hooft, R.; Kuhn, T.; Kok, R.; Kok, J.; Lusher, S. J.; Martone, M. E.; Mons, A.; Packer, A. L.; Persson, B.; Rocca-Serra, P.; Roos, M.; van Schaik, R.; Sansone, S. A.; Schultes, E.; Sengstag, T.; Slater, T.; Strawn, G.; Swertz, M. A.; Thompson, M.; Van Der Lei, J.; Van Mulligen, E.; Velterop, J.; Waagmeester, A.; Wittenburg, P.; Wolstencroft, K.; Zhao, J.; Mons, B. Comment: The FAIR Guiding Principles for Scientific Data Management and Stewardship. *Sci Data* **2016**, *3*. https://doi.org/10.1038/sdata.2016.18.
20. Fleige, S.; Pfaffl, M. W. RNA Integrity and the Effect on the Real-Time QRT-PCR Performance. *Molecular Aspects of Medicine*. **2006**, 27(2-3), 126–139. https://doi.org/10.1016/j.mam.2005.12.003.
21. Ewels, P.; Magnusson, M.; Lundin, S.; Käller, M. MultiQC: Summarize Analysis Results for Multiple Tools and Samples in a Single Report. *Bioinformatics* **2016**, *32* (19), 3047–3048. https://doi.org/10.1093/bioinformatics/btw354.
22. Andrews, S. FastQC: A quality control tool for high throughput sequence data. *Babraham Bioinformatics*. **2010.** URL: https://www.bioinformatics.babraham.ac.uk/projects/fastqc/
23. Langmead, B.; Salzberg, S. L. Fast Gapped-Read Alignment with Bowtie 2. *Nat Methods* **2012**, *9* (4), 357–359. https://doi.org/10.1038/nmeth.1923.
24. Gierliński, M.; Cole, C.; Schofield, P.; Schurch, N. J.; Sherstnev, A.; Singh, V.; Wrobel, N.; Gharbi, K.; Simpson, G.; Owen-Hughes, T.; Blaxter, M.; Barton, G. J. Statistical Models for RNA-Seq Data Derived from a Two-Condition 48-Replicate Experiment. *Bioinformatics* **2015**, *31*(22), 3625–3630. https://doi.org/10.1093/bioinformatics/btv425.
25. Benjaminit, Y.; Hochberg, Y. Controlling the False Discovery Rate: A Practical and Powerful Approach to Multiple Testing. *Journal of the Royal Statistical Society* **1995**, 57, 289-300. https://academic.oup.com/jrsssb/article/57/1/289/7035855.
26. Morschhäuser, J. The Development of Fluconazole Resistance in *Candida albicans* – an Example of Microevolution of a Fungal Pathogen. *Journal of Microbiology*. **2016**, 54, 192-201. https://doi.org/10.1007/s12275-016-5628-4.
27. de Oliveira Santos, G. C. de O.; Vasconcelos, C. C.; Lopes, A. J. O.; Cartágenes, M. do S. de S.; Filho, A. K. D. B.; do Nascimento, F. R. F.; Ramos, R. M.; Pires, E. R. R. B.; de Andrade, M. S.; Rocha, F. M. G.; Monteiro, C. de A. Candida Infections and Therapeutic Strategies: Mechanisms of Action for Traditional and Alternative Agents. *Frontiers in Microbiology*, **2018**, 9, 1351. https://doi.org/10.3389/fmicb.2018.01351.

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.

© 2025 by the author(s). Distributed under a Creative Commons CC BY license.