The role of Pentraxin-3 in the immunometabolic regulation of antifungal immunity

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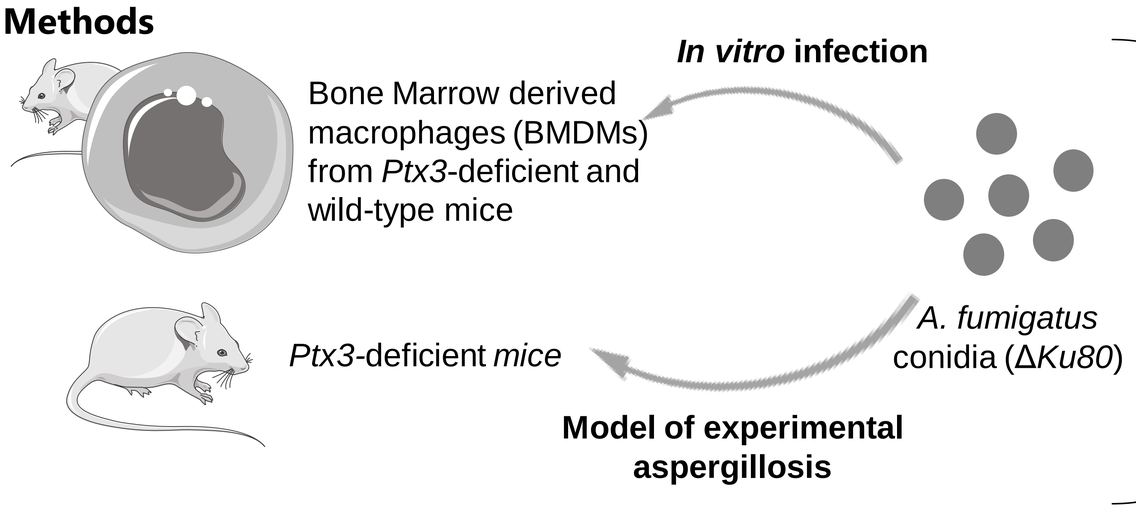
Introduction

The susceptibility to life-threatening fungal infections, including invasive aspergillosis, represents an emerging problem as the consequence of the expanding populations of immunocompromised individuals. In response to infection, immune cells rapidly adapt their cellular metabolism to fuel specialized antimicrobial effector functions. The reprogramming of cellular metabolism is a fundamental mechanism through which innate immune cells meet the energetic and anabolic needs during host defense against invading pathogens. The long pentraxin-3 (PTX3) plays a pivotal role in the pathogenesis of infections by *Aspergillus fumigatus* as the result of its opsonic activity facilitating immune recognition and phagocytosis. However, whether PTX3 exerts its functions by regulating the immunometabolic responses to *A. fumigatus* remains unknown.

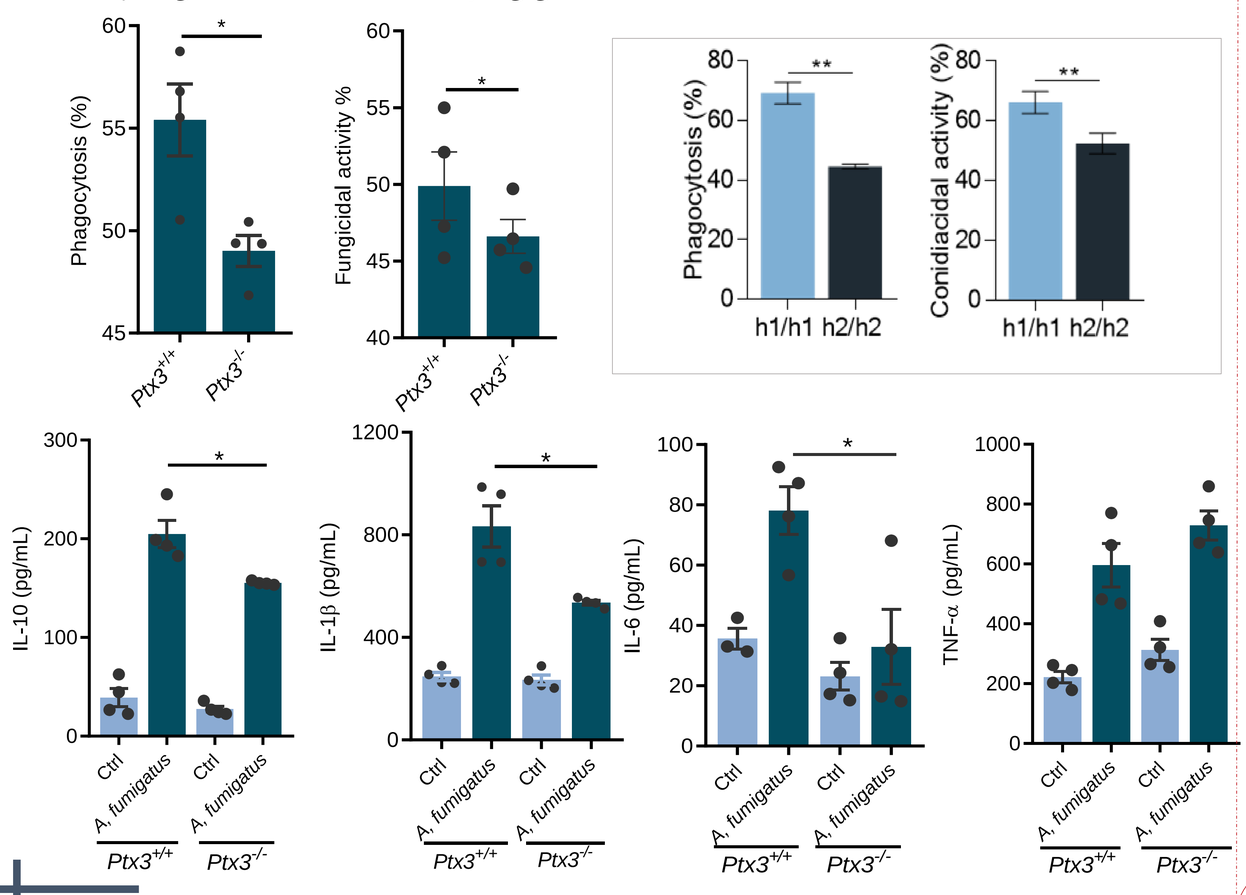
Methods



Results

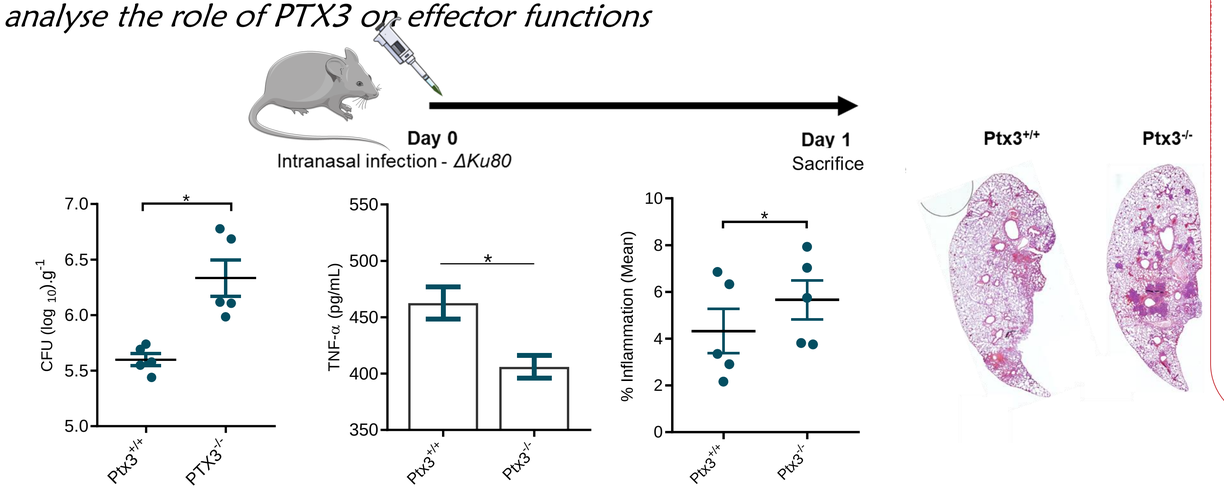
1 Role of PTX3 in the imune response against *A. fumigatus*

Analysis of the role of PTX3 on effector functions of macrophages, using BMDMs from Ptx3-deficient and wild-type mice infected with A. fumigatus conidia and macrophages from donors carrying genetic variants in Ptx3



- PTX3 deficiency impairs the phagocytosis and fungicidal activity of BMDMs and affect cytokine production

In vivo model of experimental aspergillosis resorting to PTX3-deficient mice to analyse the role of PTX3 on effector functions

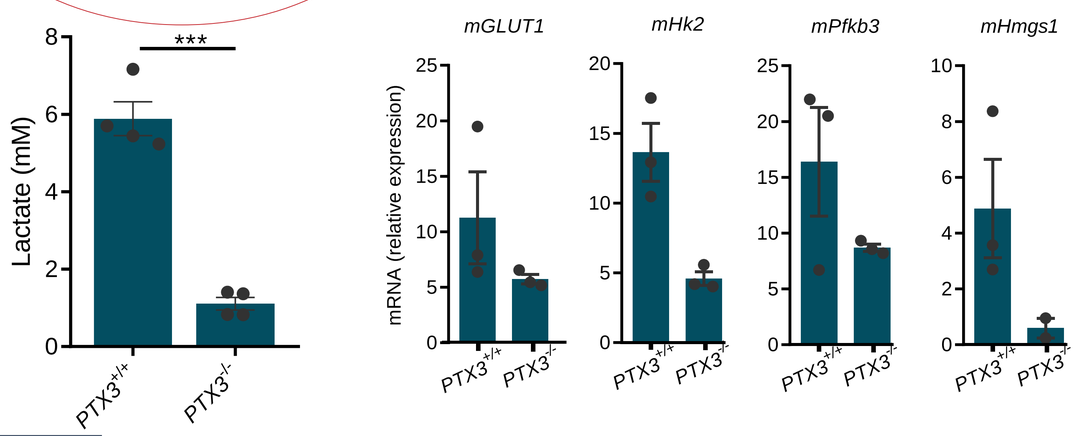


2 Role of PTX3 in metabolic reprograming during *A. fumigatus* infection

Glucose metabolism was analysed through lactate production and the expression of glycolitic enzymes

The glycolytic pathway is required for protective immune responses to A. fumigatus *(unpublished data)*

Reprograming caused by the lack of Ptx3?



- PTX3 deficiency compromises the metabolic reprogramming of macrophages
  - Glucose homeostasis of macrophages is impaired upon infection with *A. fumigatus*, as revealed by the decreased levels of **lactate secretion** and **expression of glycolytic enzymes**

Conclusion

We suggest a novel PTX3-regulated mechanism contributing to anti-fungal immunity, namely by regulating adequate immunometabolic responses. PTX3 deficiency compromises the metabolic reprogramming of macrophages. These results may contribute towards the design of innovative therapeutic approaches or metabolic adjuncts to reorient host cells towards immune protection against IPA. Ongoing studies are being performed to dissect how PTX3 coordinates host cell metabolism in response to fungal infection.

References

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