

TERMS OF REFERENCE

Biology/Targets Subgroup

Objectives:

The primary purpose of the Biology/Targets subgroup is to exchange and summarize information to improve decision making for target selection and treatment strategies of *Mtb* and to help build a global vision for TB drug development. By promoting the transparency of multiple organizations, the subgroup will provide centralized, relatively open-access website to drive innovation, create opportunities for global synergy, and to facilitate recommendations in a timely manner. This process will be driven by:

- Maintaining an active subgroup that meets regularly by having telephone conference calls and face to face meetings to define specific time-bound goals and action items
 - Facilitate data sharing and information gathering and regularly updating internet pages of target based and cell based drug discovery efforts
 - Updating a member-accessible subgroup calendar for scheduling meetings
 - Generating a master list of *Mtb* targets and/or group projects (i.e. database of all known drug targets, including the status of research activities) and maintaining the succinct master list, including group projects that are no longer active (and why) as well as projects under priority consideration
 - Define parameters for selection of specific targets, propose targets from specific pathways learned from *Mtb* biology, define metrics for drug-ability of targets and prioritize targets that are most likely to shorten therapy, target persistent, latency, as well as MDR/XDR isolates, and work in synergy with drug candidates and existing drugs
- Identifying challenges and unmet needs in new targets and *Mtb* biology
 - Solicit ongoing feedback on specific biological/target that are not being adequately addressed including operational challenges
 - Promote understanding of *Mtb* and human immunologic and metabolic relationships to map out new strategies for *Mtb* drug therapeutics and to seek new ways of optimizing the contribution of the immune system.
 - Identifying resources and opportunities for funding to support progression of *Mtb* targets
- Providing direction and recommendations for the overall WGND strategy and in the global *Mtb* community
 - Define resources available to facilitate target based drug discovery and improving compound penetration of *Mtb* for efficacy
 - Increase visibility and help drive global policy development
 - Provide clear direction and illustrate opportunities by drafting white papers, presentations and review articles to inspire interest and to accelerate drug discovery and assay development for biologically relevant *Mtb* targets predicted to shorten TB therapy

Host Targeting and Immunotherapy Task Force

The purpose for the Host Targeting and Immunotherapy Task Force is to help create a new vision for TB treatment regimens by leveraging host targets and the immune system to shorten TB therapy when combined with existing TB antibiotics. This process will be achieved by:

- Meeting regularly at a scheduled time and place to define specific goals and action items
 - Facilitate data sharing and information gathering and regularly updating a member-accessible subgroup calendar
 - Update the Working Group for New Drugs Website to keep the information current and relevant
 - Coordinate a scientific conference or meeting, if deemed necessary
 - Generate a working list of host targets and therapeutics with defined mechanisms of action and prioritize them according to their strengths and weaknesses
 - Define parameters for selection of specific host targets from specific pathways learned from *Mtb* biology including transcriptional profiling and metabolomic approaches
 - Define realistic parameters for drug-ability and potential synergy with existing drugs and drug candidates
- Identifying challenges and critical issues for host targets in *Mtb* biology
 - Solicit ongoing feedback on specific host target or immuno-therapeutic that is not being adequately addressed including operational challenges
 - Develop a better understanding of host immunologic and metabolic relationships to map out new strategies for *Mtb* drug therapeutics and to seek new ways of optimizing the contribution of the immune system.
 - Identifying resources and opportunities for funding to support preclinical and clinical advancement of host targeted and immunotherapeutic candidates
- Help structure the overall WGND strategy
 - Define resources available to facilitate host target based drug discovery, hit follow up and lead optimization
 - Increase visibility, make recommendations and help shape TB drug development policy

Provide clear direction and illustrate opportunities by drafting white papers, presentations and review articles to inspire interest and to accelerate drug discovery as it relates to host targets and immuno-therapeutics. The task force will be evaluated after one year.