

Repurposing anti-mycobacterial drugs targeting InhA and Ag85 to combat *Nocardia* infection

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SUMMARY

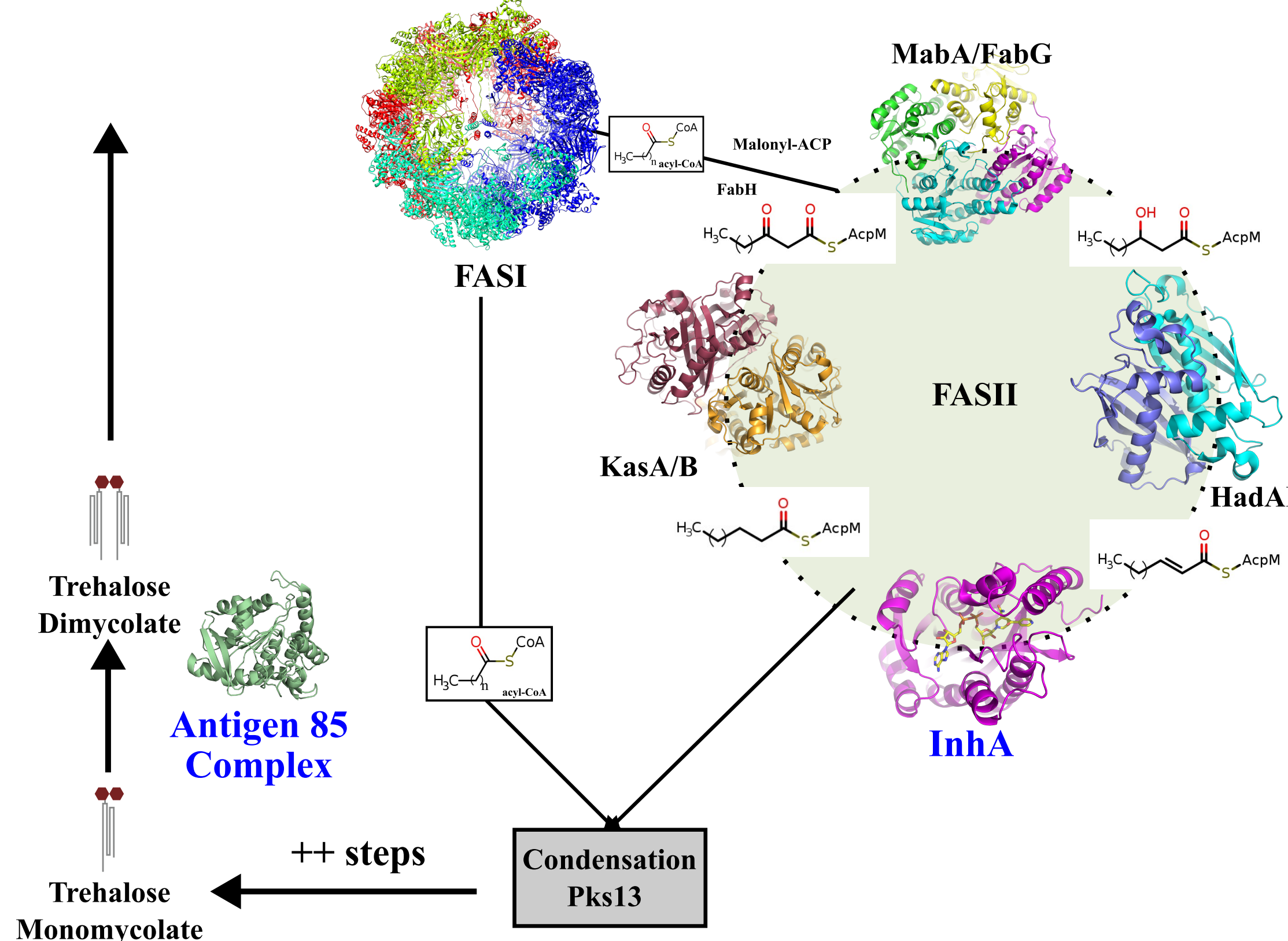
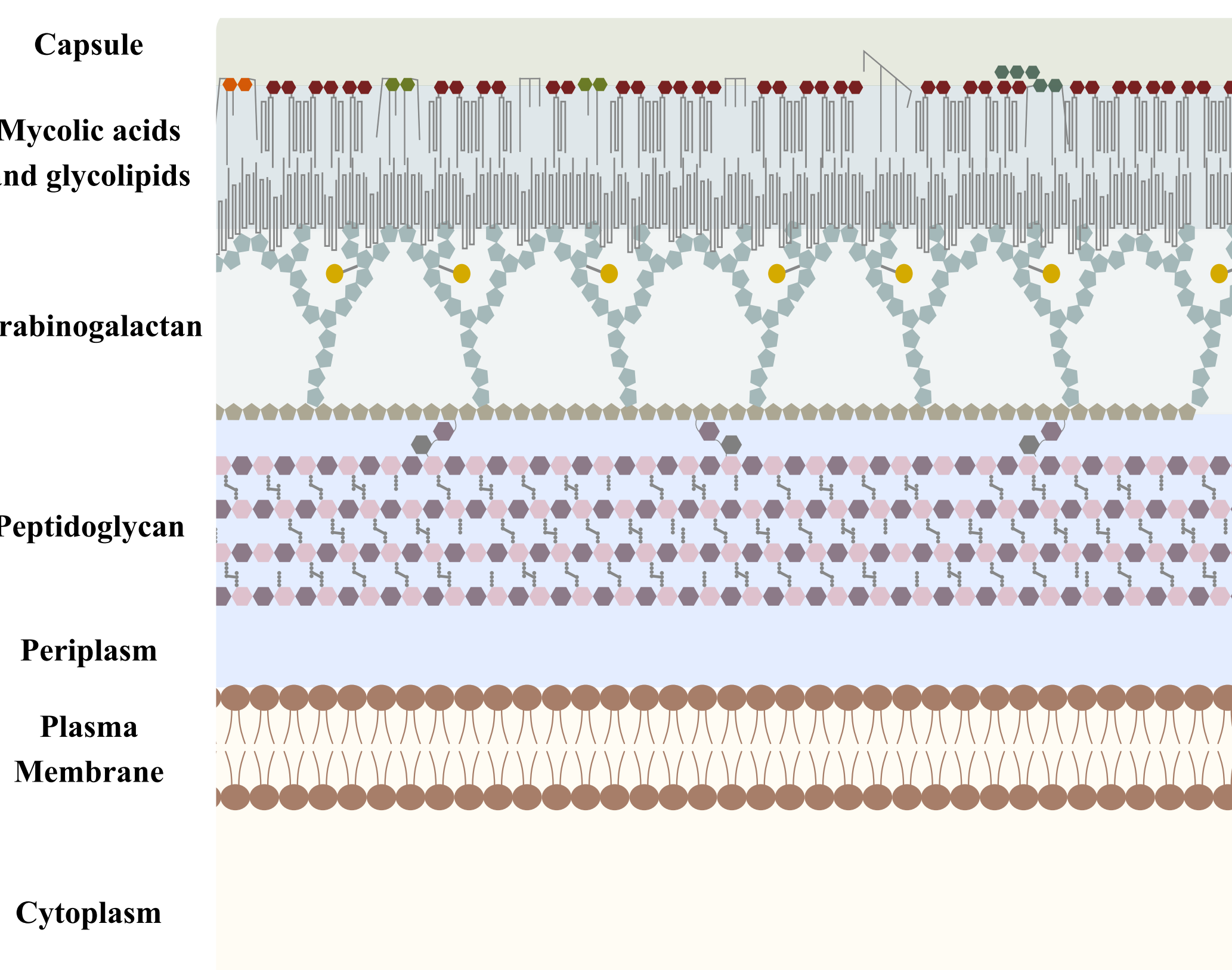
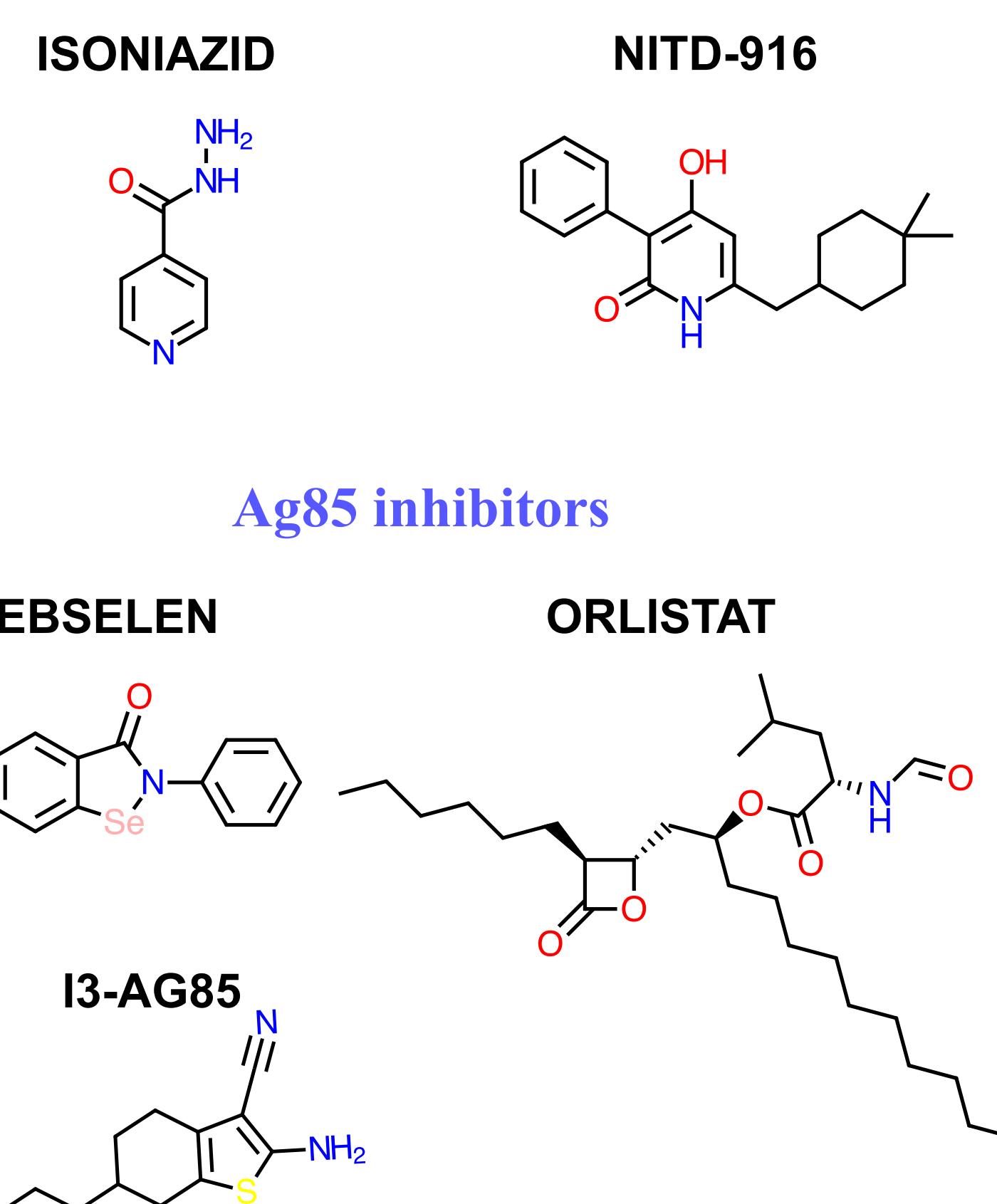
Nocardia species (spp.) are opportunistic intracellular pathogens responsible for pulmonary and disseminated nocardiosis, particularly in immunocompromised patients. Current treatment relies on prolonged multidrug antibiotic regimens that are associated with toxicity, treatment failure, and emerging antimicrobial resistance. The identification of new therapeutic strategies is therefore needed.

Nocardia and mycobacteria belong to the order Actinomycetales and share highly conserved pathways involved in mycolic acid biosynthesis and cell wall assembly. In particular, the enoyl-acyl carrier protein reductase (InhA) and the antigen 85 (Ag85) mycolyltransferase are both essential and are conserved in *Nocardia asteroides*, making them attractive candidates for drug repurposing. We hypothesize that anti-mycobacterial inhibitors targeting these enzymes, including isoniazid and derivatives (InhA pathway) and existing Ag85 inhibitors, will retain activity against *Nocardia* spp., providing a rapid and cost-effective strategy to identify new therapeutic options.

The waxy cell wall of bacteria from the Mycobacteriales order

Mycolic acids synthesis pathway in Mycobacteria

InhA inhibitors

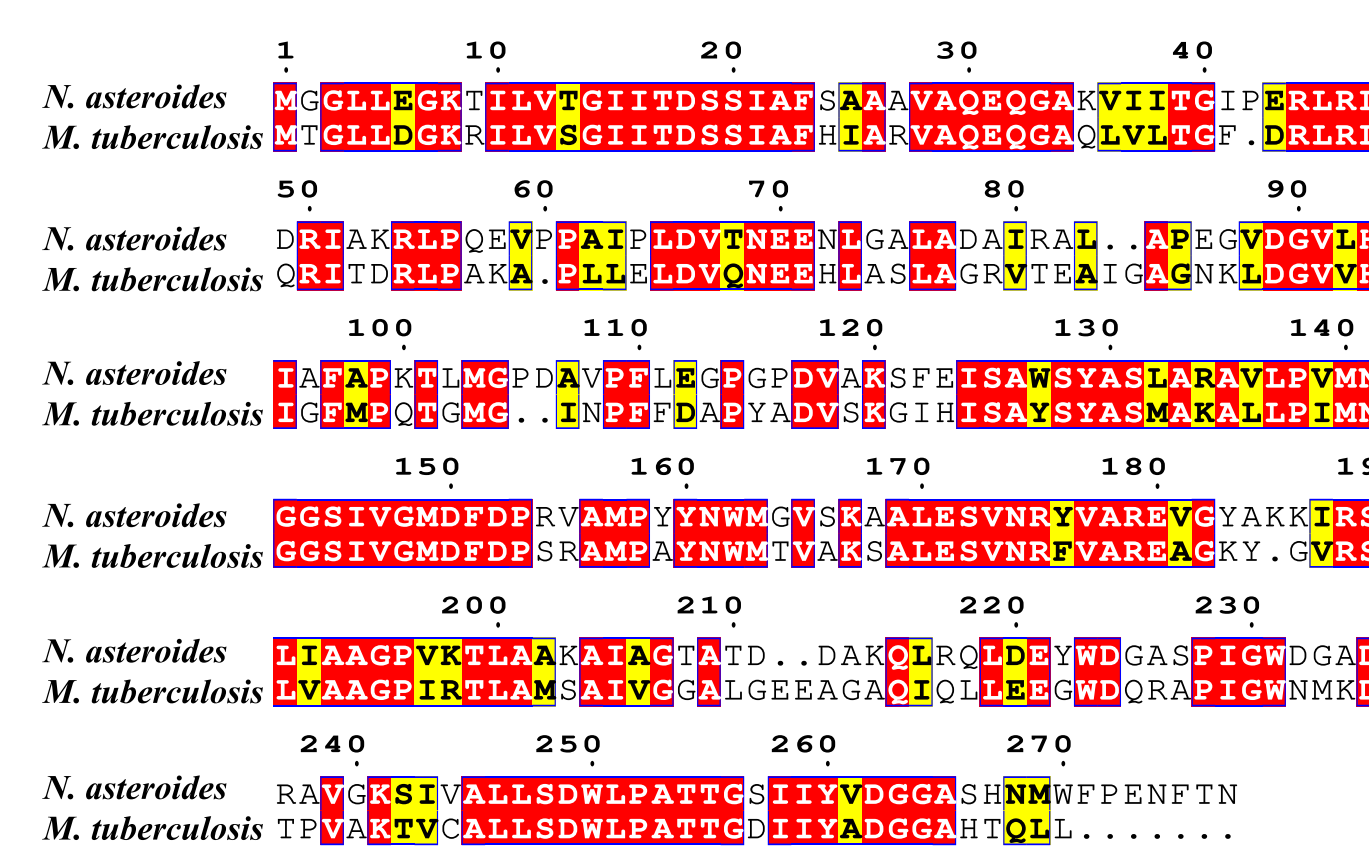


HIGH CONSERVATION BETWEEN NOCARDIA AND MYCOBACTERIA FASII PROTEINS

N. asteroides possesses several homologues of Ag85



N. asteroides and *M. tuberculosis* InhA share high identity



OBJECTIVES

Scientific

- Express, purify and crystallize recombinant Ag85 and InhA from *N. asteroides*
- Determine if *Nocardia* Ag85 and InhA can be inhibited *in vitro*
- Address *Nocardia* spp. susceptibility to these drugs alone or in combination with other antibiotic classes

Educational

- Acquire experimental technical skills in microbiology, molecular biology, biochemistry and structural biology
- Analyze, interpret, and draw valid conclusions from experimental data
- Organize and present research findings through lab notebooks, written and oral reports

TECHNIQUES AND APPROACHES

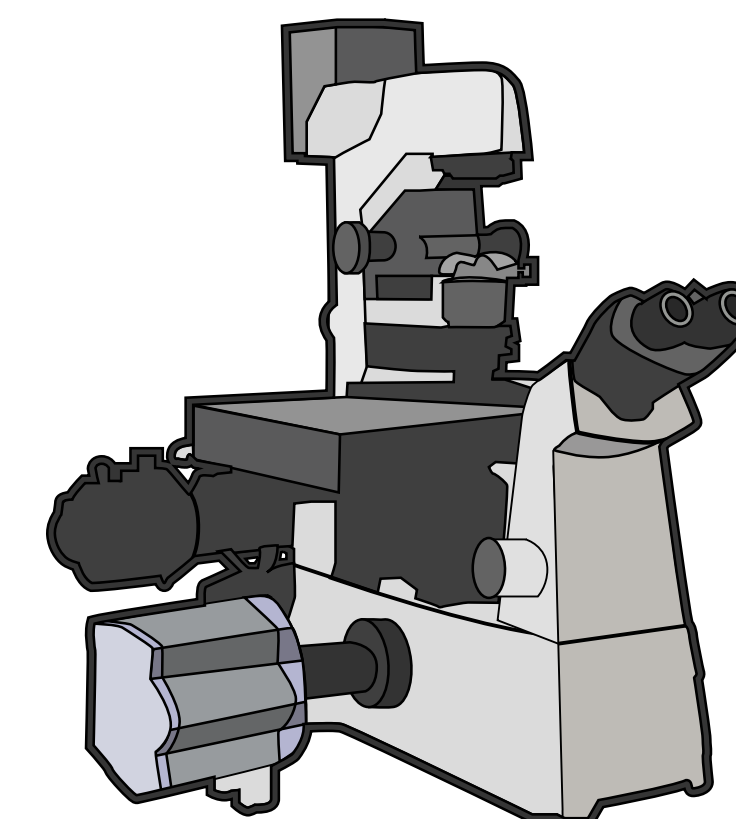
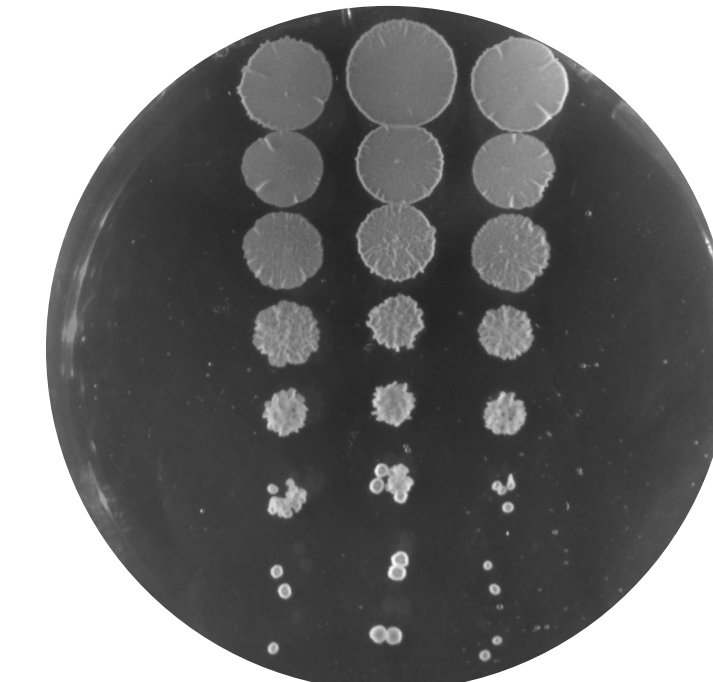
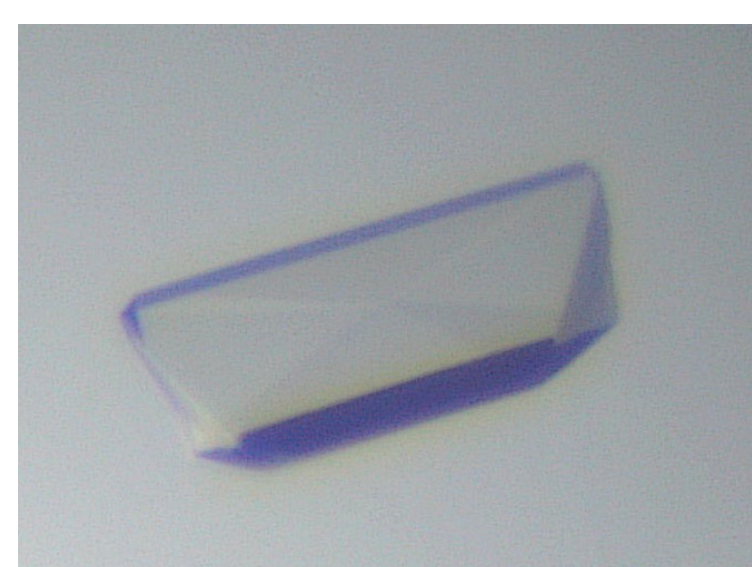
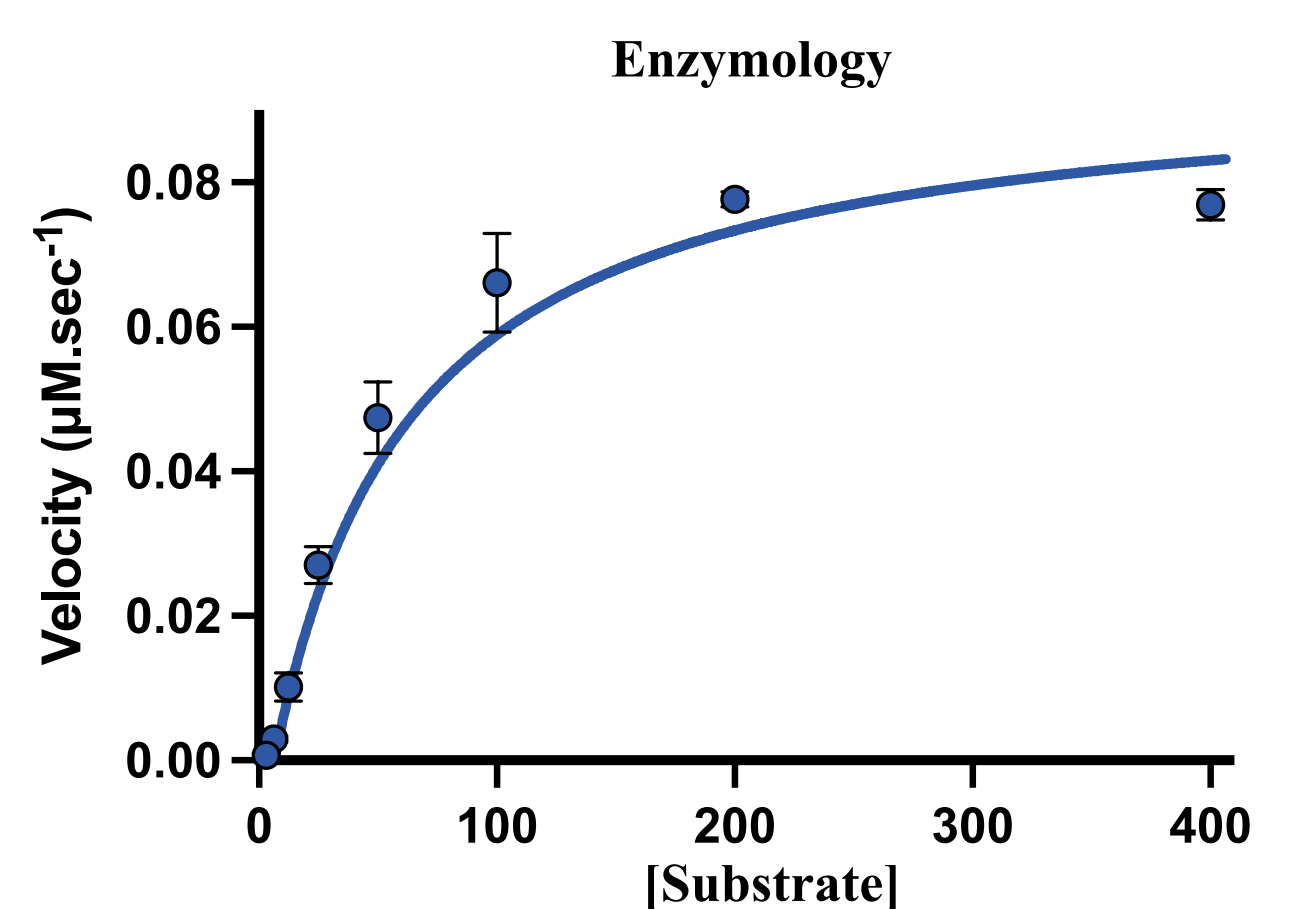
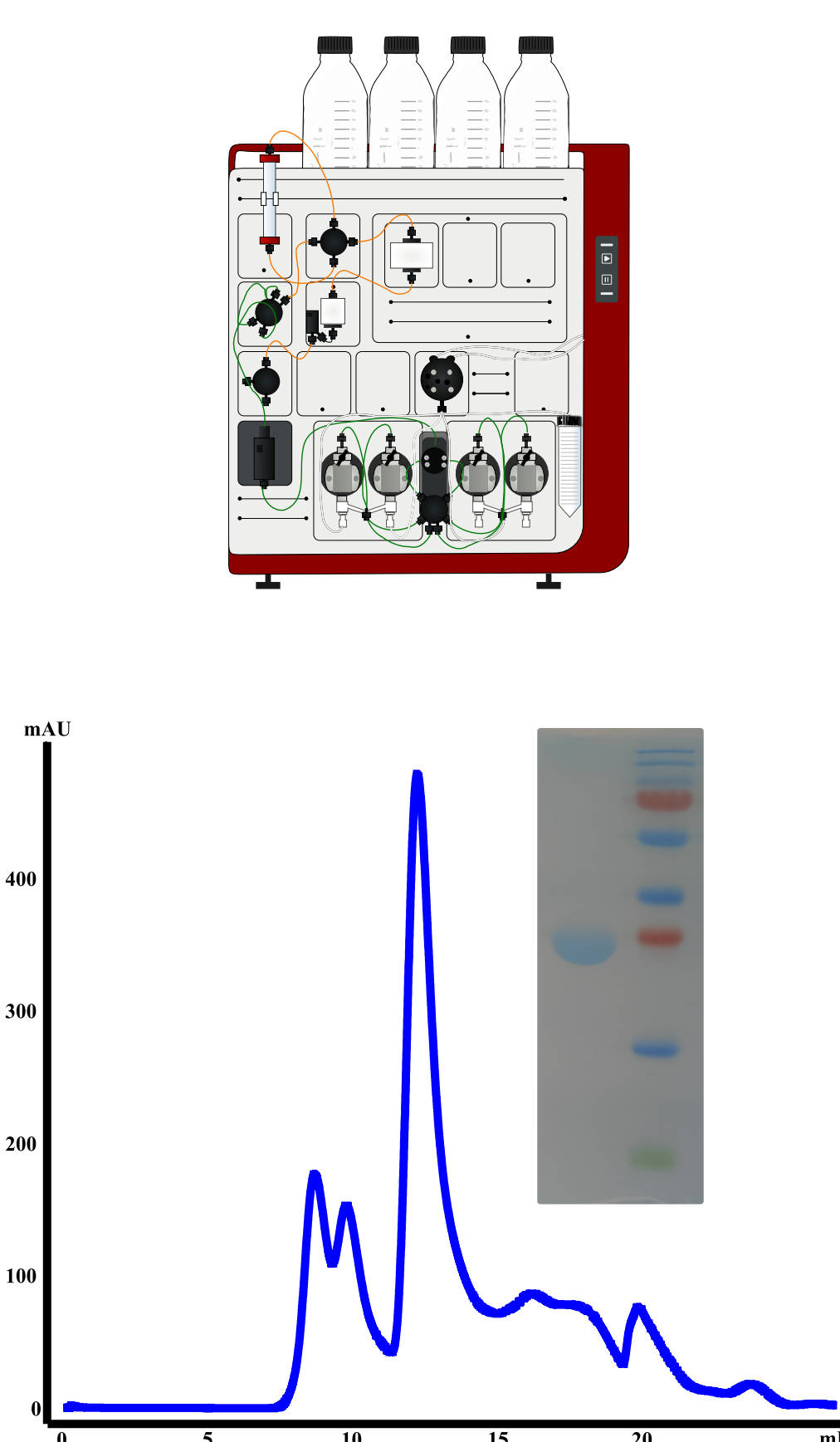
Protein expression and purification

Activity assay

Structural biology

Microbiology

Cell biology and microscopy



Human macrophage infected with *Nocardia*

