Accelerated Cure Project for MS

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Accelerating research towards a cure for multiple sclerosis

The Microbiome and MS

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Human… What is a *human*? We think of the human being as a singular organism, but in fact a human being is an ecosystem – which we call the human microbiome. This ecosystem is the collective combination of human cells, microbial cells (microbiota), and the genes within these cells,that exist on and in a human being. Actually, the human microbiome is more *other* than it is *human* – only a third (if that) of the cells and <1% of the genes we carry around in this human ecosystem are human (**Figure 1**). Don't be grossed out though, most of these bacterial and fungal cells are really important to our existence – as a human, we live in a symbiotic relationship with these *other* cells. We provide shelter, resources, and food through what we eat, and they in turn provide protection and help break down certain foods, aiding our digestion. The microbial cells exist on all our surfaces, but they are predominantly within our gut – hence you may have heard the term gut microbiota. NPR created this neat must-watch animation describing the

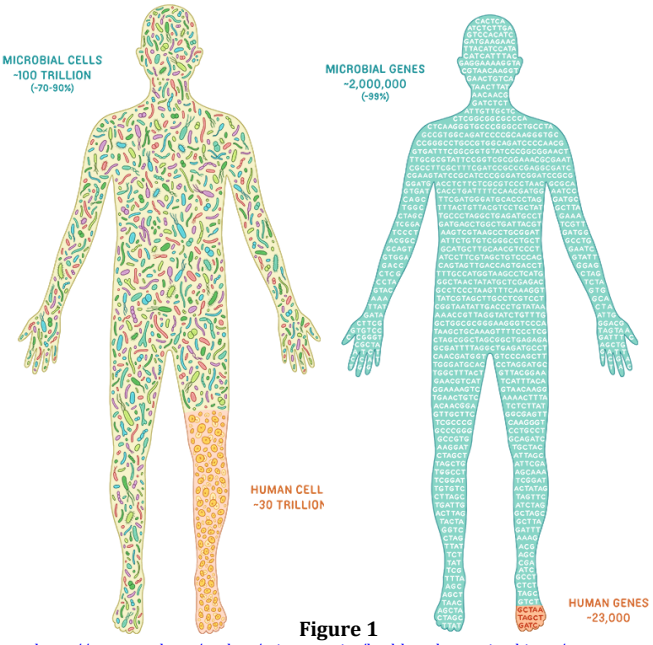
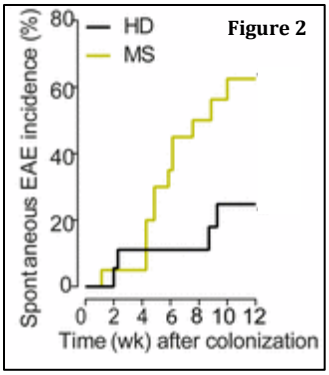


Figure 1
https://www.amnh.org/explore/science-topics/health-and-our-microbiome/meet-your-

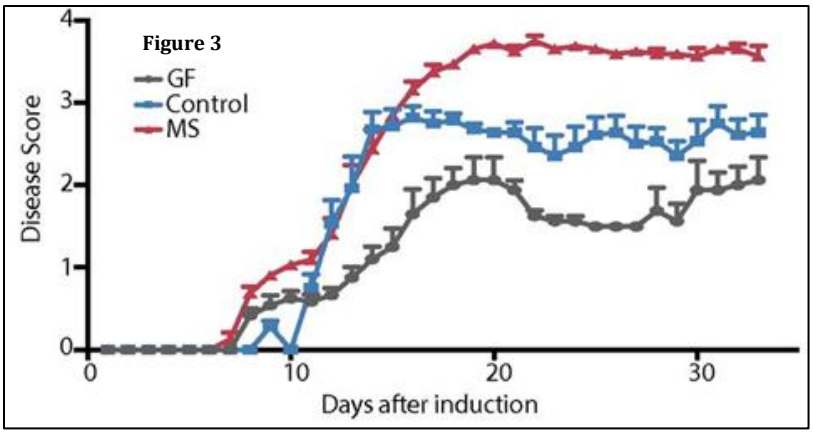
human microbiome and the important role these *other* cells play in our lives (click here to see the video). Unfortunately, we have barely scratched the surface of understanding how changes in the human ecosystem impact our health and vice versa.

This month, two papers were published simultaneously in the official journal of the National Academy of Science (*PNAS*) shedding light on the possible role the microbiome may have in MS. In both *PNAS* papers the gut microbiota (from fecal samples) was compared between persons with MS (PwMS) to those without MS, and then the researchers assessed the impact of the human microbiota on mice susceptible for neurological autoimmunity. The results were surprisingly and intriguingly similar. The first study out of Germany, compared the gut microbiota of 34 identical twins pairs.[1] In each twin pair only one sibling had MS (thus, the twins were discordant for MS). The microbiota between the twins with and without MS did not differ dramatically. However, half of the MS twins were on disease-modifying therapies. When the analysis was restricted to drug-naïve MS twin pairs, there was an elevated abundance of *Akkermansia muciniphila* in the fecal sample from the MS twins compared to their healthy co-twins. The researchers then transplanted the human microbiota into unique mice that could spontaneously develop a MS-like phenotype. As one would expect, only a handful of the human-derived microbiota were able to colonize the gut of these mice. Well, the mice who received the microbiota of the MS twin were more likely to spontaneously develop the MS-like condition than the mice who received the microbiota from the healthy twin (HD) (**Figure 2**). These mice with the MS microbiota produced less immune cells secreting IL-10 (an anti-inflammatory molecule), than the mice with the HD microbiota.



[1] https://www.ncbi.nlm.nih.gov/pubmed/28893994 (or http://www.pnas.org/content/early/2017/09/05/1711233114.full)

The second *PNAS* paper describes an American study where the gut microbiota of 71 drug naïve PwMS were compared to 71 unaffected controls. [2] There were no major differences in the microbiota composition, but they did observe *Akkermansia muciniphila* and *Acinetobacter calcoaceticus* as being increased in PwMS (similar to the German study). The researchers took gut bacteria and immune cells from each individual and mixed them. The MS immune cells stimulated with the MS gut bacteria were not fully functional (they were impaired) – this demonstrated the microbiota may influence the immune system in PwMS. Then mice prone to another MS-like condition were colonized with the microbiota from PwMS and unaffected controls. In these mice, they will all develop the MS-like condition. What was interesting, was the severity (disease score) of the MS-like condition was worse in mice who received the PwMS microbiota, compared to those from the unaffected controls, and much worse than the mice who stayed germ-free (GF) (**Figure 3**). And similar to the prior study, the mice with the MS microbiota produce few immune cells secreting the anti-inflammatory molecule IL-10.



It is rare to have two studies complement each other so well, particularly with such unique study designs and results. Nonetheless, these results should be cautiously interpreted, as there is so much yet to uncover. However, they do suggest a strong role for the gut microbiota in MS (in mice, so far), both at onset and on severity. Many things influence microbiota hitching a ride in/on our bodies, particularly diet (there is robust work demonstrating switching between animal- and plant-based diets rapidly and reproducibly alters the gut microbiota). [3] All in all, these results are exciting, and I am sure we will see many more diet-related studies in MS, with specific considerations for our hitchhikers, in the next few years!

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[2] https://www.ncbi.nlm.nih.gov/pubmed/28893978 (or http://www.pnas.org/content/early/2017/09/05/1711235114.full)

[3] http://www.nature.com/nature/journal/v505/n7484/full/nature12820.html