## **KEY POINTS/BENCHMARKS**

## F. LINKING PROBIOTIS AND THE HOLOGENOMIC THEORY OF CO EVOLUTION

- Improving a) General Health OR b) targeted diseases by making an informational change at the cellular and/ or molecular level with activity enhanced by a Prebiotic, together, SYNBIOTIC, providing co-active libraries of genomic information (macrobe and microbe), collectively the hologenome.
- Microbiont's derive their lineage from co evolution (Hologenomic Theory of Co Evolution ) together of procaryotes and eucaryotes, recognizing evolving "Dual Citizenship" and symbiosis (SYNBIOTA) and the importance of the microbiota acting as an unstructured organ system with individual members assigned specific duties analogous to individual tissue/organs, addressing potential use of Mini (Oral/Skin ) or Maxi (Enteral) "transplants."
- Recasts the individual macro holobiont as subject to evolutionally genetic forces brought about by changes in the microbiome, including acquisitions of new microbes (Natural or drived, Probiotic), horizontal gene transfer (HGT), and/or changes in abundance (Ratio) within the macrobe (host), and transferable to offspring.
- Recognize the importance of "Missing Microbes ", a declining information library (microgenome) over time (M Blaser), often focused in targeted metabolic diseases (chronic) in our Microbioal Clock and the potential of Replacement Therapy or Restorative Microbiology (probiotics), recognizing "loss of microbial diversity", (particularly low frequency background isolates) may directly contribute to pathogen selection and persistence (VAP).
- Emphasize the importance of recognizing "who we are" as a individuals (macrobe and microbe holobiont's)(S Mukherjee) and the CENTRISTS feature of the latter as Partners in Life, short and long, health and disease, possibly aging, acting as a "declining biomedical network" or intergenomic association, potentially amenable to probotics.