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Promotionsverfahren von **Herrn M.Sc. Steffen Schindler**
Auslage der Dissertation und Gutachten sowie Termin der mündlichen Prüfung
Anlage: Einseitige Zusammenfassung der Dissertation

Sehr geehrte Damen und Herren,

in dem oben genannten Promotionsverfahren wird die Annahme der Dissertation

Functional characterization of potential new drug target candidates in Mycobacterium tuberculosis

von den Berichterstattenden Prof. Dr. R. Kalscheuer und Prof. Dr. K.-E. Jaeger beantragt. Sie kann zusammen mit den Gutachten in der Zeit

vom 02.12.2024 bis 11.12.2024

eingesehen werden. Bitte wenden Sie sich zur Einsicht an das Promotionsbüro (promotionmnf@hhu.de).

Einsprüche gegen diese Dissertation können nur zwei Tage nach der vorgenannten Frist geltend gemacht werden. Erfolgt kein Einspruch, so gilt die Dissertation als angenommen (§ 7 Ziffer (5) PO).

Sofern die Dissertation angenommen wird, findet die mündliche Prüfung am

16.12.2024 um 13:00 Uhr

im **Hörsaal 6G** statt. Als Prüferinnen bzw. Prüfer sind vorgesehen:
Juniorprof. Dr. J. Cramer, Juniorprof. Dr. M. Hacker und Prof. Dr. Eva Nowack.

Die Öffentlichkeit ist bei der Befragung nicht zugelassen.

Mit freundlichen Grüßen
im Auftrag

Daniela Schleiffer

3. SUMMARY

Although *M. tuberculosis* was replaced as the deadliest pathogen during the SARS-CoV-2 pandemic, TB remains a global threat. Millions of people are infected and killed by TB each year, and the emergence of antibiotic resistances exacerbates the current situation. Unlike assumed, antibiotic resistance is not limited to high incidence areas, highlighting its importance on a global scale. The drivers for resistance development are diverse as a number of factors ranging from misuse to economics are involved.

During the so-called golden era of antibiotics (1940 - 1960), antibiotic discovery using hit identification-based antimicrobial screening methods was successful. After this period rich in antibiotic discoveries, humanity faces the challenge of not being outcompeted by the evolution of antibiotic resistance, as the outcome is likely to be catastrophic in terms of mortality from multidrug-resistant pathogens by 2050. To counteract this trend, scientists are striving to find and develop new antibiotics and/or innovative methods to combat pathogens.

The aim of this work was to characterize new drug targets in *M. tuberculosis* to enable, for instance, the rational design of antibiotics. Rational design uses information about a target protein to engineer structure-specific molecules that interfere with the protein's function. This target-to-drug approach supports drug development based on screening approaches that analyze the effects of molecules on pathogens. Due to our efforts to generate knowledge about different genes involved in cell wall assembly, we have been able to expand the spectrum of antibiotic target candidates to include Rv3277, Rv2509 and *glgE*.

In addition to analyzing components associated with the cell wall, we also investigated ncRNAs as potential drug targets. Since the world of ncRNAs is a relatively young and underrepresented area in *M. tuberculosis* research, advances could have a great impact on drug development. We functionally characterized the two highly abundant ncRNAs MTS1338 and MTS2823 in *M. tuberculosis* and uncovered crucial regulatory functions, as both ncRNAs have been shown to be involved in the repression of gene expression during transition to and/or in stationary phase. The involvement in the regulation of essential mechanisms such as ribosomal silencing that, for instance, enables latent infections, renders these ncRNAs valuable drug targets.