

Abstract

Exposure to Mycovirus-Containing *Aspergillus flavus* Alters Transcription Factors in Normal and Leukemia Cell Lines [†]

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[†] Presented at the 4th International Electronic Conference on Cancers, 6–8 March 2024; Available online: <https://sciforum.net/event/IECC2024>.**Keywords:** etiology; cancer; leukemia; leukemogenesis; carcinogenesis; mycovirus; fungi; aspergillus; virus

Transcription factors bind specific DNA motifs to regulate the expression of target genes in order to maintain normal hematopoiesis. The dysregulation of these factors can lead to hemopoietic disorders, including leukemias. Mutations, translocations, or the aberrant expression of several transcription factors in various leukemias have been well documented. Mycoviruses are known to alter the genetics of their fungal host and transform their biological characteristics. We have evaluated the effects of the products of a certain mycovirus-containing *Aspergillus flavus* (MCAF), which we have isolated from the home of a patient with leukemia, on the transcription factors of acute lymphoblastic (ALL), acute myelogenous leukemia (AML) cell lines, and controls. This organism does not produce any aflatoxin. Our previously published studies have shown that patients with B-cell ALL, unlike controls, have antibodies to MCAF, and the exposure of the mononuclear leukocytes from ALL patients in complete remission to its products results in the re-development of genetic and cell-surface markers characteristic of ALL. In additional investigations, ALL and AML cell lines and controls were exposed to incremental doses of the supernatant of the culture of MCAF. Prior to and after exposure, the levels of PAX-5 and Ikaros (75 and 55 kDa) in ALL cell lines, and AML-1,c/EBP-a and PU.1 in AML cell lines, as well as NF-κB(p65) transcription factors in both cell lines, were assessed. Cellular viability was also evaluated. The exposure of the 'normal' cell line to the MCAF resulted in apoptosis, and the downregulation of all tested transcription factors, with no detectable levels remaining. In leukemia cell lines, exposure to MCAF also caused cell death; however, while there was a downregulation of all tested transcription factors, some residual levels were retained. The genetic alterations caused by MCAF are novel findings and of significance. Further studies on the possible role of mycovirus-containing *Aspergillus flavus* in leukemogenesis are warranted.



Citation: Tebbi, C.K.; Sahakian, E.; Yan, J.; Patel, S.; Mediavilla-Varela, M. Exposure to Mycovirus-Containing *Aspergillus flavus* Alters Transcription Factors in Normal and Leukemia Cell Lines. *Proceedings* **2024**, *100*, 19.

<https://doi.org/10.3390/proceedings2024100019>

Academic Editor: Stephen Geoffrey Ward

Published: 27 March 2024



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Author Contributions: C.K.T. has authored the abstract. J.Y. has performed technical works. E.S., S.P. and M.M.-V. have contributed to planning and review of the experiment. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: No new data were created.

Conflicts of Interest: The authors declare no conflict of interest.

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