

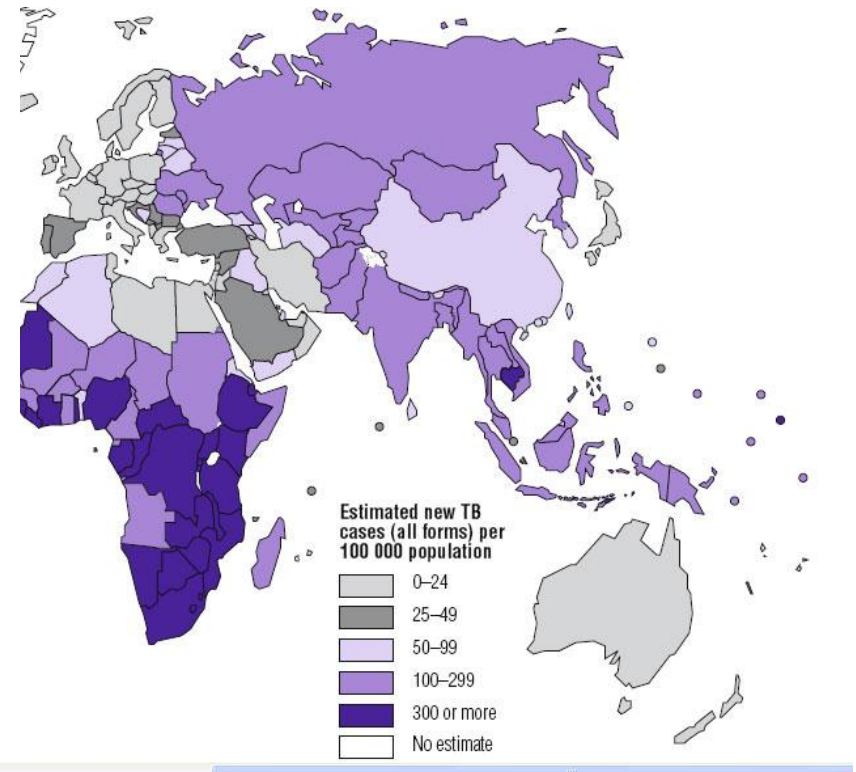
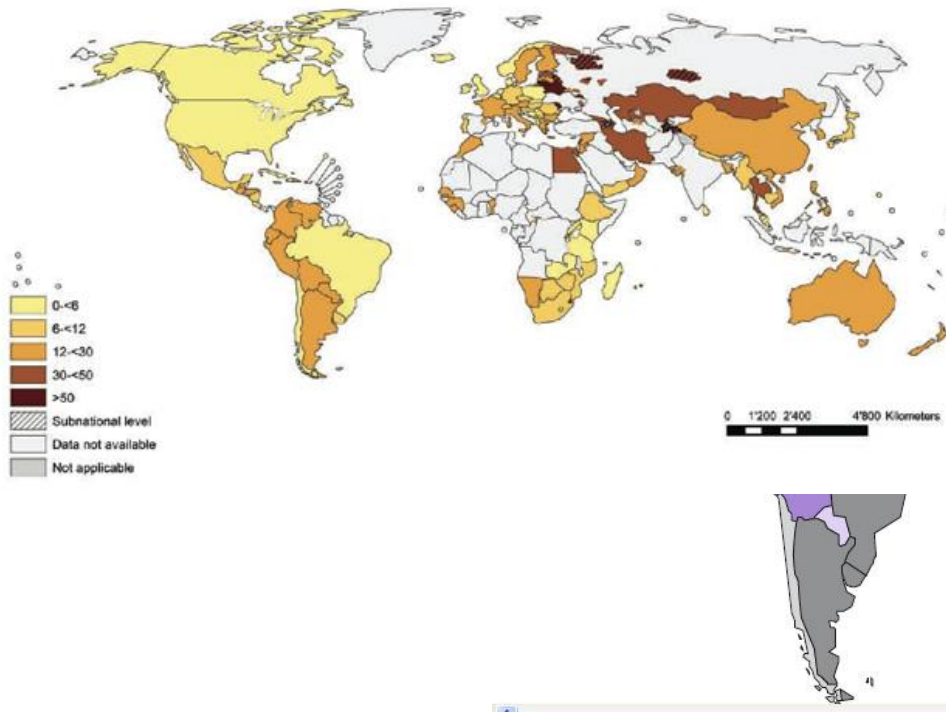
noTBsec

New intervention strategy for tuberculosis: blocking multiple essential targets

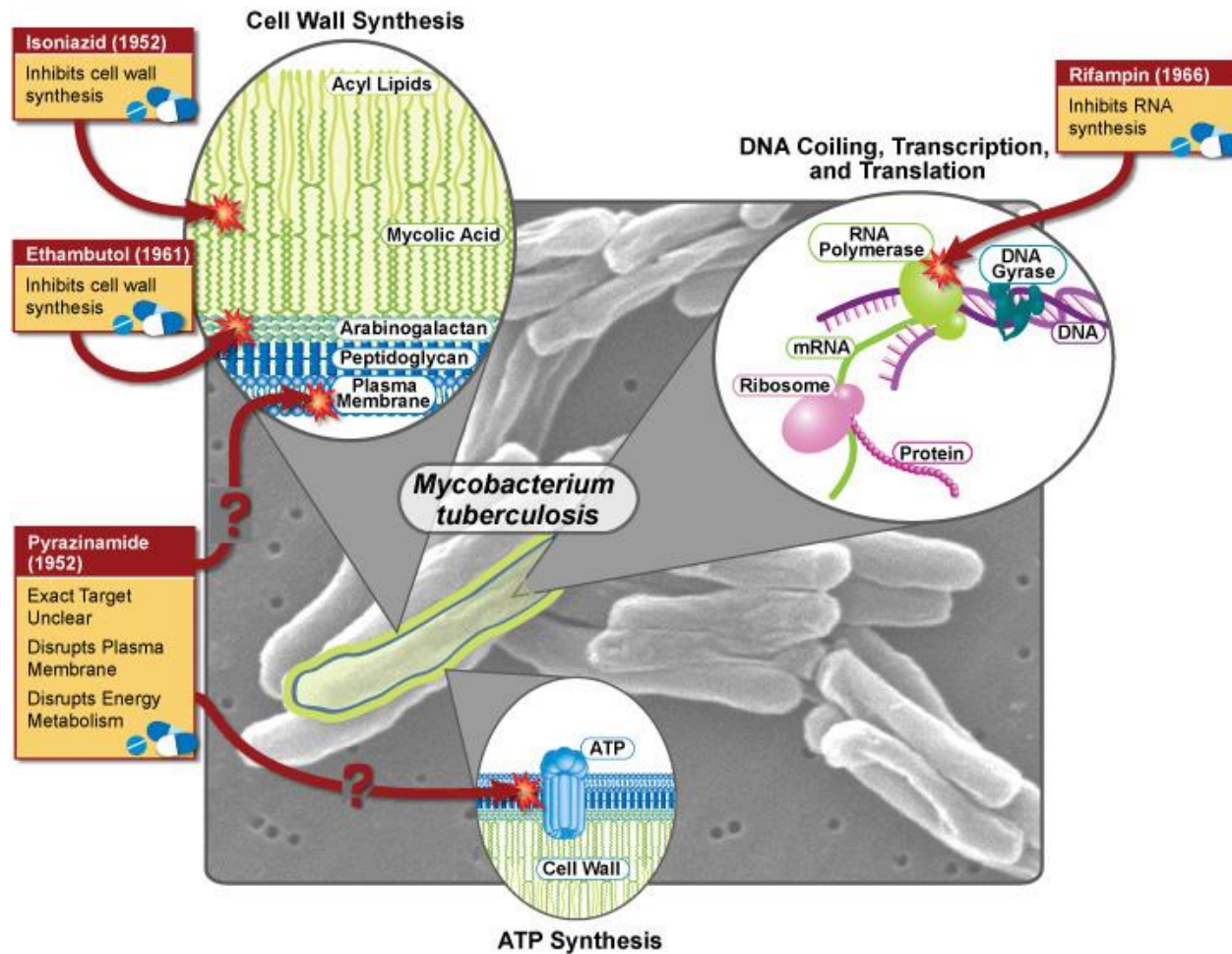
Magnus Steigedal
NTNU - Norwegian University of Science and Technology
Trondheim
Norway

Why focus on tuberculosis?

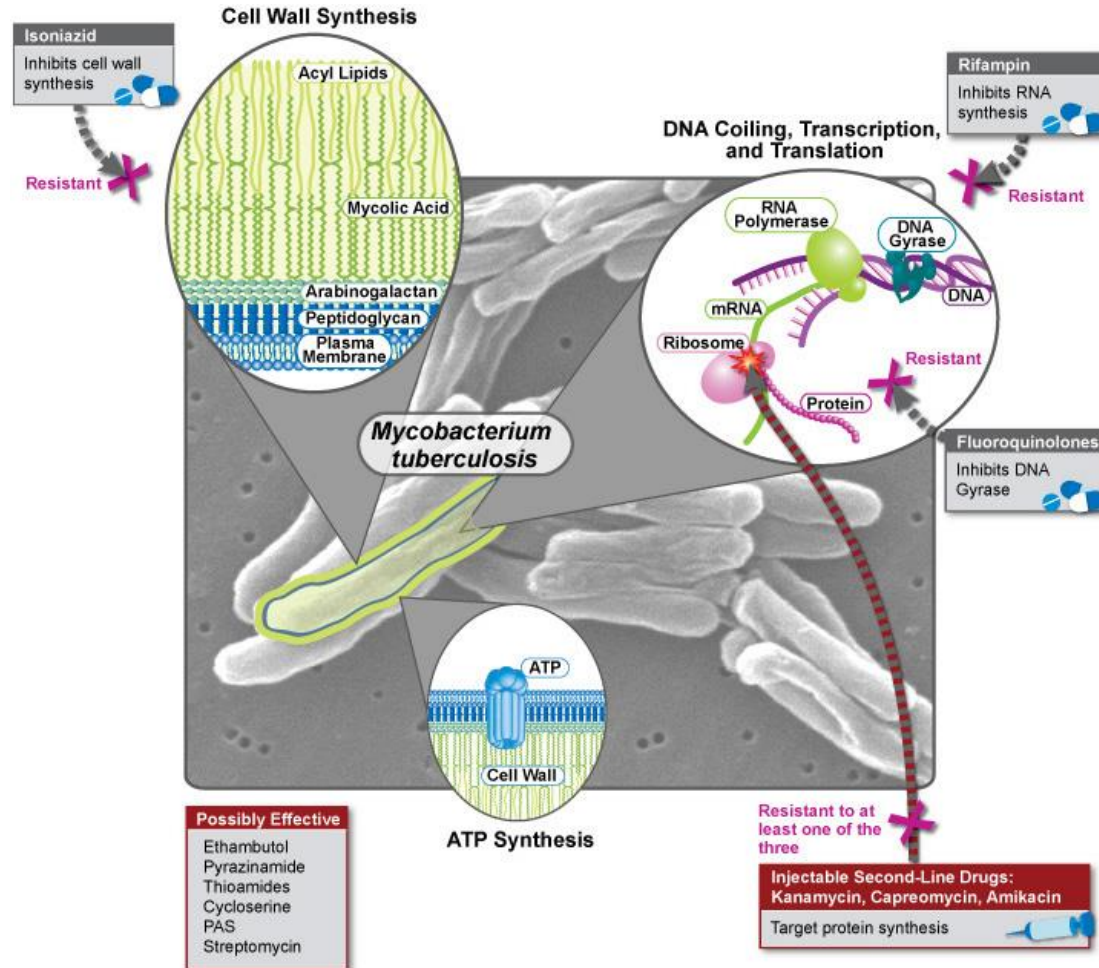
Fig. 3. Percentage of previously treated tuberculosis patients with multidrug-resistant tuberculosis (MDR-TB)



Treatment regime in tuberculosis



Antibiotic resistance in tuberculosis



JPIAMR project: noTBsec

- New intervention strategy for tuberculosis: blocking multiple essential targets

What is our idea?

Identify drugs that target several essential processes in the bacterium

Type VII secretion systems

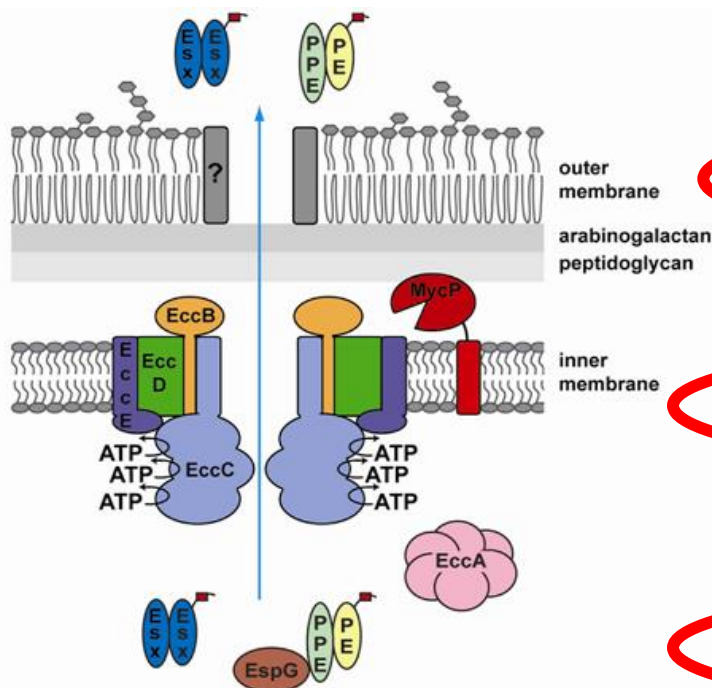
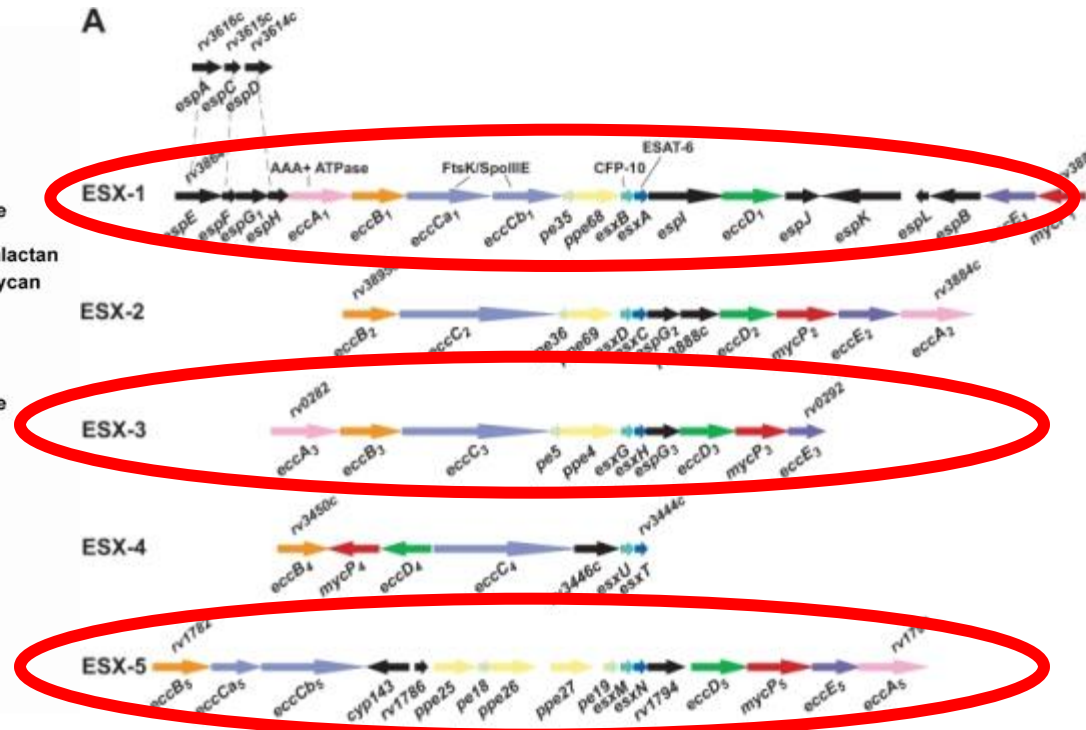
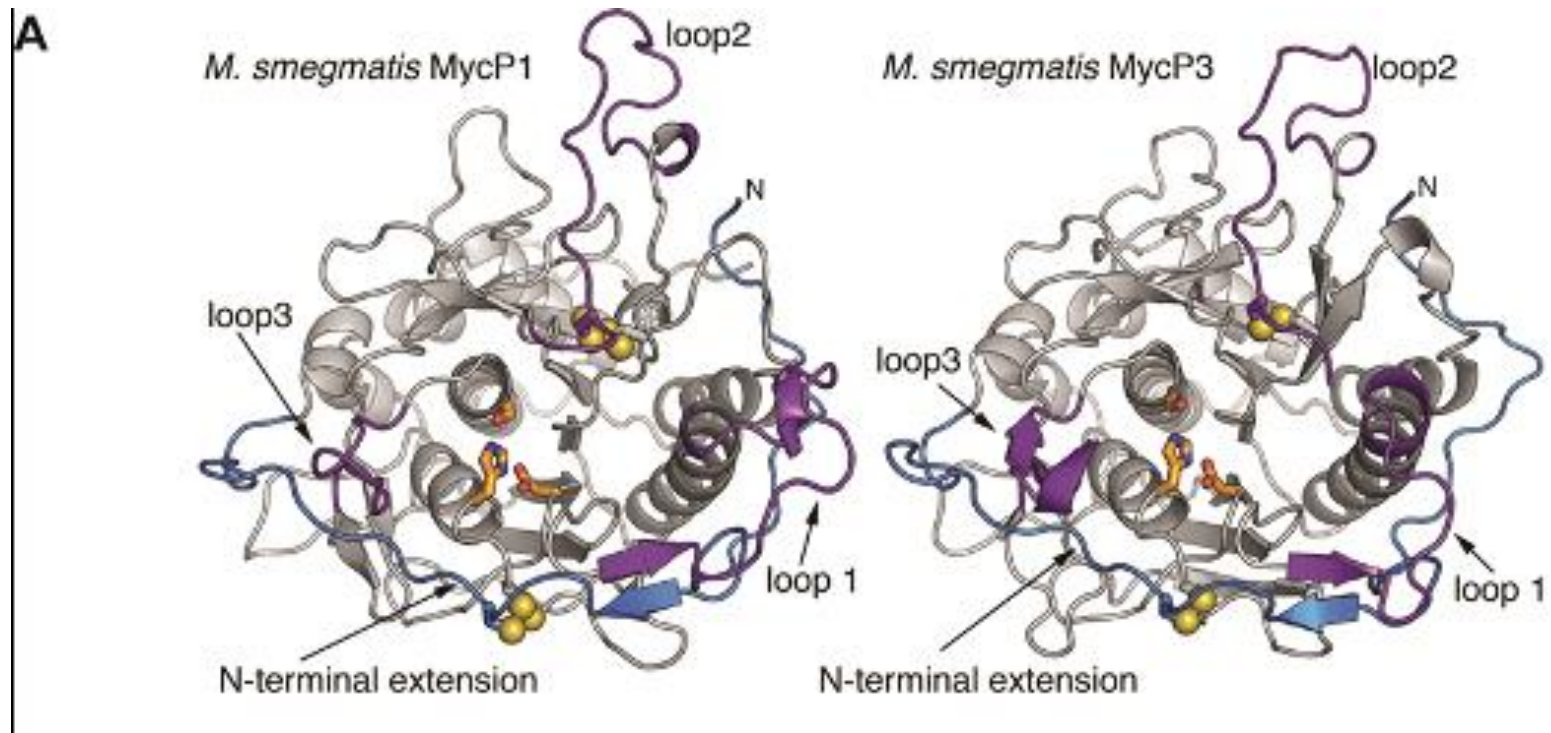


Figure 1. Model for type VII secretion.



Structural similarity between ESX-homologues



Who's part of the project in addition to CEMIR?



VU Medical Center, Amsterdam, Netherlands

Wilbert Bitter and Edith Houben

- Secretion system ESX-5
- Zebrafish model of Tuberculosis
- Compound library



Institute Pasteur, Paris, France

Roland Brosch

- Secretion system ESX-1
- Mouse model of Tuberculosis



University of British Columbia, Vancouver, Canada

Charles Thompson

- Novel antibiotic combinations in mycobacteria
- Library of known antibiotics



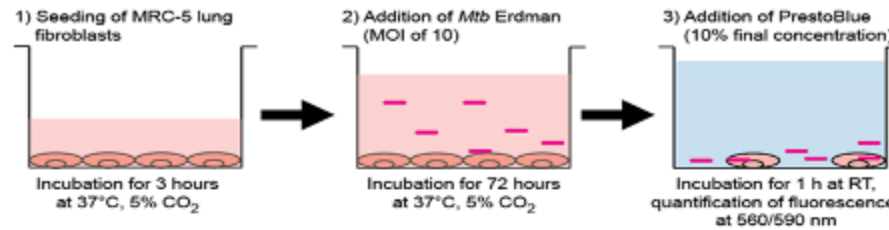
EPFL, Lausanne, Switzerland

Stewart Cole

- Secretion system ESX-1
- Drug discovery screening
- Compound library

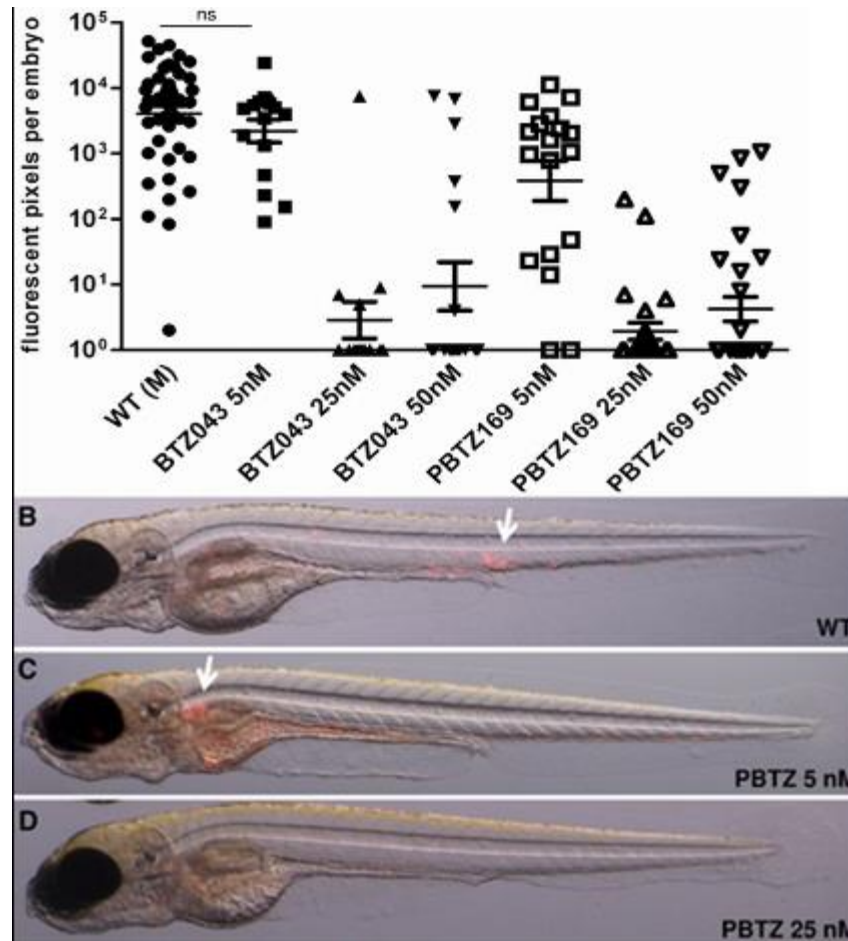
What is our approach?

Example with protein secretion inhibitors



What is our approach?

Validation and combination with known drugs



Summary: What, when and who?

