USTTB-UCRC-MALI

Antituberculosis Therapy and Gut Microbiota: Review of Potential Host Microbiota Directed-Therapies

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Background

Tuberculosis (TB) remains a major public health concern with millions of deaths every year. HIV co-infections, long treatment duration, and the emergence of drug resistance are significant obstacles to the TB control. Indeed, the standard TB first-line treatment takes at least six months and even longer for the second-line. Many reports have proven prolonged and significant damage (dysbiosis) of the gut microbial community from anti TB drugs that can detrimentally persist several months after the cessation of treatment. Host microbiota-directed therapy (HMDT) is a new proposed strategy for shortening treatment duration, correct damage occurred during anti-TB therapy.

Goals

This review aimed to study the role of the gut microbiota in both TB infection and treatment, and its potential link with treatment duration. Will be also discussed, the new concept of Host Microbiota Directed-Therapies (HMDT) as a potential adjunctive strategy.

Strategies

Pubmed and google Scholar were used as library to search ‘’Tuberculosis treatment”, “gut microbiota”, and “Host Directed-Therapies, dysbiosis”. References found were then reviewed.

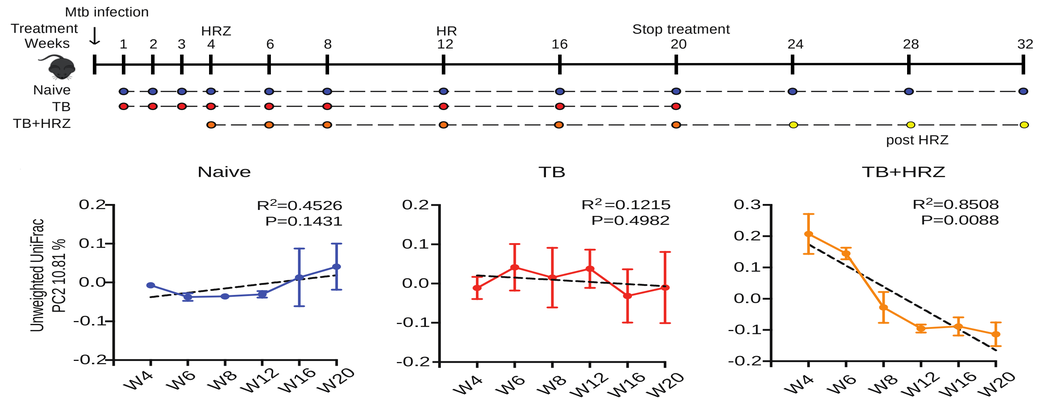

Figure 1: TB first-line drugs, in mouse model induce a distinct and long lasting dysbiosis.[1]

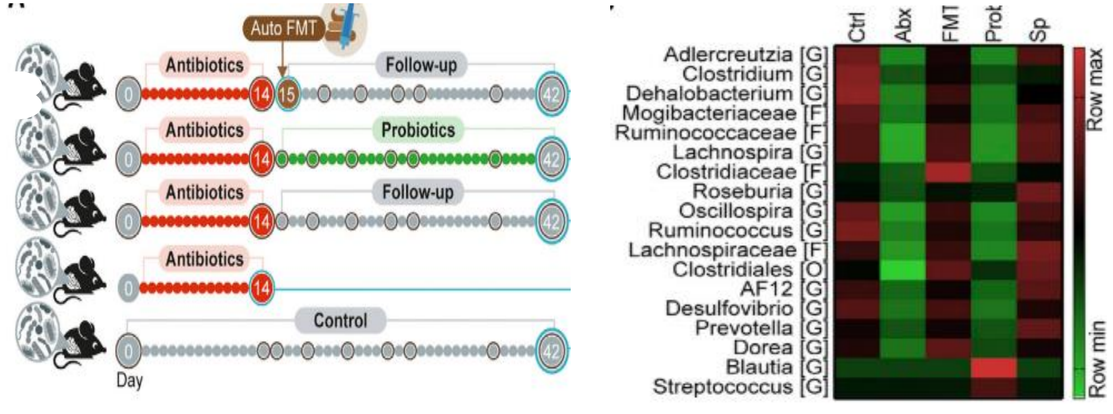

Figure 2: Taxa reconstitution after antibiotics treatment with aFMT[2]

Ctrl: uninfected mice; **Abx**: Post antibiotics sacrified mice; **FMT**: Fecal microbiota transplantation; **Prob**: Mice under probiotics; **Sp**: Spontaneous recovery

Findings

- Anti-TB drugs cause profound dysbiosis to host gut microbiota (Fig 1). The genera Acetivibrio, Robinsoniella, Alkaliphilus, Stomatobaculum, Butyricicoccus, Acetanaerobacterium, Tyzzerella, Ruminococcus, and Peptococcus were significantly lost.

- Oral administration of autologous stool microbiota enhances rapid reconstitution of gut microbiome following antibiotics therapy compared to probiotics or spontaneous groups.

Conclusions/Perspectives

Application of this innovative solution could lead to HMDT as an adjunctive tool to shorten TB treatment, which will have enormous public health impacts for the End TB Strategy worldwide. Studies showed several metabolic pathways interrupted during TB treatment, more investigations are needed for choosing the best to allow as TB therapy.

References

1. Namasivayam S, Sher A, Glickman MS, Wipperman MF. The microbiome and tuberculosis: Early evidence for cross talk. *MBio*. 2018;9(5). doi:10.1128/mBio.01420-18
2. Suez J, Zmora N, Zilberman-Schapira G, et al. Post-Antibiotic Gut Mucosal Microbiome Reconstitution Is Impaired by Probiotics and Improved by Autologous FMT. *Cell*. 2018;174(6):1406-1423.e16. doi:10.1016/j.cell.2018.08.047

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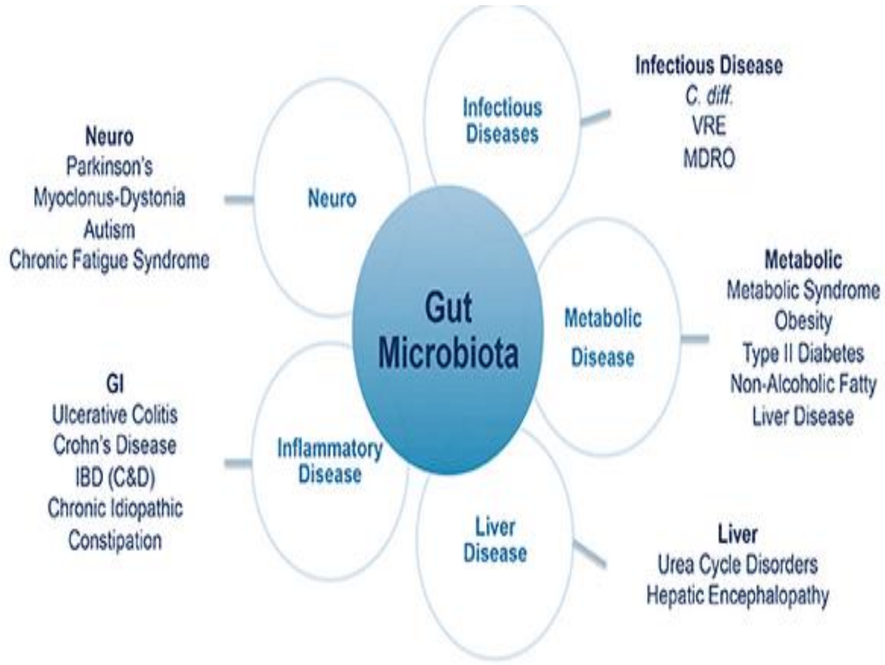
Background

- Tuberculosis (TB) remains a major public health concern with millions of deaths every year.
- HIV co-infections, long treatment duration, and the emergence of drug resistance are significant obstacles to the TB control.
- Standard TB first-line treatment takes at least six months and even longer for the second-line.
- These antibiotics cause profound and persistent dysbiosis of the gut microbial community.
- Targeting this microbiota may be essential for faster bacterial clearance and a better treatment outcome.



https://www.rebiotix.com/our-therapy/microbiota-restoration-therapy/

We aimed in this review to study the role of the gut microbiota in both TB infection and treatment, and its potential link with treatment duration. Will be also discussed, the new concept of Host Microbiota Directed-Therapies (HMDT) as a potential adjunctive strategy.

Strategies

- Pubmed and google Scholar were used as libraries.
- Tuberculosis, gut microbiota, Treatment and Host Directed-Therapies, dysbiosis were used as keywords.
- Collected references have been then reviewed.

Findings

- Three mice groups (Naïve, TB infected and mice treated with HRZ) were included. Anti-TB drugs cause profound dysbiosis to host gut microbiota (Figure 1). The genera Acetivibrio, Robinsoniella, Alkaliphilus, Stomatobaculum, Butyricicoccus, Acetanaerobacterium, Tyzzerella, Ruminococcus, and Peptococcus were significantly lost, all of which belonging to the class Clostridia of the phylum Firmicutes.

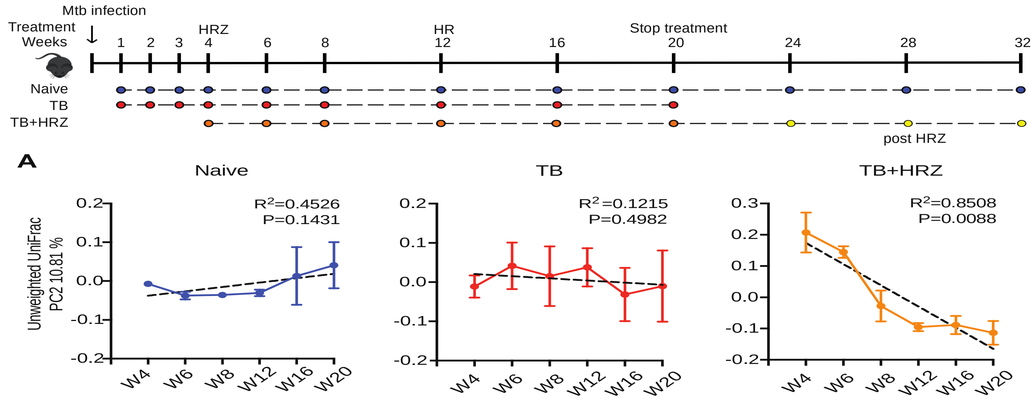


Figure 1: TB first-line drugs, in mouse model induce a distinct and long lasting dysbiosis.[1]

- Two weeks antibiotics therapy mice were followed up and divided by 4 groups (auto pre-therapy fecal microbiome transplant, commercial probiotics, spontaneous recovery). Mice receiving aFMT showed quick recovery of gut microbial population.

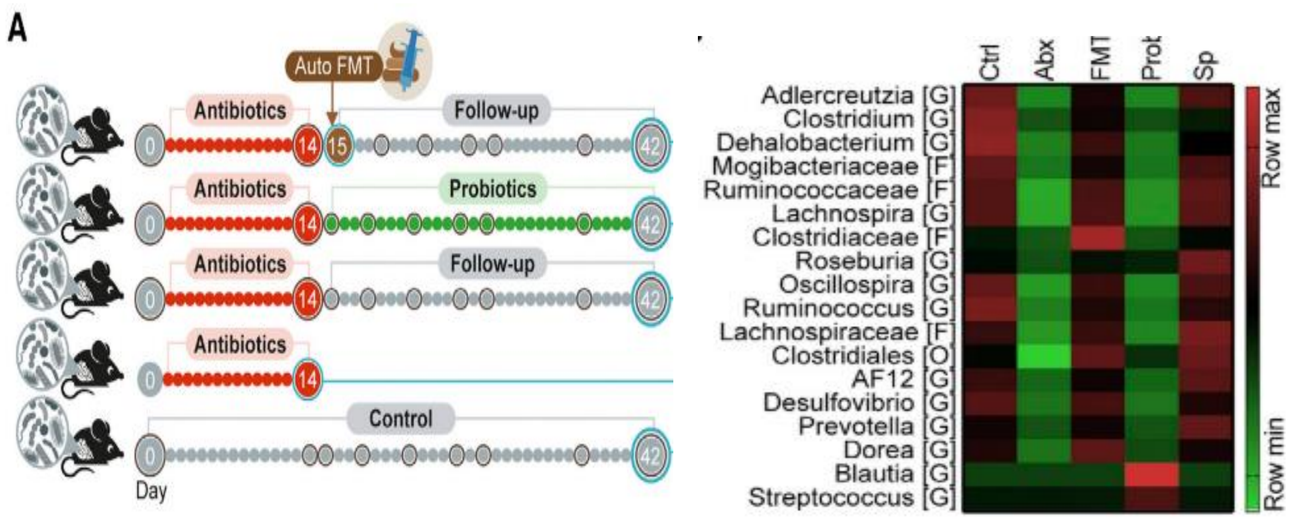


Figure 2: Taxa reconstitution after antibiotics treatment with aFMT[2]

Conclusion and Perspectives

- This review come as a proof of gut microbiota dysbiosis and HMDT feasibility in the management of TB.
- Application of this innovative solution could lead to HMDT as an adjunctive tool to shorten TB treatment, which will have enormous public health impacts for the End TB Strategy worldwide.
- Studies showed several metabolic pathways interrupted during TB treatment, more investigations are needed for choosing the best to allow as TB therapy.