Microbial Clock, Aging and Probiotics (Beneficial Microbes) 

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INTRODUCTION: 
We previously (2015) recognized the theme of ‘Dual Citizenship’ (Prokaryotes and Eukaryotes) in humans (Hologenomic Theory) (REF 1) (Fig. 1), while introducing the concept of our Microbial Clock (Fig. 2) linking ten diseases in a common pathway in 4 Quad Hs (color coded). Followed (2015) by our Oral Phylotype Signature as unique markers of dementia and aging (Fig. 3), uncovering potential targets of ‘Restorative Microbiology’ and shared genetic information (Probiotics/Beneficial Microbes).

OBJECTIVE: 
As a completion of our Trilogy, we wanted to expand our Searchable Decision Tree Probiotic Database, Patents-4U (www.globalbugs.com) (REF 2), as a research adjunct in interventional studies for age and age-related co-morbidities, recognizing the NIH has recently proposed that aging is a disease (REF 2)

RELEVANCE: 
Age related cognition impairment is a global health problem; in US Alzheimer’s Disease (AD) affects 5.5 million patients at an annual $1.5 trillion dollars, not including catastrophic family efforts estimated at $296 billion, yearly. AD is 6th leading cause of death in US, highlighting 1 in 3 deaths for seniors over 65 years. Reversing local microbial driven inflammatory aging functions via age matched probiotics, optimized by a searchable database linked, ultimately, to Artificial Intelligence (AI), could unmask, evolve, co-evolve research strategies and benefits of Restorative Microbiology (Intelligent Symbiosis), inexpensively compared to palliative care.

METHODS: 
In 2013, we introduced the website Bas-2-Health, (www.globalbugs.com) highlighting microbiology educational tools, particularly the data from 310 manuscripts on probiotics focusing on 11 diseases/conditions, (Fig. 4) organized into a 2 layered decision tree, (Fig. 5) with each graded a to d) 20% and b) strength of research, searchable by 3) user. Here we expanded the data sets to include review of an additional 67 manuscripts addressing aging and probiotics, 35 selected, highlighting the growing awareness of a declining microbiota with age and the unrecognized functions of the human mycoclast/myobiome (fungi).

RESULTS: 
Reviewed manuscripts focused on the Red Zone (>55 YO) of our Microbial Clock, unmasking the importance of 4 missing bacterial phylotypes, (Fig. 6) and the unrecognized, significant contribution of fungal phylotypes with aging and the use of probiotics. Most articles were international in nature, focusing on Alzheimer’s Disease (AD) and were arbitrarily divided into 1) the Microbiome of Aging (TABLE 1) and 2) Probiotics in Aging (TABLE 2). Changes were most evident in the gut microbiota. We constructed a ‘Phylo Signature’ (Fig. 7) integrating a unique five circle Microbial Construct (AllMICRO), each circle matching age, disease and the phylotypes present, missing and fungal. A sixth circle matched the probiotic by disease and age, describing composition of 3x11 microphylotypes of the limited fungal state, highlighted the usage of a fungal probiotic, Saccharomyces beneficial.

CONCLUSION: 
By heralding the evolution of our Microbial Clock in three stages (The Trilogy), lastly, the missing ‘Phylotype Signature’, and the importance of the missing microbes in aging and age related diseases, we wanted to provide a searchable, educational decision tree for developing new strategies and research approaches; this would emphasize tailored (Precision Medicine) (REF 3) ‘Restorative Microbiology’ (linkable to AI), while integrating the Hologenomic Theory of ‘Dual Citizenship’ and our new Hologenomic Center (Fig. 8) for intervention and treatment in cognitive impairment via the brain-GUT axis.

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