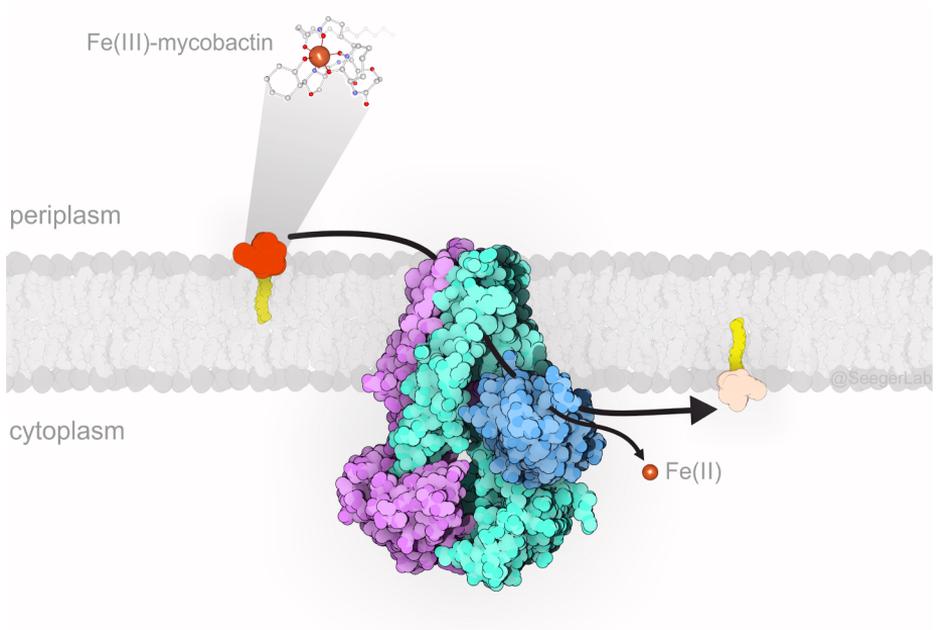# The ABC exporter IrtAB imports and reduces mycobacterial siderophores
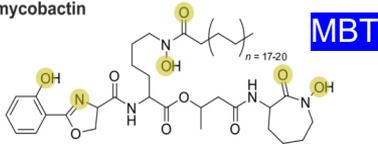
Fabian Arnold, Miriam Weber, Imre Gonda
Tuberkulose Symposium
25. März 2021
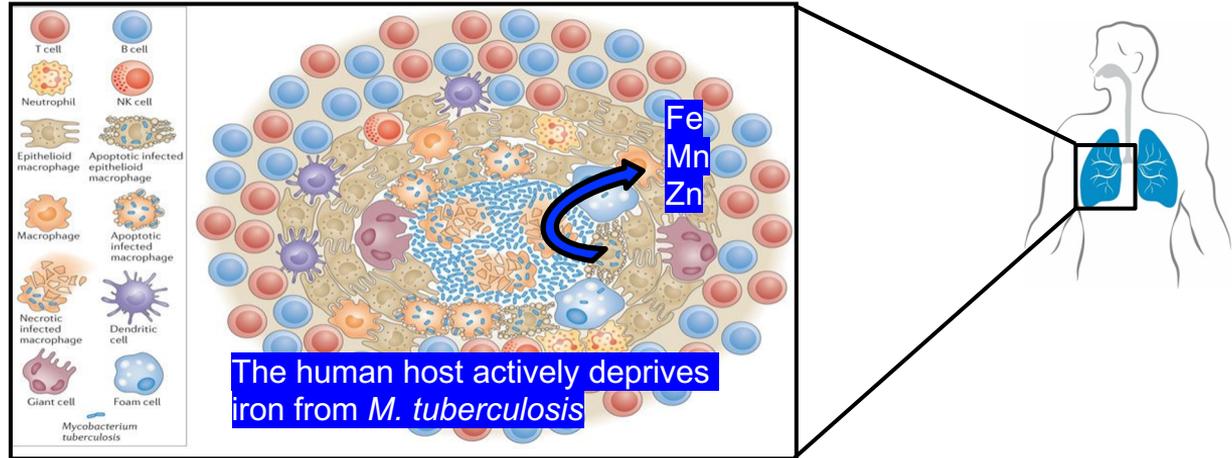
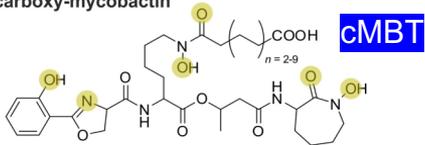# Why does *M. tuberculosis* need siderophores?

Siderophores of *M. tuberculosis:*

mycobactin

MBT

$n = 17-20$

carboxy-mycobactin

cMBT

$n = 2-9$

COOH

Fe
Mn
Zn

The human host actively deprives iron from *M. tuberculosis*

- A 'Nutritional Immunity' is present in the human host against M. tuberculosis: the host deprives the essential element iron from *M. tuberculosis* by trapping it into host proteins
- *M. tuberculosis* synthesizes siderophores to scavenge and 'steal' iron from the host in order to survive
- *M. tuberculosis* strains with impaired siderophore synthesis or transport show drastically decreased virulence, highlighting the importance of siderophores for *M. tuberculosis* infection

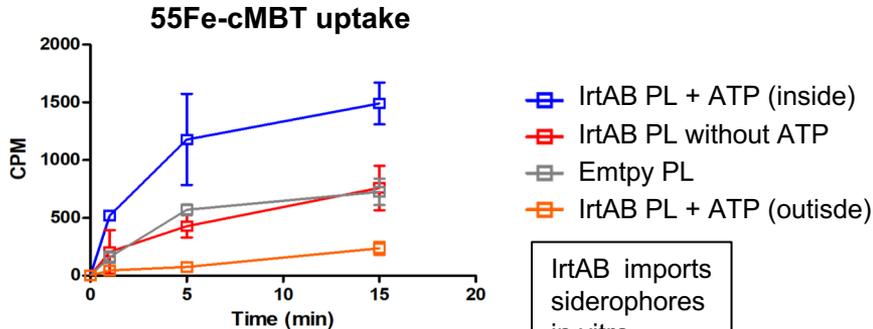# IrtAB is responsible for the uptake of siderophores

In vivo uptake experiments in the model organism *M. smegmatis*
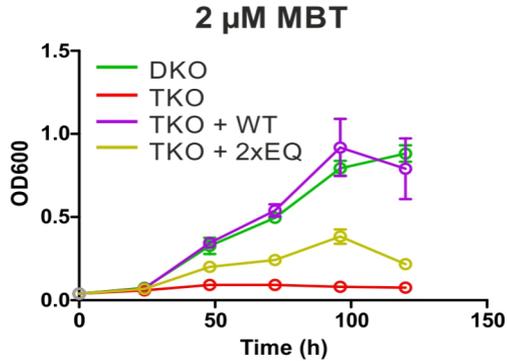
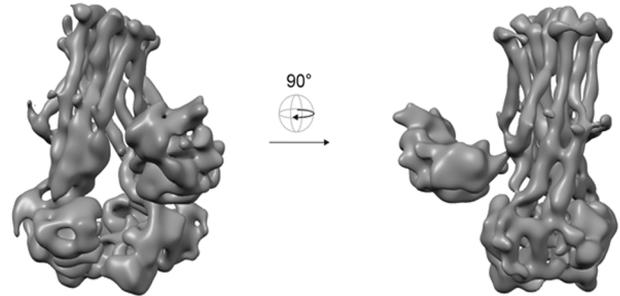IrtAB is essential for the uptake of siderophores in iron-limiting growth conditions

In vitro uptake experiments with purfied IrtAB protein in liposomes

IrtAB imports siderophores in vitro

The molecular structure at atomic resolution of IrtAB was determined y combining X-ray cristallography and Cryo-EM
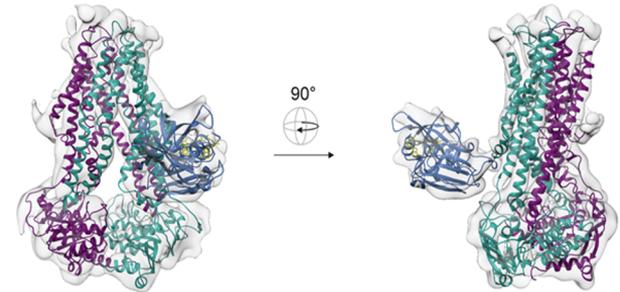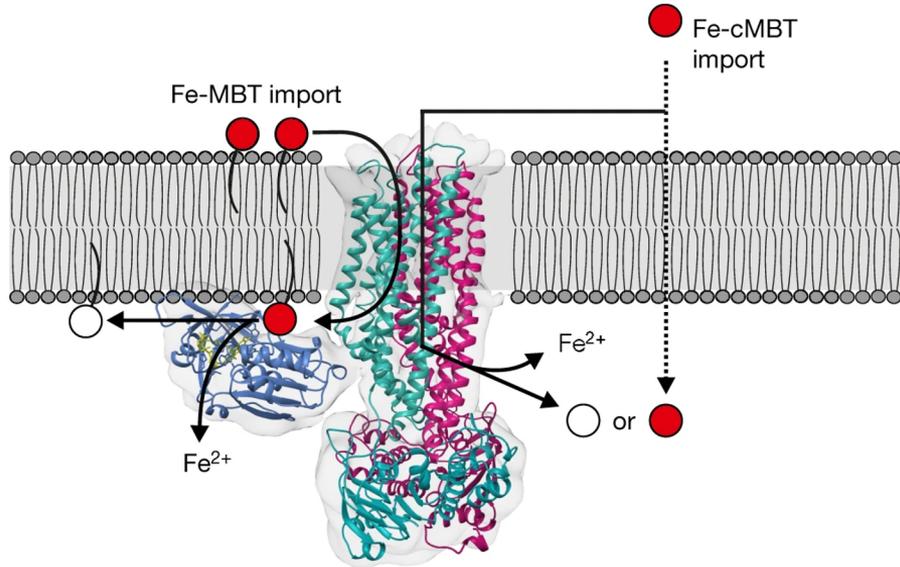
Conclusion and Outlook

- IrtAB plays a **crucial role in the uptake of siderophores** in mycobacteria. Experimental IrtAB-knockout strains are not able to take up siderophores and grow in iron-limiting conditions

- IrtAB is responsible for the **import** of both cMBT and MBT siderophores

- The main role of IrtAB is the import and reduction of MBT, while the uptake of cMBT is seems to be a more «accessory» role

Outlook

→ How does IrtAB **recognize** and **transport** mycobactins?

→ How can we **exploit** IrtAB for antituberculotic **drug development**?

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Article

The ABC exporter IrtAB imports and reduces mycobacterial siderophores

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