

## Newsletter May 2022

Update on the projects: For almost three years now both RespiTB and RespiNTM have been steadily working on finding novel assets to battle infections caused by *Mycobacterium tuberculosis* and non-tuberculous mycobacteria.

The RespiTB project has continued their successful collaboration between the different partners to push further the development of novel drug candidates for a more efficient drug regiment against TB. Despite the world-wide corona crisis that has had a profound impact on the work, we have made great strides and reached crucial milestones that place us in a favorable position to move the project forward. Some examples include: 1) multiple cryo-EM structures of cytochrome  $bc_1aa_3$  that enables the study of the binding mode of different inhibitors, 2) first generation inhibitors of the Mycothione reductase, as well as the determination of the first crystal structure of a mycobacterial Mycothione reductase, 3) first studies of combinatorial regiments in Mtb-infected macrophages. Hence, all three avenues of drug development (cytochrome bc & cytochrome bd, mycothione reductase, and host-directed therapies) are progressing well along the drug development pipeline.

RespiNTM is also making considerable progress, although it has taken a different path. In the initial plan of the RespiNTM consortium, several different approaches were laid out to be explored and to select the most promising drug candidate down the line. As part of this exercise, the consortium has decided to stop pursuing the cytochrome bc and bd targets for NTM, which had been initially selected based on promising data in *Mycobacterium tuberculosis*. Newly generated data indicated that the impact of inhibiting these targets in NTM is much less pronounced when compared to *M. tuberculosis*. The removal of the cytochrome bc and bd avenue allows the consortium to focus their efforts on profiling antibacterial candidates that are more suited for NTM.

Unfortunately, due to the COVID-19 pandemic we were not able to meet face to face for our annual general assembly over the past two years. Even though the



online meeting was very successful and great results and insights were shared, we are very pleased to announce that we will meet again this June in real life. The upcoming face to face meeting will find place in Paris, hosted by Sorbonne University. We are really looking forward to it!