# *5-hydroxytryptamine receptor 1A* (*5-HT1A*) is involved in the host defense of *Drosophila melanogaster* against *Aspergillus fumigatus* infection and the mycotoxin it secrets

R Yan[1], A C Chen[1], R Xu, D Ferrandon[1,2*]

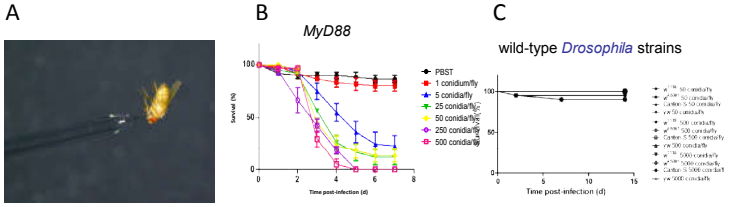
[1]Sino-French Hoffmman Institute, Guangzhou Medical University, Guangzhou, China

[2]Universite de Strasbourg, UPR9022 du CNRS, Strasbourg, France

**Abstract**: *Drosophila melanogaster*, as a simplified and powerful model organism, has been used widely in various aspects of life sciences researches, including innate immunity. *Aspergillus fumigatus* is a mammalian opportunistic pathogen that is ubiquitous in the environment and its spores are deadly if they enter into the lungs of the immunocompromised patients, which lead to invasive pulmonary aspergillosis with high morbidity and mortality rates. Recently, our team established an *Aspergillus fumigatus*-infected *Drosophila melanogaster* model by injecting its spores into *MyD88* mutant flies and utilized this model to perform genome-wide large-scale screening that is susceptible to this fungal infection. Numerous candidates have been screened so far and *5-hydroxytryptamine receptor 1A* (*5-HT1A*) exhibits high susceptibility to *Aspergillus fumigatus* infection and its mycotoxin, restrictocin. Furthermore, tissue specificity analyses show that *5-HT1A* expression in the glial cells of the brain could play an essential role in the host defense against this fungal infection.

## Introduction

*Aspergillus fumigatus* is a mammalian opportunistic pathogen that is ubiquitous in the environment, which floats in the air and can be deeply inhaled into human lungs. It normally is harmless to humans, however, its spores are deadly if they enter the lungs of the immunocompromised patients, which lead to invasive pulmonary aspergillosis with high morbidity and mortality rates. So, it is useful and helpful to gain more insights into the mechanism of host defense against this fungal infection.




Our team established an *Aspergillus fumigatus*-infected *Drosophila melanogaster* model by injecting its spores into the thorax (A) of the *MyD88* mutant flies (B) and wild-type flies (C) with capillary. This model shows that Aspergillus fumigatus is pathogenic to *MyD88* mutant flies, however, it does not kill wild-type flies efficiently.

## Results

### 1. *5-HT1A* RNAi and mutant flies are specifically susceptible to *Aspergillus fumigatus* infection.

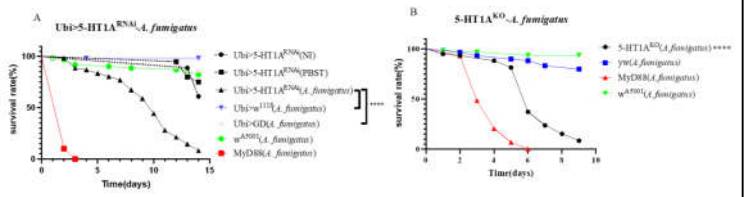
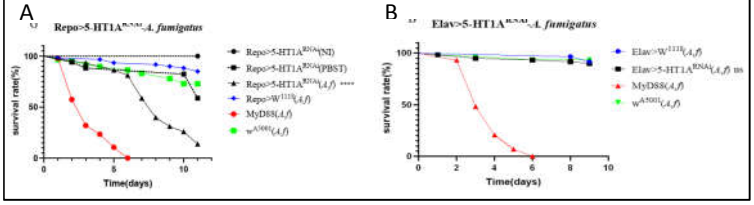



Figure 1. Survival rates of *5-HT1A* RNAi and mutant flies injected with *Aspergillus fumugatus* spores. (A) Survival rates of *5-HT1A* RNAi flies infected with *Aspergillus fumigatus* for 14 days. (B) Survival rates of *5-HT1A* knock-out flies with *Aspergillus fumigatus* for 9 days.

### 2. *5-HT1A* knock-down in glial cells is susceptible to *Aspergillus fumigatus* infection.



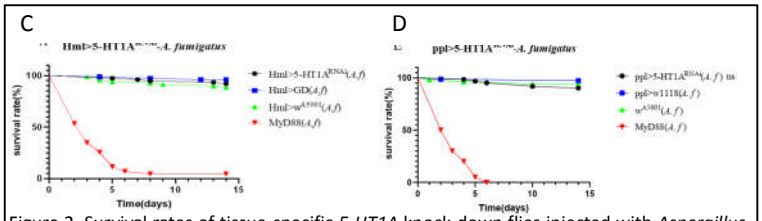




Figure 2. Survival rates of tissue-specific *5-HT1A* knock-down flies injected with *Aspergillus fumugatus* spores. (A) Survival rates of glial cell-specific *5-HT1A* knock-down flies infected with *Aspergillus fumigatus*. (B) Survival rates of neuron-specific *5-HT1A* knock-down flies infected with *Aspergillus fumigatus*. (C) Survival rates of hemocyte-specific *5-HT1A* knock-down flies infected with *Aspergillus fumigatus*. (D) Survival rates of fat body-specific *5-HT1A* knock-down flies infected with *Aspergillus fumigatus*.

### 3. *5-HT1A* RNAi flies are specifically susceptible to the restrcitocin.

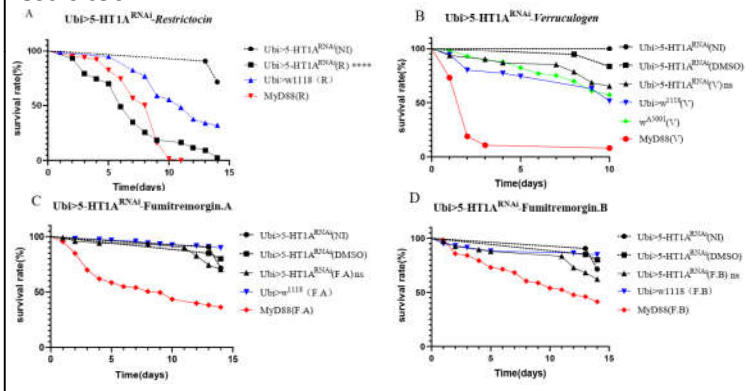



Figure 3. Survival rates of *5-HT1A* RNAi flies injected with the mycotoxins Restrcitocin (A), Verruculogen (B), Fumitremorgin A (C), Fumitremorgin B (D).

### 4. *5-HT1A* may not be involved in the phagocytosis or the melanization.

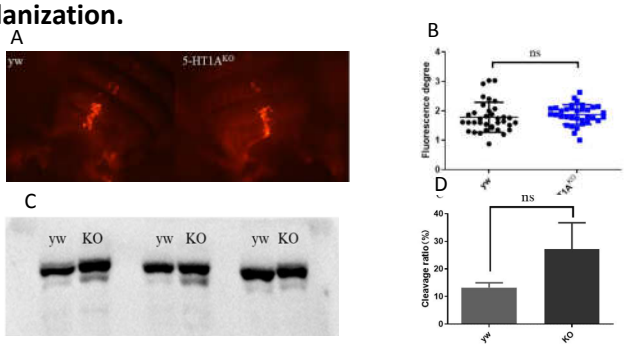



Figure 4. The phagocytosis efficiency (A, B) and melanization response (C, D) of *5-HT1A* mutant flies.

## Conclusion

*5-HT1A*, not other *5-HT* receptors, is specifically involved in the host defense against *Aspergillus fumigatus* infection and restrictocin injection in the *Drosophila* model, which may not be involved in the phagocytosis or the melanization.