

Benoît Henry¹, Wajiha Gohir¹, Deepali Kumar¹, Atul Humar¹, Claire Aguilar^{1,2}, Shahid Husain¹

¹Transplant Infectious Diseases, Toronto General Hospital, University Health Network, University of Toronto, Toronto, Canada, ²Université de Paris, Centre d'Infectiologie Necker Pasteur, IHU Imagine, Hôpital Necker-Enfants Malades, Assistance Publique- Hôpitaux de Paris (AP-HP), Paris, France.

INTRODUCTION

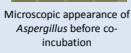
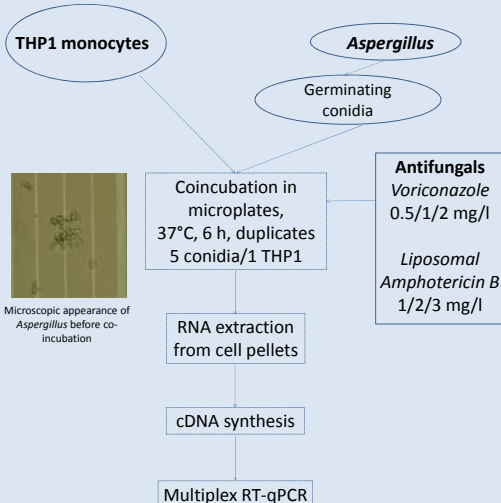
- Across the various classes of antifungals used against *Aspergillus fumigatus*, differences regarding *in vitro* and *in vivo* activities have been observed, leading to varied clinical responses in patients.
- Aside from direct antifungal effects, immunomodulatory properties of antifungals may account for these variations in clinical response.
- Human monocytic cell lines such as THP1 are model of human phagocytes, which can represent a convenient and well characterized model for exploratory studies

OBJECTIVE

To explore the effect of different antifungals on the gene expression of major components of innate and adoptive immunity in human phagocytes.

METHODS

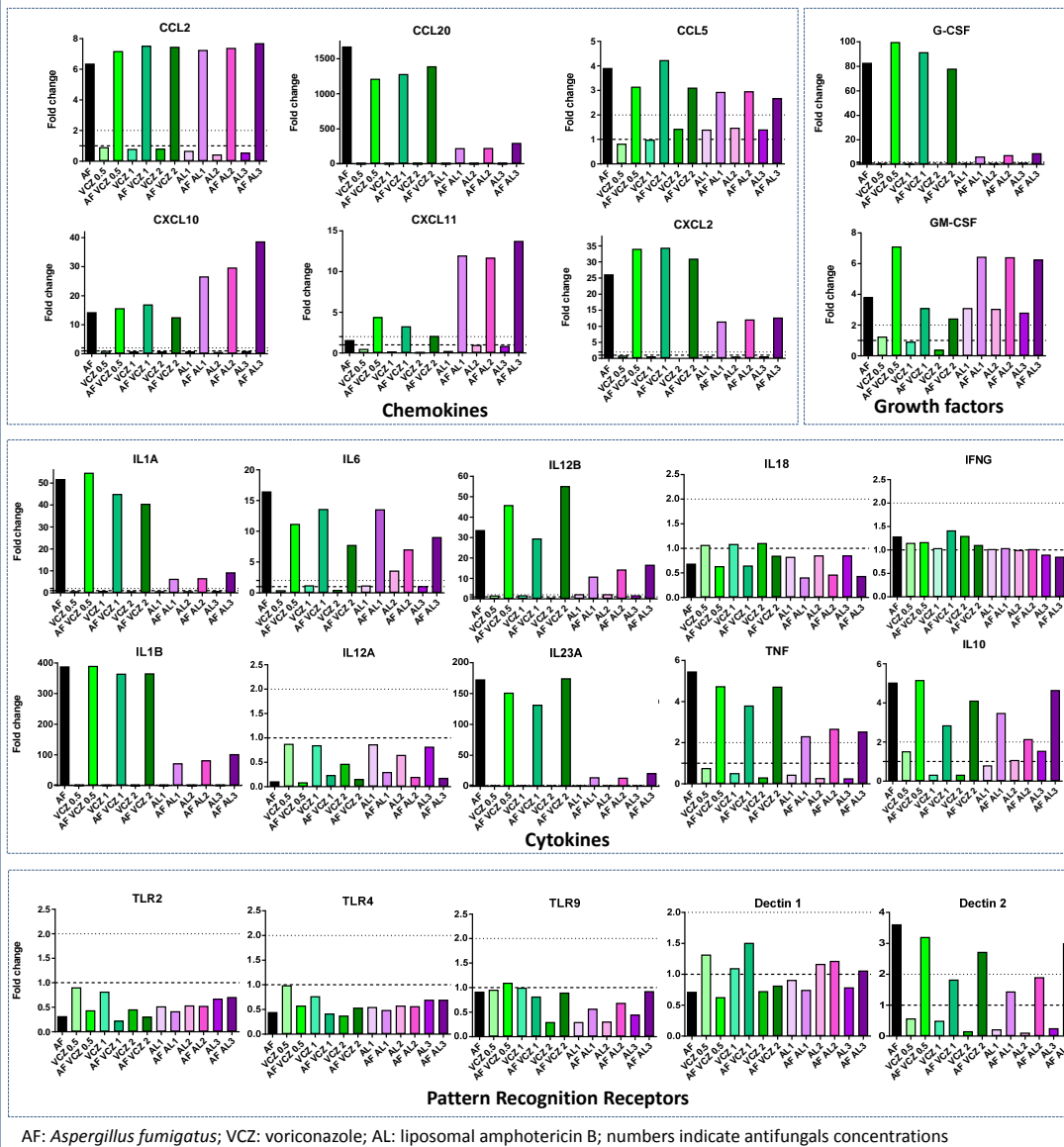
- Human THP1 monocytes were coincubated with a variable combination of *Aspergillus fumigatus* (ATCC® 13073TM; NIH 5233 strain) and antifungals for 6 hours
- THP1 cells were cultivated in classical medium (RPMI, FBS, Penicillin-Streptomycin)
- *A. fumigatus* was grown on PDA plates, then germinating conidia were obtained through incubation in Sabouraud liquid medium, at 37°C, continuous agitation, for 7-8 hours
- Antifungals were diluted in DMSO (voriconazole) or culture medium (liposomal amphotericin B), then adjusted to the target concentrations.



Microscopic appearance of *Aspergillus* before co-incubation

RESULTS

All results are expressed as fold changes in gene expression, using untreated, uninfected THP1 cells as controls, and are normalized through a panel made of 5 housekeeping genes.



CONCLUSIONS

- Upon coincubation with *A. fumigatus* germed conidia/hyphae, voriconazole appears to maintain in THP1 cells an innate immune response oriented at phagocytes attraction trough chemokines, and towards Th1 and Th17 responses, whereas this response appears diminished when liposomal amphotericin B is used.
- These preliminary result point out to a potential anti inflammatory role of liposomal Amphotericin B during the initial response to the infection, and result in differences in clinical outcomes as compared with voriconazole.
- Further and ongoing experiments will address the effect of deoxycholate amphotericin B and caspofungin in this context; validation through the use of immunocompromised patients immune cells and animal models of *Aspergillus fumigatus* infections is envisioned.