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## Accepted Manuscript

Are non-communicable diseases chronically communicable: a role for the human microbiota?

Ali Abbasi

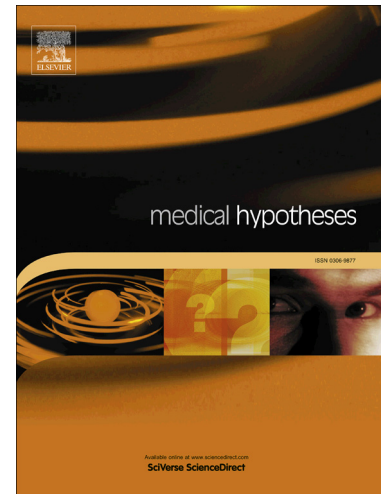
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**Are non-communicable diseases chronically communicable: a role for the human microbiota?**

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There is increasing amount of information about the role of gut microbiome composition in communicable –or infectious diseases– and antibiotic resistance, but also how the human microbiota can be involved in chronic non-communicable diseases (NCDs) like diabetes and diabetes-related endophenotypes.(1) While much interest has recently been awakened that perturbations in gut microbiota are associated with the burden of antibiotic resistance(2), recent efforts investigating the potential causal effects or predictive value of information on the composition of microbiota, or their metabolites (e.g., Trimethylamine N-oxide (TMAO) in the circulation) or their functions (like changes in the gut-blood barrier (GBB) permeability) will open new avenues of research.(3-5)

Recently, experimental studies demonstrated how administration of *Akkermansia muciniphila*, one of the most abundant members of the human gut microbiota, to mice can prevent the development of obesity and associated complications.(3) In other words, pasteurization of *A. muciniphila* enhances its capacity to reduce insulin resistance and dyslipidemia in mice.(3) These findings were in line with previous evidence that microbiota transfer from adult male to female mice yielded in protection against diabetes development.(6) Moreover, there is evidence in human adults how taking metformin can influence the several microbial populations such as an increase in *A.muciniphila*.(7) As such evidence in human studies provides valuable insights into our understanding of metabolic disorders, it is time to re-think about the underlying host gene-environment and host-microbiome interactions to explore missing players and predictors for the prevention and treatment of non-communicable diseases.

So far, epidemiological observations or clinical trials have been mainly focused on genes, endophenotypes and the host gene- environment interactions.(8) Research studies in humans show that the host-microbiome communication is essential to maintain vital functions

of the healthy human over the life course.(1, 8) Therefore, the effect estimates (for human genes, biomarkers or interventions) obtained in the classical settings can be modified if one could take into account the transmission of human microbiota between people within a certain population.(1, 9, 10) Given the fact that microbiome traits are considered heritable and the trait associations tend to be small(8), complementary evidence from an integrative analysis of how the host gene-environment interaction can influence diversity and structure of the human microbiome and vice versa may find right matched pieces of the puzzle in these diseases.

Another aspect of research for microbiome-disease associations is to investigate whether additional information on the composition and structure of the human microbiota is of value to improve the risk prediction for NCDs. In this context, the performance of prediction models including classical risk factors and the utility of microbiome traits needs to be formally quantified using prognostic metrics and clinical reclassification. (11, 12). Few out of several studies on microbiota metabolites or functions have conducted a formal quantification to support predictive utility of these phenotypes for NCDs.(4, 5)

So, future lines of research need to focus on two hypotheses; human microbiota or a panel of microbiota-related phenotypes would improve risk prediction or be causally associated with NCDs. Such complementary strands of evidence may demonstrate if information about human microbiota can serve as prognostic markers for predicting clinical health outcomes and behavior; or as novel targets for new therapeutic and prevention strategies in clinical or public health practice.

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The author has no competing interests.

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