

**Release Notes 2023-10-25 :** This is an alternative analysis of a simple differential abundance measure between control and AD brains from one recent publication [111]. The differential abundances suggest loss of beneficial organisms may be acquired at conception. The title derives from literature on some of these organisms being symbionts with plants. As soon as I can figure out how to download the Bioproject data I hope to look at sequence level analysis. This may be another case of the mixed taxonomy getting in the way of seeing what is really there. A good database on metabolism may be helpful too. If nothing else, compare the list here to those most abundant in the endometrium [189]. Also repeats warnings on static measures of all kinds :) This is just released in current form due to hitting a time constraint. It seems to motivate important speculation with acceptable editing issues for now. **This is a draft and has not been peer reviewed or completely proof read but released in some state where it seems worthwhile given time or other constraints. Typographical errors are quite likely particularly in manually entered numbers. This work may include output from software which has not been fully debugged. For information only, not for use for any particular purpose see fuller disclaimers in the text. Caveat Emptor.**

**I am not a veterinarian or a doctor or health care professional and this is not particular advice for any given situation. Read the disclaimers in the appendices or text, take them seriously and take prudent steps to evaluate this information.**

**This work addresses a controversial topic and likely advances one or more viewpoints that are not well accepted in an attempt to resolve confusion. The reader is assumed familiar with the related literature and controversial issues and in any case should seek additional input from sources the reader trusts likely with differing opinions. For information and thought only not intended for any particular purpose. Caveat Emptor**

## Brain Microbiome : Make Your Garden Grow? Feed Your Head

Mike Marchywka\*

44 Crosscreek Trail, Jasper GA 30143

(Dated: October 24, 2023)

A recent work comparing the post-mortem brain microbiome of those who died with Alzheimer's to controls [111] provides insightful differential measurements of the two states. The authors mostly interpreted results to support a causal role for the associated organisms in disease progression. They found common skin bacteria such as *Staphylococcus epidermidis*, among others, to be more common in AD brains and these occasional pathogen may be one of several contributing organisms yet to be understood. Their results also suggest the diseased brain has different nutritional or metabolic status. The AD brains had lower abundances of organisms prone to overgrowth in benzoate rich conditions ( *Pseudomonas* ) while the skin bacteria in the AD brains are thought to benefit from low Trp or 5HT ( *Cutibacterium* ). Other AD associated organisms benefit from higher iron ( *Acidovorax* ) and methanol ( *Methylbacterium* ). Many of these organisms promote plant growth in various environments which may or may not be relevant in the brain. Observations from pre and peri-natal microbiome work suggest the possibility the AD brains lost beneficial organisms, such as *Acinetobacter junii*, acquired as early as conception. The response of organisms sensitive to tryptophan, iron, and methanol helps validate the microbiome results as being consistent with known properties of the disease state such as microbleed and endogenous methanol increases. The nutrients highlighted by these organisms tend to support earlier interest in uptake of lipophilic neurotransmitter precursor amino acids as well as vitamin K. The bacteria in healthy brain may help nutrient uptake in plants consistent with solubility as a performance limiting issue. Contrarily, histidine is not implicated as an issue while endogenous methanol production may be an important surprise. Methanol may derive from GI bacteria or SAM and methionine. GI bacteria then could still be causal and methionine may be a relative issue due to loss of other amino acids although I had not explicitly considered it before. Interventions such as dietary absorption aids including surfactants and acids then may be considered to improve nutrient uptake and minimize methanol production. The possibility of symbiotics or commensals suggests caution in antibiotic usage especially if they are only easily acquired before the development of the blood brain barrier.

---

\*Electronic address: [marchywka@hotmail.com](mailto:marchywka@hotmail.com); to cite or credit this work, see bibtext in [G](#)

## Contents

<b>1. Introduction</b>	3
<b>2. The Extremely Differentially Abundant OTU's</b>	4
<b>3. Microbes, Nutrients, and Disease</b>	8
3.1. Tryptophan related	8
3.2. Tyrosine related	9
3.3. Histidine related	9
3.4. Methanol related	9
3.5. Iron and Vitamin K related	9
3.6. Exposure, Vulnerability, and Uptake into CNS	10
<b>4. Discussion</b>	11
4.1. Informing Interventions	11
4.2. Plant Symbionts in Brain : Coincidence or Nurse Bacteria ?	12
<b>5. Conclusion</b>	13
<b>6. Supplemental Information</b>	13
6.1. Computer Code	13
<b>7. Bibliography</b>	13
<b>References</b>	13
<b>Acknowledgments</b>	25
<b>A. Statement of Conflicts</b>	26
<b>B. About the Authors</b>	26
<b>C. Interpretation Issues- General and Specific</b>	26
<b>D. Symbols, Abbreviations and Colloquialisms</b>	26
<b>E. General caveats and disclaimer</b>	26
<b>F. A baseline nutrient outline</b>	27
<b>G. Citing this as a tech report or white paper</b>	27

## 1. INTRODUCTION

Despite many interesting discoveries in the lab and clinic, cause and effect in many biological settings remains difficult to determine stifling the design of therapeutic interventions. Alzheimer's Disease is one important unresolved medical issue which may exemplify this limitation. For decades, amyloid beta and tau had both been considered as causal in the sense that removing either one would reduce disease processes and produce significant clinical benefits or even a cure ( see citations in any of the AD citations below ). That state of affairs is well documented in the works that hint at it unravelling[45] such as a 2002 work suggesting that "tauists" and "baptists" could 'shake hands" and look for other causes [114]. Efforts continued and recently Aducanumab was approved despite trials having been stopped for futility [166] followed by Lecanemab [180] [174]. Other approaches target cholinesterase [56] due to decreased acetylcholine and NMDA receptors [88] to control glutamate and Ca with limited success.

The infectious disease hypothesis has recently gained credibility [62]. [111] [76] considering direct CNS infection as the disease cause but currently without a particular tractable set of responsible organisms. This was the motivation for the microbiome work [111] examined here. Perhaps most interesting is the similarities between infections such as *Treponema pallidum* and AD [108] especially as syphilis cases continue to escalate although in younger high-risk fringe groups [5] distinct from the typical AD patients.

AD has also been attributed to autoimmunity but autoimmune disease always invites the "undetected pathogen" concern and hence an interest in infectious etiology. A 2022 work concluded AD is an autoimmune disease modulated by Trp metabolites [40]. Immune activation and Trp depletion associated with AD were recognized as early as 2000 [188]. Similarly, Parkinson's has been considered as autoimmune [36] with possible undetected infection.

Other work has continued on age related cognitive decline in general exploring GI microbes, their metabolites, and nutrition. Metabolites may also exist in ingested food independent of host microbiome. Animal studies have show links between gut microbiome and behaviors [105]. Tryptophan metabolism is now being explored as a mediator from GI microbiome to brain function [49] with particular interest in 5HT [121] Some work appears to just emphasize the role of Trp metabolites and various details [148] without considering the likely context pointing to deficiency. One interesting work from 2007 identified tryptamine as a cause of neurodegeneration through Trp-tRNA synthetase and the effects may not be overcome with excess Trp [127]. Recent literature on microbially derived tryptamine and indeed tRNA related signalling and particularly Trp-tRNA- related signalling has added details but not resolved issues completely. One work suggesting amino acid and tryptophan restriction to counter aging suggests that can impair cognition [22]. Given the observations of decreased acetylcholine in Alzheimer's, dietary choline is a popular choice [179]. In the case of choline deficiency, given that gut organisms are thought modulate choline availability to the host [145], nutrient and neurotransmitter deficiency could be mediated by infection with the wrong microbes.

Another recent study demonstrated that AD symptoms and reduced adult hippocampal neurogenesis could be caused by fecal microbiome transplant from AD but not control humans [54] tending to support an infectious or transmissible attribute contained in the GI tract.

In any case, the observed age distribution of Alzheimer's needs to be explained by any constructive theory. Microbe exposure is not as age specific as Alzheimer's Disease and an infectious etiology suggests a good intervention will be host directed attempting to restore the successful "youthful" response. Often this is just dismissed by glib terms like senescence or "inflammaging" that don't do much to explain cause and effect behind the age related vulnerabilities. There are special events such as conception at which time exposure and response to microbes is unique and difficult to replicate at other points in life but in general most other variations are quantitative. By finding associations between groups of organisms and clinical trajectory, work on the infectious hypothesis will greatly aid evolving hypotheses that consider the microbial environment such as barrier function and nutrient flows even if the organisms are better observers than pathogens. Making meaningful or "functional" measurements can be difficult and blood levels don't measure nutrients on the other side of the vessels. Microbe ecology may be more meaningful if more complicated to interpret or ambiguous.

The present work supports a nutritional hypothesis, without or without microbial involvement, that cognitive decline and correlates of aging in general are due to nutrient deficiencies caused by common age related digestion declines with idiosyncratic adaptive responses. This builds on my earlier efforts with the age dependence of covid-19 [99] [101] that suggest other neurotransmitters, notably those derived from the "WHY" ( tryptophan histidine tyrosine ) amino acids, possibly along with vitamin K, are most important. A complete solution will probably address all the age related bottlenecks and include absorption aids [93] [97] [95] [94] [96].

While little of this has been tested, some interest has recently been expressed in age related GI damage suggesting interferon-gamma per se may be part of a problem [122] and a recent analysis of long covid points to serotonin deficiency and nutrient issues [190]. While generally well known, GI damage due to SARS-Cov-2 may be under appreciated. In general this can be a complicated issue as treating a measured deficiency for clinical benefit may involve more than supplementing and measurements may be deceiving.

Seemingly unrelated work can be linked to nutritional status. For example, a causal role for lncRNA such as

MEG3 in mediating neuron death in AD has been described [7]. But this had previously been implicated in apoptosis and endothelial cell dysfunction related to high glucose [186] [169] as well as pathogen [132] and tumor control [193] through mTOR. Absent any conclusive data, it is interesting that dietary tryptophan was found to improve a glucose issue in fish via lncRNA [64]. Another line of attack is aquaporin 4 read through rates [109] but there is some indication linking Trp ( and Tyr) or its tRNA to this [13] as may be expected. In many of these cases, compensatory or adaptive responses can probably obscure deficiencies by "correcting" blood levels even as things become desperate intracellularly.

The work interprets the microbiome results from figure 4 in [111] in terms of the literature on the most differentially abundant organisms ( those at either end of the curve) which have been listed in Table I. This analysis tends to confirm that their results have some validity as organisms can be rationalized in term of previously known attributes of AD. They also suggest higher availability of tryptophan and aromatics like tyrosine in the healthy brain consistent with my earlier works. At least one disease preferring organism benefits from methanol oxidation suggesting that may be an important part of the disease so the existing literature on methanol in the elderly is explored. Iron or mineral metabolism may be more prominent in the diseased brain which may be attributed to microbleeds although other causes are possible.

Two known sources of methanol are GI bacteria and one carbon metabolism from the SAM system. Increasing stomach acidity may reduce GI methanol production and that is discussed as a low risk approach to explore although contrary to many notions that encourage PPI usage. GI bacteria methanol production would then make AD "infectious" although also dependent upon phenotype. The possibility to too much methionine due to too little protein translation is also discussed and could benefit from extra protein digestion possible with more stomach acid.

Further consideration of these organisms in this context suggests that some of the differences may be due to loss of symbionts<sup>1</sup> that could have been present since conception This hypothesis appears to be novel for AD but does explain several observations related to antibiotic usage and the age distribution. If they were seeded during conception it may be difficult to re-establish in old age and the use antibiotics would need to be considered carefully.

## 2. THE EXTREMELY DIFFERENTIALLY ABUNDANT OTU'S

Table I lists the organisms associated with health or AD as taken from figure 4 in [111] . they are discussed in order of magnitude in either direction. Discussions vary among genus and species or strain level depending on the literature. Taxonomy is a bit confusing and later alternatives may include direct appeal to the 16s sequence features. Host-organism relationships can be quite diverse and many organisms tend to be benign or beneficial to humans but are also found to become pathogenic under conditions that may not be well defined. Table entries as well as following descriptions remain in note form to stay concise although may be a little confusing.

Title	
Six OTUs are more abundant in the control group:	
Acinetobacter junii	common in soil animals human water soil, plant growth promoter, from birth?
Comamonas jiangduensis	plant symbiont, genus uses Trp
Cloacibacterium normanense	breast milk aromatic degrading
Pseudomonas putida,	denitrifyin,benzoate overgrowth breast milk
Pseudomonas thermotolerans	may not use benzoate
Diaphorobacter nitroreducens	sludge not benzoate, methanol, or sugars tetracycline favored
Seven OTUs are more abundant in the AD group:	
Cutibacterium acnes	skin resident, overgrowth in 5HT depletion
Staphylococcus epidermidis	skin resident, known pathogen in infant brains
Acidovorax ebreus	Fe oxidation
Acinetobacter tjernbergiae	sludge uses histidine but not others
Acidovorax temperans	Fe oxidation
(Novi)herbaspirillum soli	volcanic burned soil plant enhancer
Methylobacterium goeisingense	methanol consumer

TABLE I: Miscellaneous features of OTU's identified in [111] that are more or less common in AD vs control post mortem brain sections after minimal processing. In order of "Extremism" with first entry being the most extreme in each category.

<sup>1</sup> The distinction between symbiosis and commensalism may be important but the benefits to the organism are generally assumed and symbiosis will be used by default.

**Cutibacterium :** *Increased in AD :* Prior to 2016, *Cutibacterium acnes* was in the genus *Propionibacterium* and a 2019 proposal made subspecies *defendens* and *elongatum* the latter of which is associated with progressive macular hypomelanosis rather than acne [39]. The species is itself quite diverse with *defendens* associated with prostate cancer and even friend/foe status is questioned [17]. Interestingly, it is blamed as the pathogen in many infections [18]. with a strain-specific antibiotic, thiopeptide cutimycin, which is supposed to kill *S. epidermidis* [32] although the interaction appears to be two-way [18]. *C. acnes elongatum* is related to a pigmentation disorder suggesting possible interaction with tyrosine or tyrosinase. Treatments of hypomelanosis may include benzoyl containing products [79] although transformations remain unknown. More generally, *C. acnes* is associated with post inflammatory hypopigmentation disorders for which antibiotics appear to be part of the cure [142]. An antibiotic would be surprising given that *S. epidermidis* abundance has increased too but again numbers and fitness are relative. This could be a candidate for an AD pathogen but given its ubiquity it would need other changes in the host. In very recent work on fungal infection found *Cutibacterium* expansion in Tph-/- mice which were unable to convert tryptophan into 5HT [143]. Even though this intervention may have raised tryptophan levels, it acted similarly to tryptophan depletion or loss of serotonin producing cells in that the tryptophan metabolite 5HT was missing allowing for proliferation. "Serotonin degeneration" has been implicated in cognitive declines [158] and it may not be clear in which direction cause and effect operate but degeneration in response to limited tryptophan would be quite plausible. Skin ecology may involve many factors and exposure to ketoconazole may have favored *C. acnes* for unclear reasons although biotin synthesis was considered [53].

**Staphylococcus :** *Increased in AD :* Until recently *Staphylococcus epidermidis* was not considered pathogenic as a normal inhabitant of the skin but is now recognized as a common pathogen [124]. If there is a specific pathogen responsible for age associated cognition defects this is the most suspicious of the group. It is the most common infection in pre-term infants and activates microglia and modulates BBB permeability [55]. Like some of the other bacteria here, it has been isolated from planted areas and in particular apple orchards and found to promote the growth of clover [28]. One report suggested it is a symbiont in the female mouse reproductive tract [123]. It was found in higher amounts in infant fecal microbiome when vitamin K deficient [12] which may be expected as "leakage" or diffusion from the skin and reduced coagulation barrier function or it may reflect other competitive factors. As a coagulase-negative *Staphylococcus*, it can secrete antibacterials such as 6-thioguanine a purine analog inhibiting purine synthesis in susceptible organisms [29]. It would be interesting to check community for overall entropy and susceptibility to see if this is a relevant factor. In particular, determine if *A. junii* is susceptible. Trp metabolites have some activity against it [116] suggesting its presence may indicate low Trp metabolism due to lack of tryptophan or reduced activity of any Trp metabolizing cells.

**Acidovorax :** *Increased in AD, 2 species :*

*Acidovorax temperans* may be considered a non-plant species more common in "environmental and clinical" samples [205] and is frequently found in petroleum contaminated sites with polycyclic aromatic hydrocarbon content [157]. *Acidovorax ebreus* has been studied in detail for its iron oxidizing capability as part of a uranium immobilization scheme [33].

Besides acetate, *Acidovorax* can use lactate and citrate as carbon sources [26]. It is notable for oxidation of Fe-II and encrusting mineralization [27]. Although the benefits of iron oxidation have been demonstrated, encrustation depends on iron concentration and perhaps absence of chelators [26]. This may generate a distinctive "green rust" [206] [130]. Arguably precipitation is a better fate for excess iron than some alternatives so even this may be mitigating although not sustainable as minerals accumulate.

As with some other genera, some *Acidovorax* species interact with plants [19]. *Acidovorax* was found in root endosphere of Chinese Chives [162]. Beneficial and pathological relationships have been distinguished by genomes with beneficial abilities to sense, transport, and synthesize useful molecules while pathogens have secretion systems and ability to use plant synthesized lipids [154].

**(Novi)herbaspirillum :** *Increased in AD :* Originally isolated from plants in volcanic ash, and assigned to *Herbaspirillum*, *Noviherbaspirillum soli* is thought to be siderophore producing and plant growth promoting and will assimilate lactate and hydroxybenzoate [25]. Lactate usage could be simply using astrocyte output that is not consumed by dysregulated neurons or it could be starving neurons. The distinction between "parasite competing for scarce lactate" and "symbiont benefiting from excess benzoate" is discussed in Appendix C as there is a lot of ambiguity in all cases without networked rate equations reflecting feedback mechanisms. It changed genus circa 2014 from *Herbaspirillum* after proposal in 2013 [85]. *Noviherbaspirillum* was one of a few genera to increase in abundance in a soil sample with the addition of pyrogenic organic matter [198]. In a study of raw quarry waste soil compared to undisturbed and organic amended soils, *Noviherbaspirillum* appeared to do best in the raw quarry waste soil with no additional organic matter [144]. In general then it may be an early colonizer of previously abiotic settings and benefit from low organic high mineral conditions. A relative, *Noviherbaspirillum denitrification* HC18, can methylate methyl-As<sup>3</sup> but not As<sup>3</sup> [200]. Another relative, *Herbaspirillum* sp. WT00C, is an endophytic selenite reducer specific to tea-plants [192]. Species of *Herbaspirillum* considered plant growth promoting bacteria (PGPB) were described



as having low siderophore production but P solubilizing ability as endophytes [38].

**Methylobacterium :** *Increased in AD :* Methylobacterium are notable for metabolism of methanol and succinate in beneficial association with plants [134] . Associations with plants may be endophytic or epiphytic and appears to be largely due to methanol released during pectin metabolism [164].

Increased methanol derived formaldehyde is observed in neurological patients and the elderly [41] suggesting the presence of Methylobacterium is indicative of methanol accumulation and perhaps mitigation of formaldehyde damage by methanol oxidation. Methylobacterium converts methanol to formaldehyde

inside the cell ( by a periplasmic dehydrogenase ) but then quickly forms CO<sub>2</sub> or assimilates it in the cytoplasm [164].

**Comamonas :** *Increased in healthy :*

The properties and history of this genus have been well summarized and quoted verbatim here,

Comamonas spp. have been isolated from a broad variety of environments, including water, aircraft water, soil, plants, and animals [8–12]. Several Comamonas spp. have been investigated for their potential to degrade xenobiotic pollutants and for heavy metal detoxification under a variety of environmental conditions [13–19]. Comamonas spp. are thought to be of low virulence. They have, however, caused infections, including serious infection such as septicemia or endocarditis, in immunocompetent hosts [20–22] [ ...] Analysis of the scientific/medical literature showed wide-ranging types of infections resulting from Comamonas spp. These were resistant to numerous different antibiotics. The data uncovered that this genus is a more commonplace pathogen than hitherto believed, with numerous infections/conditions caused by Comamonas spp. being severe and incapacitating. The purpose of this study was to give a general summation of infections caused by Comamonas spp., any underlying disorders/illnesses in patients that predispose them to infections with these bacteria and the antibiotic therapies that can be used for the management of these infections to aid medical professionals. 2. Genus Comamonas Previously designated as Pseudomonas rRNA homology group III, the family Comamonadaceae now includes the genera Comamonas, Delftia and Acidovorax. The genus Comamonas, assigned to the Comamonadaceae lineage in the -Proteobacteria, was originally proposed by Davis and Park [23] and the name validly published with the revival of the genus and the type species Comamonas terrigena by De Vos et al. [24]. In 1987, two Pseudomonas species, Pseudomonas acidovorans and Pseudomonas testosterone, were transferred to the genus Comamonas as Comamonas acidovorans and Comamonas testosterone, respectively [24]. Based on a detailed 16S rRNA gene sequence-based phylogenetic study of the Comamonas [146].

The Comamonas genus was also observed to be less abundant in intestinal microbiome of AD patients [184] suggesting the brain and intestinal abundances may correlate although not mentioned in a similar 2017 analysis [181] or a 2018 review article [82].

#### Thinking aloud

check for obsolete names etc

Comamonas jiangduensis is known for producing biosurfactant in agricultural soil [161] Other species such as Comamonas acidovorans, as part of plant rhizobacteria, was observed to promote lettuce seedling root elongation when tryptophan was included [8] although 10mM tryptophan inhibited its growth. Comamonas testosterone makes a variety of tryptophan containing cyclic dipeptides with antimicrobial effects [118]. Comamonas testosterone and Comamonas jiangduensis have some anti-nematode activity [117]. Comamonas genus is also considered metal tolerant [23]. Potentially then low levels of heavy metals could favor these organisms leading to increases in absolute abundance. Depending on the numbers then, it is possible that some cognitive benefits could result from small amounts of these toxic elements. While perhaps not likely, its important to remember issues like this especially when the obvious interpretations don't lead to useful interventions or "go over like a lead balloon."

**Cloacibacterium :** *Increased in healthy :*

Isolated from municipal wastewater by 2006 [2], Cloacibacterium normanense is also listed as an endophyte of plants grown in textile waste water [153]. Cloacibacterium was found abundant in stem endosphere of Chinese Chives [162]. Cloacibacterium normanense is electrochemically active [6] [196] Along with P. putida, it is a component of breast milk ( Guatemalan mothers ) and both also have aromatic hydrocarbon degrading capabilities [52]. Its route to the milk is controversial [90]. It was also prominent in one study on breast cancer and another in lung cancer.

#### Thinking aloud

check direction and numbers with author, also note right next to Geobacillis not Geobacter

It was one of the most increased genera in recurrence free patients' BAL fluid prior to resection of early stage non-small cell lung cancer [131] . Cloacibacterium was detected in an exploration of breast microbiome and metabolites such as TMAO in triple negative breast cancer [183] From their file mmc4, it looks like several p-values are lower than TMAO including lactate, Trp, and Trp derivatives. Exploration of their data may be useful but I was unable to determine from the supplementary information which samples were in the beneficial "IM" state.

**Thinking aloud**

need a choline section for this: The role of TMAO has been a matter of debate and has featured some of the same issues related to causal role now being explored for brain microbes and metabolites [178]. As choline status is likely relevant to AD, it may be useful to determine if Cloacibacterium has any impact here although other genera such as Desulfovibrio [50] and a variety of others [145] are known to generate trimethylamine from choline. While TMAO is often considered uniformly unhealthy, it may be beneficial in cancer [31] the choline deficiency could be collateral damage from an otherwise adaptive response.

The genus Cloacibacterium was also found differentially abundant in certain types of arteritis along with metabolic changes [75].

**Thinking aloud**

The reference also mentions FISH which may be useful in localization. Curious what this would look like with just the 16s primer FISH ?

**Pseudomonas** : *Increased in healthy* : Two species of Pseudomonas, putida and thermotolerans, were overabundant in health. Pseudomonas in general tend to overgrowth in benzoate rich settings. Like other soil dwelling organisms, they are known for degrading benzoate derived from lignin [160] and it could also be derived from tyrosine or neurotransmitters. Studies relating P putida and aeruginosa response to aromatic amino acids as in cystic fibrosis sputum have shown some common and species specific features. [128]. Repeated application of quaternary benzylalkonium chlorides to the Lascaux Cave created an overgrowth dominated by Ralstonia and Pseudomonas [11]. This suggests a competitive advantage in aromatic rich settings Swimming and surfactant production as a function of amino acid exposure have been investigated at least for P. aeruginosa [66].

However, P. putida is also known for flexibility [110] [150] suggesting its presence is not particularly informative without phenotype or mRNA information. It can be denitrifying [67]. However, its potential utility in bioproduction has created a significant amount of literature on it including glutarate sensing and metabolism [201]. While glutarate is a toxic product of amino acid metabolism, it would not be clear if P putida would be more fit in a high or low concentration setting but may be able to remove it. A rough form has been found in biofilms along with Acinetobacter species [58]. Pseudomonas thermotolerans is notable for possibly not using benzoate [91]. Although the real issue is aromatic amino acid usage and early work did suggest a strain specificity at least with P aeruginosa, "28 of 29 strains grew on tyrosine as a sole source of carbon, whereas only seven grew on phenylalanine as a sole source of carbon" [21].

**Diaphorobacter** : *Increased in healthy* : Diaphorobacter nitroreducens was first isolated from activated sludge in 2002 and found to use polyhydroxybutyrate but no common sugars and notably not used were, "methanol, caprylate, citrate, benzoate, serine, and histidine" [65]. At least one strain degrades a variety of polycyclic aromatic hydrocarbons [187] and other(s) degrade phenylurea herbicides [204]. A strain found in coking waste could use phenol and cresol as carbon and energy sources although beef broth sped up the phenol degradation and it was inhibited by various metals [107]. Common in mining wastes and can oxidize sulfur to thiosulfate [147] which may have significance in a metal handling. Several species are notable for "simultaneous nitrification and denitrification using acetate as carbon source" [203]. Diaphorobacter along with Pseudomonas increased in abundance with addition of tetracycline into a nitrogen reducing reactor with mixed bacteria culture [191].

**Acinetobacter** : *Species fluctuate* : The Acinetobacter distribution is the most confusing with A. junii being the most overabundant in the control group and Acinetobacter tjernbergiae overabundant in the AD brains. The Acinetobacter species are described in general as versatile plant growth promoters with beneficial effects on availability or buffering of nutrients like phosphate and metals [115]. Some works compare the species in detail, such as [172] [9] [177], although no obvious differences between A junii and tjernbergiae were apparent. A junii was originally identified in 1985 however by its ability to use L-histidine [69] [16] and pathogenic species of Acinetobacter appear to rely on histidine [89]. It is possible that its presence reflect CNS histidine status but refer to Appendix C for a more complete description. Interestingly, some species can live off of tryptophan metabolite kynurenine and both of these species lack a putative Mn transporter [9]. At least in combination with other organisms A. junii appears to promote plant growth [126] and has been described as "hypertolerant" to metals such as arsenic [103] and lead [73] [156]. A junii is rarely a human pathogen but infections have been documented and more likely in those with prior antibiotic use, invasive procedures, or cancer [197]. and in preterm infants [87]. Intriguingly, it is much more common in the fecal microbiome of those delivered by vaginal birth than cesarean [129] and exposure of cesarean infants to maternal vaginal fluid improved some aspects of neurodevelopment [207]. The literature on A. tjernbergiae is not as extensive but one work claims, "A. baylyi, A. bouvetii, A. grimontii, A. tjernbergiae, A. townneri, and A. tandoii are commonly found in natural environments but occasionally isolated in activated sludge and have not been found associated with humans (19, 85). They are able to store phosphate as polyphosphates and may have potential applications in the biological removal of phosphates (2)." [43]. Substrate selections for A. tjernbergiae were listed as, [24]

Using the method of Kaempf et al. (1993), L-arginine, L-histidine and quinate are all used as sole sources

of carbon and energy and some strains utilize DL-aspartate and L-leucinamide. cis-Aconitate, pimelate, trans-aconitate, adipate, 4-aminobutyrate, azelate, citrate, glutarate, malonate, oxoisocaproate, suberate, b-alanine, L-aspartate, L-glutamate, L-leucine, L-phenylalanine, L-tryptophan, 4-hydroxybenzoate and phenylacetate are not utilized.

The most well known pathogen, *A. baumannii*, appears to have genetic features that define a pathogenic *calcoaceticus-baumannii* cluster [171].

### 3. MICROBES, NUTRIENTS, AND DISEASE

Organisms or communities may be considered pathogenic, beneficial, or neutral, causal or responsive with these attributes defined by the result of the subject's removal from the host. Novel data such as these abundances also needs to be "sanity checked" or validated. There are recurring issues with this kind of data even in this short work and some common caveats are described in Appendix C. The original work [111] analyzes the data to suggest that a pathogenic organism or community is causing Alzheimer's Disease and removal or attack can have clinical benefit. However, looking at the most differentially abundant OTU's, along with other known or suspected characteristics of the disease state, it is easy to make a case for pre-existing beneficial organisms being replaced by disease related emergent organisms largely reacting to and even mitigating a changed environment. The distinction is important because in the former case broad spectrum antibiotics with good CNS penetration may be explored but in the latter case restoration of nutrient flow and targeted eradication or seeding may be more prudent. The easy reconciliation between observed abundance variation and disease properties also helps validate the microbiome results. Taken together, these differential abundances can suggest that the diseased brain is reduced in the supply of tryptophan or metabolites, benzoate or parents like tyrosine, while having an excess of iron and methanol. Reduced levels of vitamin K may also be a factor.

Most or all of these genera, notably *Comamonas*, *Methylbacterium*, *Pseudomonas*, *Acinetobacter* and *Herbaspirillum*, have shown some members that have activity as plant growth promoting bacteria (PGPB) [51]. *Comamonas jiangduensis*, more common in health, is known for producing biosurfactant in agricultural soil [161] while *Noviherbaspirillum soli*, more common in AD, is found in volcanic or low-organic soils and may be an early colonizer presumably suited to lower fertility conditions suggesting in general the diseased brain may be nutrient poor. On an entity by entity basis, this generalization is plausible.

#### 3.1. Tryptophan related

Excess tryptophan or metabolites may suppress the skin bacteria, the *C. acnes* and *S. epidermidis*. Reduced tryptophan may be due to decreased intake with age, decreased uptake due to GI or vascular impairment, or decreased signalling to bring peripheral Trp to the brain. Metabolite decreases may be purely due to Trp decrease or decreased functions of host cells and bacteria that would produce metabolites such as 5HT. Similar considerations apply to all entities including benzoate and tyrosine with all caveats in Appendix C applying. Some reference works exist on various aspects of metabolism and taxonomy. One work on tryptophan synthesis and IAA ( indole pyruvic acid ) production shows for example the abilities of *A. junii* and *P. putida*, which have IPA pathways, in the context of others [159]. While IAA appears be deleterious at mg/kg for animal fetus [47] [48] and correlates with cognitive decline in CKD patients [86], to the brain, IPA has been investigated as a therapeutic in phase II clinical trials [135] and it other brain related effects [113][10]. Note that the above "IPA" is indole pyruvic acid NOT indole propinoic acid although IPA is used for the latter in at least one work on intestinal production of Trp derivatives suggesting both may be beneficial. IAA production is also known to occur [199]. As early as 1999, indole-3-propionic acid was investigated for effects against AD [30]. It is quite possible that for a beneficial relationship the organism has to adapt its metabolism to the human host versus a typical plant.

As early as 2000, it was demonstrated that acute tryptophan depletion could worsen cognition among AD patients [137] but that does not prove that the dominant cause of the natural disease could be corrected by providing more Trp. A 2003 study of healthy and AD patients demonstrated cognitive impairment by "depleting" trp in a comparison of two amino acid drinks with and without tryptophan [138] suggesting amino acid competition may be significant in the elderly.

An interesting 2010 study in *Drosophila* demonstrated complete recovery from expression of amyloid beta with oral 1,4-naphthoquinon-2-yl-L-tryptophan which was designed based on observations of quinones preventing aggregation [149]. Presumably, vitamin K then could exert similar effects and the compound itself could act in unexpected ways such as metabolism to provide excess tryptophan of unknown significance. It is not known if follow up work occurred.



### 3.2. Tyrosine related

Direct evidence of tyrosine related effects is lacking but the overgrowth of organisms associated with benzoate is suggestive of a change in monocyclic aromatic content. Benzoate consumption has a putative benefit in dementia [84] and it could act to feed symbiotics or aid absorption of nutrients including phenylalanine, tyrosine, and tryptophan.

However, given the involvement of dopaminergic systems in Parkinson's, there is some literature that may be relevant for context. One work explored interaction between antibiotics and MPTP treatment on clinical outcomes and microbiota suggesting antibiotics could protect against MPTP neurotoxicity [141]. While none of these organisms was mentioned, *Proteus mirabilis* was found to create some damage pointing to possibility of common pathogens having impact on the brain. Other works on dopamine or Parkinson's and microbiome do not highlight any of these organisms more generally [57]. Some association was found between microbial tyrosine synthesis and schizophrenia [168] of unknown relevance. Some organisms have been identified that metabolise levodopa with tyrosine decarboxylases [176] but again no organisms identified in this work appear relevant.

#### Thinking outloud

D-tyrosine but only in combination with an antibiotic incredible synergy in kill rates [63]. D-amino acids such as D-serine and D-amino acid oxidase are well known in the brain.

### 3.3. Histidine related

Nothing of substance can be said about histidine from this work. The only obvious relationship to histidine suggests it is probably adequate or more or less consistent based on *Aceinetobacter*. See however Appendix C for general ambiguities.

### 3.4. Methanol related

The alert to methanol was a surprise but supported by significant literature. As early as 2014, exploration of chronic methanol feeding relationship to AD pathology was explored [194] with feeding to monkeys producing tau phosphorylation and amyloid plaques [195] similar to AD. Increased methanol concentration is known in old age [42]. Interestingly, investigation on APOE-4 and ethanol consumption [81] may be consistent with an important role for methanol in AD pathology. Two endogenous sources of methanol include bacteria and SAM. Bacteria may also metabolize methanol into longer acids such as butyrate isomers [37].

Supplement usage related to SAM may need to be more carefully considered [46].

#### Thinking outloud

this is a duplicate citation used earlier IIRC

. Balance of the amino acid pool was considered in passing before [99] and perhaps methionine, best known for translation initiation, is over supplied as protein synthesis is hindered by limitations of tryptophan or other amino acids. Some evidence suggests excess methionine may impair memory, for example [167]. A link to Parkinson's-like symptoms had already been considered as early as 2010 [77].

Another recent study focused on transmission of AD into healthy young rats with fecal microbiome transplants, found that *Desulfovibrio* were more common in AD microbiome than controls [54]. There appears to be some literature on this genus [155] and may be useful for further understanding of the issue as well as methanol-ethanol interactions.

### 3.5. Iron and Vitamin K related

The abundance of iron and methanol responsive organisms is also consistent with prior expectations helping to validate their initial results. iron metabolizing organisms would presumably benefit from heme influx due to vascular issues like CAA or microbleeding which is common in AD [59] and presumably could be reduced with more effective clotting. Vitamin K deficiency was also recognized as early as 2001 as a contributor to AD and cardiovascular disease [3] with modern work continuing to assess the situation [1]. Vitamin K in particular may not be fully appreciated but it is important for CNS sulfatide regulation [163] [136] and the sulfatides themselves have important but confusing effects on coagulation [74]. There is a tendency to jump to anticoagulants with the appearance of inappropriate coagulation but it is likely beneficial to isolate damage and more vitamin K may be indicated [98].

Acidovorax iron oxidation is intriguing as I suspected mineral deposits were part of "old age pathology" but the question remains if the growth is due to extra iron supply from heme suggesting it is just a symptom of a large leakage problem. Initially, I would have suspected calcium minerals and a role for vitamin K.

Another reason for iron accumulation may be a group of diseases called "Neurodegeneration with brain iron accumulation"(NBIA) which is normally defined by genetic defects, motor symptoms, and spatial iron distribution although in some cases specific defects have yet to be identified [72] . NBIA is considered to be related to AD among other brain diseases [185] but cause and effect not established. As there are reports iron accumulation can be mitigated with vitamins [4] [165] its quite likely to include an exaggerated phenotype of vitamin deficiencies in normal brains. As defects exist in specific enzymes it is unclear if iron removal fixes everything and in fact so far removal attempts have had some but limited clinical results [61]. Recently some age related iron accumulation was observed in healthy adults using susceptibility-weighted imaging (SWI ) MRI [173] and the imaging patterns are still being investigated [78].

### 3.6. Exposure, Vulnerability, and Uptake into CNS

Initial expectation of an acquired pathogen may have to be modified based on this analysis as symbionts acquired early in life are quite probable with some evidence suggesting exposures at birth could matter while the conception environment contains many of these overabundant presumed beneficial organisms. Loss of a symbiont in old age due to nutritional or other factors that was acquired at conception may be difficult to re-seed. At least one study did find an increased risk of dementia with antibiotic usage [68] and a very recent review provides more context for the issue [182]. This is consistent with loss of symbiont(s).

While *C. acnes* and *S. epidermidis* could both be considered possible pathogens, their lifelong residence on the skin appears difficult to reconcile with the age distribution of AD. However, as would be expected with lower quality barriers due to protein quality correlating with old age, their ability to colonize the brain would be approaching that which existed at birth ( with vitamin K deficiency ). They probably still need an age-related fitness benefit which would compare well with the nutritional issues outlined above.

The case for infection-at-conception is greatly motivated by a recent work on the microbiome of endometrium and cervix compared to other body surfaces. The endometrial organisms are ambiguous at the species level but include all of those here,

A BLAST analysis (i.e. comparison of a 16S rRNA gene sequence to those in the BLAST taxonomy database) revealed that the consensus sequence for OTU 1 was identical to that of eight *Acinetobacter* type strains within seven species that have been isolated from clinical samples: *A. bereziniae*, *A. colistiniresistens*, *A. glylbergii*, *A. junii*, *A. modestus*, *A. proteolyticus*, and *A. vivianii*. A BLAST analysis of OTU 30 showed identical matches for multiple strains of *Pseudomonas aeruginosa*, and an analysis of OTU 19 revealed identical matches for multiple *Pseudomonas* species within the *Pseudomonas putida* group (*P. monteilii*, *P. plecoglossicida*, *P. putida*, and *P. taiwanensis*)<sup>77</sup>. A BLAST analysis of OTU 39 showed identical matches for six type strains within the species *Cloacibacterium normanense*, *C. caeni*, and *C. rupense*. Lastly, a BLAST analysis of OTU 29 (a member of the family Comamonadaceae) revealed identical matches for *Comamonas jiangduensis* and *C. kerstersii*. [...] Specifically, the bacterial profiles of cervical and endometrial samples were dominated by *Acinetobacter* (OTU 1), which accounted for 49.0% and 44.4% of sequences from these body sites, respectively. Other prominent taxa in the endometrium included *Pseudomonas* (OTUs 19 and 30), *Cloacibacterium* (OTU 39), Comamonadaceae (OTU 29), and *Escherichia* (OTU 21).

[189].

Implicating possibility of *A. junii* ( OTU 1 ) , *P. putida*( OTU 19) , *C. normanense* ( OTU 39) and *C. jiangduensis* ( OTU 29) or pretty much a possible exact match except for *P. thermotolerans* and *Diaphorobacter nitroreducens* the two least overabundant on the list. OTU 30 is assigned to *P. aeruginosa* which was not found in brain results. However, the overabundant *P. thermotolerans* is most nearly related to *P. aeruginosa* among the *Pseudomonas* species known at the time [92]. Possibly the semen carries some of the speculated symbionts [70] [112] making "infection-at-conception" possible from two sources.

There is also some indication that delivery method and vaginal microbiome impact early neurological development. Intriguingly, *A. junii* is much more common in the fecal microbiome of Indian infants delivered by vaginal birth than cesarean [129] and exposure of cesarean infants to maternal vaginal fluid improved some aspects of neurodevelopment [207]. There may be some benefit then to vitamin K deficiency at birth if it allows more organism migration.

## 4. DISCUSSION

This analysis is only an outline of what could become a more complex or rigorous analysis given enough information on organism pathways and metabolic state along with algorithms or "AI." However, from this initial manual investigation several interesting observations can be considered.

### 4.1. Informing Interventions

Many aspects of old-age disease may be more an issue of frailty than anything else. As this resembles classical starvation, it motivates an interest in more subtle forms of nutrient deprivation in old age. In fact a 2023 work suggested that frailty more than age per se correlated with covid-19 severity as well as cognitive issues [104]. A link between sarcopenia and cognition is suspected in general at least in some populations [83]. However, attempts at clinical trials of specific nutrients are not likely to work well without some understanding of cause and effect leading to the problem. A single point of failure may require multiple vitamins be replaced or that issues of solubility be addressed. Real world anecdotes may have some merit as specific vitamins are combined with "other stuff." In the present case, the data point to specific nutrients but that does not exclude the loss of other nutrients that obstruct flow of these nutrients. Based on the following considerations, improving stomach acid may be a simple approach to explore along with supplements of the missing nutrients.

I outlined a lot of unpublished work in my initial response to covid-19 including the specific problems with low stomach acid and issues with emphasizing tryptophan, tyrosine, and vitamin K [99]. While not considered originally, it later turned out that histidine may be a factor in older age and correspondingly in covid-19 [93]. Some of the issues related to nutrient mix and solubility are explored in work with dogs [97] [95] [94] [96] . A 2022 literature review tends to support that amino acid fluxes in sarcopenia, in essence frailty, reflect low tryptophan levels [34],

However, a study showed that the levels of isoleucine, leucine, tryptophan, serotonin, and methionine in the participants with low muscle quality were significantly higher than that in the participants with high muscle quality, which may be attributed to impaired metabolism of amino acids, resulting in reduced uptake of skeletal muscle, and thus increased circulating plasma amino acid levels (15). Inconsistencies in amino acid profiles in patients with sarcopenia will lead to variations in clinical practice and research.

even if low blood levels of Trp are not observed, I have called this "stress transport" or mention dynamics [93]. There is a related issue with biotin, for example, where the liver imports less during starvation while brain metabolism is largely preserved [125] and you could consider export in response to other signals. It is known that Trp consumed with BCAA's may not be well transported to the CNS presumably raising blood levels but not brain levels although magnitudes and clinical relevance in athletes are a matter of debate [14] [175] and competition with other nutrients may vary with age [120]. See also Appendix C.

#### Thinking aloud

there is a recurring problem with equating a blood level with a production or consumption rate when the sources and sinks or rate equations are not known to be stable.

As methanol appears to be influencing the microbiome in the diseased state, it may be prudent to minimize production. While control of methyl donors may be a part of the solution, pH control of the stomach may be important. In fruit mashes, fermentation pH can be a large factor in methanol production as well as pectin content [15]. Reduction of acidity from 2.5 to pH 3.5 may almost double methanol content. Interestingly, endogenous production of ethanol from consumed sugars may be reduced with citric acid consumption [44] while no direct experiments with methanol production have been found in the literature yet. PPI usage has a controversial relationship to dementia in general. One recent study found a significant increase after years of usage [119] and another 2022 study found associations including a bias towards APOE4 carriers [202]. Although some meta-analyses and reviews have concluded the association is not there [20] or only a problem in those using two rather than one type of PPI [170]. In cases of discordant results, it helps to look at details and meta-analyses may include issues like too low a dose, too little lag time or confounding factors. Results may vary with population as the users and non users were not randomized. In general, stomach acid is expected to decrease with age and the use of PPI's is being questioned [106] since they may not have much impact except for limited indications. Low stomach acid is just one of many possible conditions that impair nutrient uptake in aging populations. However, it appears to be easy to correct with more dietary acids, such as citric, acetic, or phosphoric in diet soft drinks, taken with meals. At least in humans, with Diet Coke has been used before to aid dissolution of accumulated matter [71]. Note also that "short chain fatty acids" ( including butyrate and acetate ) often associated with microbiome and health through many specific mechanisms [152], are themselves acids although overall effect on GI tract pH distribution would need to be explored. Interestingly, methanol can also be

bioconverted into butyrate [35] which is probably not as beneficial to the organism as methanol oxidation. Some of the regulatory issues have been worked out in controlled settings [60] Chloride sources may include potassium chloride with meals. As ethanol consumption inherently generates methanol while also preventing methanol conversion into toxic formaldehyde [41] , the resulting effects may be moderated and could change "sign". The work with dogs continues to focus on combinations similar to deep eutectic solvents i[96]. The association of AD with APOE4 may in fact be related to transport of lipid soluble nutrients.

#### Thinking outloud

( and at least one topology with methanol and formate is interesting as functionally the toxic product formate would encourage consumption of the parent - at least appearance-wise similar probably to Trp and coagulation "cascades" )

If there is a specific organism group driving clinical dementia it still needs to be better defined as there may be risks to symbiotics with broad antibiotic treatments. Further work can be considered to obtain phenotype information such as microbial mRNA analysis and microbiomes of younger brains with known fetal and peri-natal exposure histories. Microbes then could be contributory through many mechanisms. Besides direct infection of the brain and production of toxic metabolites, modulation of nutrient availability could be achieved by direct metabolism and damage to the GI tract. The former is discussed for choline and SARS-Cov-2 is likely to cause GI damage possibly related to ACE2 and therefore tryptophan transport. As this likely accumulates with age and reaches a positive feedback stage where lack of nutrients leads to further GI decay, it could explain age distributions. On the other hand, microbes in the brain make a functional measure of the brain environment at least for bacteria. The ecology may be reflected in abundances and phenotype information from mRNA of the more flexible organisms may further help interpretation. Rate equations accounting for sources and sinks of nutrients are probably needed in many cases or machine learning/AI.

Previously published dog diets [95] [102] are similar to an unpublished baseline diet for humans that I had outlined but more specific ones could be made now. Recent experience has suggested a role for things such as benzoate which may improve solubility and uptake from GI tract of have other benefits[95] and should be a subject of a future work based on experience with dogs. Nutrient context will likely matter as much as amount. A concentrated concern for lipid solubles may be warranted.

Additionally, uncontrolled observations during food preparation suggest salmon broth and vinegar both appear to help dissolve components such as hardboiled egg yolk. For humans, ethanol may also be beneficial explaining inconsistent health benefits associated with alcohol consumption as they may only occur when consumed with appropriate food containing otherwise inaccessible nutrients.

In the case of vascular pathology such as CAA, the best remedy restore the healthy surface with normal populations of transporters. The CAA may itself be due to nutrient deficiencies and eventually correct itself but in the meantime surpluses may achieve similar results by diffusion.

Interpretation in part is difficult due to operating through taxonomy which is a combination of historical observations with some modifications for molecular "closeness." Phenotype and even genotype/plasmids are not known but may be inferred from the 16s sequence and overall ecology likely to host the given abundance sets. Adding mRNA data may reduce ambiguity with expression of nutrient synthesis or acquisition genes or known lifestyles invoked in known environments. Another approach may be to look only at the complete 16s sequence reads and determine if particular fragments or signatures segregate to disease or control and if they mean anything about phenotype range. This is a bit speculative but there is existing literature to classify organisms based only on 16s patterns for such features as temperature range [139] as this is a functional part of the ribosome.

#### 4.2. Plant Symbionts in Brain : Coincidence or Nurse Bacteria ?

The appearance of plant symbionts in the CNS and endometrium is intriguing if accurate although it could simply be the result of "literature skew" and coincidence. Some works do suggest that plant-associated organisms have specific genetic features [80] pointing to the possible significance of plant associated organisms in the brain microbiome. It would be helpful to determine where they are and how they have been missed for so long. Possibly many exist as spores or other condensed or quiescent forms. Consideration of the isolation methods may be worthwhile. If true, it may be purely coincidental but the known structure of the brain involves compartmentalized metabolism with astrocytes already acting as "nurse cells" to provide lactate to neurons for peak energy demands [133]. The existence of prokaryotic nurse cells would not be unreasonable if they are common in the conception environment. Implications for brain evolution could be significant. The status of "immune privilege" [140] then may be as much to nurture bacteria as neurons. As a BBB does not exist at conception, that is a unique opportunity to capture symbionts.

## 5. CONCLUSION

The top-line microbiome patterns of the subject paper [111] can be interpreted as demonstrating a role for symbiotic organisms acquired as early as conception or the peri-natal period combined with measurement of the brain environment properties likely to be important to neuronal functioning. The organisms more abundant in the control brains may thrive in a setting rich in amino acid derived neurotransmitter skeletons or may be beneficial for plants and consequentially or coincidentally have similar relationships to brain by aiding nutrient uptake. They generally are more competitive in environments presumed healthy for the brain and maybe with some toxic metals present. Those more abundant in the AD brain almost exclusively would benefit from presumed deleterious states of depleted 5HT, increased iron ( speculating heme derived ), and increased methanol from endogenous metabolism. The skin resident bacteria are notable as potential pathogens able to cause brain damage. Further work should explore larger patterns of possible pathogen involvement in clinical progression. While likely coincidental, the growth of axons seeking connections and roots seeking nutrients may have some similarities that facilitate symbiotic associations.

A lot of unrelated results can be unified into a nutritional framework with tryptophan being one of the prominent recurring components. Earlier predictions emphasizing Trp, Tyr, and vitamin K for covid-19 have not been significantly tested but evolving evidence explored in the light of cause and effect rather than specific coincidences supports their utility in old age conditions. Further work on microbial patterns including metabolic phenotype may be helpful. Nutritional experiments probably need to be more comprehensive including several nutrients, excluding others, and including solubility enhancements perhaps similar to those employed by the organisms overabundant in the healthy brains. Microbiomes from a wider variety of brains including much younger may help determine if any organisms are hosted during early life. A lot of metabolic information exists in the literature in scattered forms perhaps AI would be a good way to investigate nutrient patterns. And its important to continue to question assumptions just in case lead can make your garden grow and feed your head.

## 6. SUPPLEMENTAL INFORMATION

### 6.1. Computer Code

## 7. BIBLIOGRAPHY

- 
- [1] Ludovico Alisi, Roberta Cao, Cristina De Angelis, Arturo Cafolla, Francesca Caramia, Gaia Cartocci, Aloisa Librando, and Marco Fiorelli. The relationships between vitamin k and cognition: A review of current evidence. *Frontiers in Neurology*, 10, 2019. Available from: <https://www.frontiersin.org/articles/10.3389/fneur.2019.00239>, doi:10.3389/fneur.2019.00239.
  - [2] Toby D Allen, Paul A Lawson, Matthew D Collins, Enevold Falsen, and Ralph S Tanner. Cloacibacterium normanense gen. nov., sp. nov., a novel bacterium in the family flavobacteriaceae isolated from municipal wastewater. *International journal of systematic and evolutionary microbiology*, pages 1311–1316, Jun 2006. Available from: <https://pubmed.ncbi.nlm.nih.gov/16738108/>, doi:10.1099/ijs.0.64218-0.
  - [3] A.C. Allison. The possible role of vitamin k deficiency in the pathogenesis of alzheimer’s disease and in augmenting brain damage associated with cardiovascular disease. *Medical Hypotheses*, 57(2):151–155, 2001. Available from: <https://www.sciencedirect.com/science/article/pii/S0306987701913076>, doi:https://doi.org/10.1054/mehy.2001.1307.
  - [4] Monica Alvarez-Cordoba, Diana Reche-Lopez, Paula Cilleros-Holgado, Marta Talaveron-Rey, Irene Villalon-Garcia, Suleva Povea-Cabello, Juan M Suarez-Rivero, Alejandra Suarez-Carrillo, Manuel Munuera-Cabeza, Rocio Pinero-Perez, and Jose A Sanchez-Alcazar. Therapeutic approach with commercial supplements for pantothenate kinase-associated neurodegeneration with residual pank2 expression levels. *Orphanet journal of rare diseases*, page 311, 08 2022. Available from: <https://pubmed.ncbi.nlm.nih.gov/35945593/>, doi:10.1186/s13023-022-02465-9.
  - [5] Erin H. Amerson, Herbert B. Castillo Valladares, and Kieron S. Leslie. Resurgence of syphilis in the uspsptf reaffirms screening guidelines. *JAMA Dermatology*, 158, 11 2022. Available from: <http://dx.doi.org/10.1001/jamadermatol.2022.3499>, doi:10.1001/jamadermatol.2022.3499.
  - [6] P. P. Aparna and S. Meignanalakshmi. Comparison of power generation of electrochemically active bacteria isolated from the biofilm of single chambered multi-electrode microbial fuel cell developed using *capra hircus* rumen fluid. *Energy Sources, Part A: Recovery, Utilization, and Environmental Effects*, 38. Available from: <http://dx.doi.org/10.1080/15567036.2013.835363>, doi:10.1080/15567036.2013.835363.



- [7] Sriram Balusu, Katrien Horré, Nicola Thrupp, Katleen Craessaerts, An Snellinx, Lutgarde Serneels, Dries T'Syen, Iordana Chrysidou, Amaia M. Arranz, Annerieke Sierksma, Joel Simrén, Thomas K. Karikari, Henrik Zetterberg, Wei-Ting Chen, Dietmar Rudolf Thal, Evgenia Salta, Mark Fiers, and Bart De Strooper. Meg3 activates necroptosis in human neuron xenografts modeling alzheimer's disease. *Science*, 381, 09 2023. Available from: <http://dx.doi.org/10.1126/science.abp9556>, doi:10.1126/science.abp9556.
- [8] Oz Barazani and Jacob Friedman. Effect of exogenously applied l-tryptophan on allelochemical activity of plant-growth-promoting rhizobacteria (pgpr). *Journal of Chemical Ecology*, 26(2):343–349, Feb 2000. Available from: <https://doi.org/10.1023/A:1005449119884>, doi:10.1023/A:1005449119884.
- [9] Djahanschiri Bardya, Di Venanzio Gisela, Distel Jesus S., Breisch Jennifer, Dieckmann Marius Alfred, Goesmann Alexander, Averhoff Beate, Göttig Stephan, Wilharm Gottfried, Feldman Mario F., and Ingo Ebersberger. Evolutionarily stable gene clusters shed light on the common grounds of pathogenicity in the acinetobacter calcoaceticus-baumannii complex. *PLOS Genetics*, 18(6):1–40, 06 2022. Available from: <https://doi.org/10.1371/journal.pgen.1010020>, doi:10.1371/journal.pgen.1010020.
- [10] Barbara Bartolini, Cristina Corniello, Antonio Sella, Francesca Somma, and Vincenzo Politi. *The Enol Tautomer of Indole-3-Pyruvic Acid as A Biological Switch in Stress Responses*, pages 601–608. Springer US, Boston, MA, 2003. Available from: [https://doi.org/10.1007/978-1-4615-0135-0\\_69](https://doi.org/10.1007/978-1-4615-0135-0_69), doi:10.1007/978-1-4615-0135-0\_69.
- [11] Fabiola Bastian, Claude Alabouvette, Valme Jurado, and Cesareo Saiz-Jimenez. Impact of biocide treatments on the bacterial communities of the lascaux cave. *Naturwissenschaften*, 96(7):863–868, Jul 2009. Available from: <https://doi.org/10.1007/s00114-009-0540-y>, doi:10.1007/s00114-009-0540-y.
- [12] Yoshimi Benno, Ken Sawada, and Tomotari Mitsuoka. The intestinal microflora of infants: Fecal flora of infants with vitamin k deficiency. *Microbiology and Immunology*, 29, 1985. Available from: <http://dx.doi.org/10.1111/j.1348-0421.1985.tb00823.x>, doi:10.1111/j.1348-0421.1985.tb00823.x.
- [13] Petra Beznoskov, Laure Bidou, Olivier Namy, and Leo Shivaya Valek. Increased expression of tryptophan and tyrosine trnas elevates stop codon readthrough of reporter systems in human cell lines. *Nucleic Acids Research*, pages 5202–15, 05 2021. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8136774/>, doi:10.1093/nar/gkab315.
- [14] Eva Blomstrand. A role for branched-chain amino acids in reducing central fatigue. *The Journal of nutrition*, pages 544S–547S, Feb 2006. Available from: <https://pubmed.ncbi.nlm.nih.gov/16424144/>, doi:10.1093/jn/136.2.544S.
- [15] Patrik Blumenthal, Marc Steger, Daniel Einfalt, Jörg Rieke-Zapp, Andrès Quintanilla Bellucci, Katharina Sommerfeld, Steffen Schwarz, and Dirk Lachenmeier. Methanol mitigation during manufacturing of fruit spirits with special consideration of novel coffee cherry spirits. *Molecules*, 26, 2021. Available from: <http://dx.doi.org/10.3390/molecules26092585>, doi:10.3390/molecules26092585.
- [16] P. J. M. Bouvet and P. A. D. Grimont. Taxonomy of the genus acinetobacter with the recognition of acinetobacter baumannii sp. nov., acinetobacter haemolyticus sp. nov., acinetobacter johnsonii sp. nov., and acinetobacter junii sp. nov. and emended descriptions of acinetobacter calcoaceticus and acinetobacter lwoffii. *International Journal of Systematic Bacteriology*, 36, 04 1986. Available from: <http://dx.doi.org/10.1099/00207713-36-2-228>, doi:10.1099/00207713-36-2-228.
- [17] Lyudmila Boyanova. *Cutibacterium acnes* (formerly *propionibacterium acnes*): friend or foe? *Future Microbiology*, 18, 2023. Available from: <http://dx.doi.org/10.2217/fmb-2022-0191>, doi:10.2217/fmb-2022-0191.
- [18] Holger Brüggemann, Llanos Salar-Vidal, Harald M. Gollnick, and Rolf Lood. A janus-faced bacterium: Host-beneficial and -detrimental roles of cutibacterium acnes. *Frontiers in Microbiology*, 12, 2021. Available from: <https://www.frontiersin.org/articles/10.3389/fmicb.2021.673845>, doi:10.3389/fmicb.2021.673845.
- [19] S. Burdman and Walcott R. R., editors. *Plant-Pathogenic Acidovorax Species*. The American Phytopathological Society, 2018. Available from: <http://dx.doi.org/10.1094/9780890546062>, doi:10.1094/9780890546062.
- [20] Catarina Caetano, Marta Veloso, and Susana Borda. Proton pump inhibitors and dementia: what association? *Dementia & Neuropsychologia*. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10229084/>, doi:10.1590/1980-5764-DN-2022-0048.
- [21] David H. Calhoun, Duane L. Pierson, and Roy A. Jensen. Channel-shuttle mechanism for the regulation of phenylalanine and tyrosine synthesis at a metabolic branch point in *pseudomonas aeruginosa*. *Journal of Bacteriology*, 113, 1973. Available from: <http://dx.doi.org/10.1128/jb.113.1.241-251.1973>, doi:10.1128/jb.113.1.241-251.1973.
- [22] Clare-Ann Canfield and Patrick C. Bradshaw. Amino acids in the regulation of aging and aging-related diseases. *Translational Medicine of Aging*, 3:70–89, 2019. Available from: <https://www.sciencedirect.com/science/article/pii/S2468501119300082>, doi:https://doi.org/10.1016/j.tma.2019.09.001.
- [23] Anna Barra Caracciolo and Valentina Terenzi. Rhizosphere microbial communities and heavy metals. *Microorganisms*, 9, 2021. Available from: <http://dx.doi.org/10.3390/microorganisms9071462>, doi:10.3390/microorganisms9071462.
- [24] Emma L. Carr, Peter Kämpfer, Bharat K. C. Patel, Volker Gürtler, and Robert J. Seviour. Seven novel species of acinetobacter isolated from activated sludge. *International Journal of Systematic and Evolutionary Microbiology*, 53, 07 2003. Available from: <http://dx.doi.org/10.1099/ijs.0.02486-0>, doi:10.1099/ijs.0.02486-0.
- [25] Lorena Carro, Raúl Rivas, Milagros León-Barrios, María González-Tirante, Encarna Velázquez, and Angel Valverde. *Herbaspirillum canariense* sp. nov., *herbaspirillum aurantiacum* sp. nov. and *herbaspirillum soli* sp. nov., isolated from volcanic mountain soil, and emended description of the genus *herbaspirillum*. *International Journal of Systematic and Evolutionary Microbiology*, 62, 06 2012. Available from: <http://dx.doi.org/10.1099/ijs.0.031336-0>, doi:10.1099/ijs.0.031336-0.
- [26] Anirban Chakraborty, Eric E. Roden, Jrgen Schieber, and Flynn Picardal. Enhanced growth of acidovorax sp. strain 2an during nitrate-dependent fe(ii) oxidation in batch and continuous-flow systems. *Applied and Environmental Microbiology*,

- pages 8548–56, Dec 2011. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3233087/>, doi:10.1128/AEM.06214-11.
- [27] Anirban Chakraborty, Eric E. Roden, Jürgen Schieber, and Flynn Picardal. Enhanced growth of acidovorax sp. strain 2an during nitrate-dependent fe(ii) oxidation in batch and continuous-flow systems. *Applied and Environmental Microbiology*, 77, 12 2011. Available from: <http://dx.doi.org/10.1128/aem.06214-11>, doi:10.1128/aem.06214-11.
  - [28] Yuyang Cheng, Jinhang Luo, Yixuan Wang, Jianzhen Ge, Shanshan Zhou, Wenquan Yang, and Jiancun Kou. Staphylococcus hominis yj1ljh and staphylococcus epidermidis yj101 promote the growth of white clover (trifolium repens l.) by increasing available phosphorus. *Symbiosis*, 83(1):103–114, Jan 2021. Available from: <https://doi.org/10.1007/s13199-020-00739-z>, doi:10.1007/s13199-020-00739-z.
  - [29] Denny Chin, Mariya I. Goncheva, Ronald S. Flannagan, Shayna R. Deecker, Veronica Guariglia-Oropeza, Alexander W. Ensminger, and David E. Heinrichs. Coagulase-negative staphylococci release a purine analog that inhibits staphylococcus aureus virulence. *Nature Communications*, 12, 03 2021. Available from: <https://www.nature.com/articles/s41467-021-22175-3>, doi:10.1038/s41467-021-22175-3.
  - [30] Yau-Jan Chyan, Burkhard Poeggeler, Rawhi A. Omar, Daniel G. Chain, Blas Frangione, Jorge Ghiso, and Miguel A. Pappolla. Potent neuroprotective properties against the alzheimer upbeta-amyloid by an endogenous melatonin-related indole structure, indole-3-propionic acid. *Journal of Biological Chemistry*, 274, 1999. Available from: <http://dx.doi.org/10.1074/jbc.274.31.21937>, doi:10.1074/jbc.274.31.21937.
  - [31] Sona Ciernikova, Aneta Sevcikova, Viola Stevurkova, and Michal Mego. Tumor microbiome - an integral part of the tumor microenvironment. *Frontiers in Oncology*, 12, 11 2022. Available from: <http://dx.doi.org/10.3389/fonc.2022.1063100>, doi:10.3389/fonc.2022.1063100.
  - [32] Jan Claesen, Jennifer B Spagnolo, Stephany Flores Ramos, Kenji L Kurita, Allyson L Byrd, Alexander A Aksenov, Alexey V Melnik, Weng R Wong, Shuo Wang, Ryan D Hernandez, Mohamed S Donia, Pieter C Dorrestein, Heidi H Kong, Julia A Segre, Roger G Linington, Michael A Fischbach, and Katherine P Lemon. A cutibacterium acnes antibiotic modulates human skin microbiota composition in hair follicles. *Science translational medicine*, Nov 2020. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8478231/>, doi:10.1126/scitranslmed.aay5445.
  - [33] John D. Coates. Uranium immobilization through fe(ii) bio-oxidation: A column study, 09 2009. Available from: <http://dx.doi.org/10.2172/1122941>, doi:10.2172/1122941.
  - [34] Miao Dai, Taiping Lin, Jirong Yue, and Lunzhi Dai. Signatures and clinical significance of amino acid flux in sarcopenia: A systematic review and meta-analysis. *Frontiers in Endocrinology*, 12, 2021. Available from: <https://www.frontiersin.org/articles/10.3389/fendo.2021.725518>, doi:10.3389/fendo.2021.725518.
  - [35] Rathin Datta and Jacqueline Ogeltree. Methanol bioconversion by *butyribacterium methylotrophicum* batch fermentation yield and kinetics. *Biotechnology and Bioengineering*, 25, 1983. Available from: <http://dx.doi.org/10.1002/bit.260250409>, doi:10.1002/bit.260250409.
  - [36] Oriol de Fabregues, Maria Selles, David Ramos-Vicente, Gerard Roch, Miquel Vila, and Jordi Bove. Relevance of tissue-resident memory cd8 t cells in the onset of parkinson’s disease and examination of its possible etiologies: infectious or autoimmune? *Neurobiology of disease*, page 106308, 09 2023. Available from: <https://pubmed.ncbi.nlm.nih.gov/37741513/>, doi:10.1016/j.nbd.2023.106308.
  - [37] Kasper D. de Leeuw, Sanne M. de Smit, Sabine van Oossanen, Marinus J. Moerland, Cees J. N. Buisman, and David P. B. T. B. Strik. Methanol-based chain elongation with acetate to n-butyrate and isobutyrate at varying selectivities dependent on ph. *ACS Sustainable Chemistry & Engineering*, 8, 06 2020. Available from: <http://dx.doi.org/10.1021/acssuschemeng.0c00907>, doi:10.1021/acssuschemeng.0c00907.
  - [38] Rocheli de Souza, Adriana Ambrosini, and Luciane M.P. Passaglia. Plant growth-promoting bacteria as inoculants in agricultural soils. *Genetics and Molecular Biology*, pages 401–19, Oct-Dec 2015. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4763327/>, doi:10.1590/S1415-475738420150053.
  - [39] Itaru Dekio, Andrew McDowell, Mitsuo Sakamoto, Shuta Tomida, and Moriya Ohkuma. Proposal of new combination, cutibacterium acnes subsp. elongatum comb. nov., and emended descriptions of the genus cutibacterium, cutibacterium acnes subsp. acnes and cutibacterium acnes subsp. defendens. *International Journal of Systematic and Evolutionary Microbiology*, 69, 04 2019. Available from: <http://dx.doi.org/10.1099/ijsem.0.003274>, doi:10.1099/ijsem.0.003274.
  - [40] Elena DiezCecilia, Igri Kolaj, Clarissa Santos, Imindu Liyanage, Braden Sweeting, Paul Stafford, Robert Boudreau, G. Andrew Reid, Ryan S. Noyce, Leanne Stevens, Agnieszka Staniszewski, Hong Zhang, Mamidanna R. V. S. Murty, Pascale Lemaire, Solenne Chardonnet, Christopher D. Richardson, Valérie Gabelica, Edwin DePauw, Richard Brown, Sultan Darvesh, Ottavio Arancio, Donald F. Weaver, Felix S. MeierStephenson, Vanessa C. MeierStephenson, Michael D. Carter, Autumn R. Meek, Yanfei Wang, Luzhe Pan, Qiangwei Chen, Sheila Jacobo, Fan Wu, Erhu Lu, Gordon A. Simms, Laural Fisher, Alaina J. McGrath, Virgil Fermo, Christopher J. Barden, Harman D.S. Clair, Todd N. Galloway, Arun Yadav, Valérie CampagnaSlater, Mark Hadden, Mark Reed, Marcia Taylor, and Brendan Kelly. Alzheimer’s disease as an autoimmune disorder of innate immunity endogenously modulated by tryptophan metabolites. *Alzheimer’s & Dementia: Translational Research & Clinical Interventions*, 8, 2022. Available from: <http://dx.doi.org/10.1002/trc2.12283>, doi:10.1002/trc2.12283.
  - [41] Yuri L. Dorokhov, Anastasia V. Shindyapina, Ekaterina V. Sheshukova, and Tatiana V. Komarova. Metabolic methanol: Molecular pathways and physiological roles. *Physiological Reviews*, 95, 2015. Available from: <http://dx.doi.org/10.1152/physrev.00034.2014>, doi:10.1152/physrev.00034.2014.
  - [42] Yuri L. Dorokhov, Anastasia V. Shindyapina, Ekaterina V. Sheshukova, and Tatiana V. Komarova. Metabolic methanol: molecular pathways and physiological roles. *Physiological reviews*, pages 603–44, Apr 2015. Available from: <https://pubmed.ncbi.nlm.nih.gov/25834233/>, doi:10.1152/physrev.00034.2014.

- [43] Hamuel James Doughari, Patrick Alois Ndakidemi, Izanne Susan Human, and Spinney Benade. The ecology, biology and pathogenesis of *acinetobacter* spp.: An overview. *Microbes and Environments*, 26(2):101–112, 2011. Available from: [https://www.jstage.jst.go.jp/article/jsme2/26/2/26\\_ME10179/\\_pdf](https://www.jstage.jst.go.jp/article/jsme2/26/2/26_ME10179/_pdf), doi:10.1264/jsme2.ME10179.
- [44] Fouad F. Elshagabee, Wilhelm Bockelmann, Diana Meske, Michael de Vrese, Hans-Georg Walte, Juergen Schrezenmeir, and Knut J. Heller. Ethanol production by selected intestinal microorganisms and lactic acid bacteria growing under different nutritional conditions. *Frontiers in Microbiology*, 7, 2016. Available from: <https://www.frontiersin.org/articles/10.3389/fmicb.2016.00047>, doi:10.3389/fmicb.2016.00047.
- [45] Ernesto Fedele. Anti-amyloid therapies for alzheimer’s disease and the amyloid cascade hypothesis. *International journal of molecular sciences*, 09 2023. Available from: <https://pubmed.ncbi.nlm.nih.gov/37833948/>, doi:10.3390/ijms241914499.
- [46] Kazuki Fukumoto, Kakeru Ito, Benjamin Saer, George Taylor, Shiqi Ye, Mayu Yamano, Yuki Toriba, Andrew Hayes, Hitoshi Okamura, and Jean-Michel Fustin. Excess s-adenosylmethionine inhibits methylation via catabolism to adenine. *Communications Biology*, 5, 04 2022. Available from: <https://www.nature.com/articles/s42003-022-03280-5>, doi:10.1038/s42003-022-03280-5.
- [47] Satoshi Furukawa, Masayoshi Abe, Koji Usuda, and Izumi Ogawa. Indole-3-acetic acid induces microencephaly in rat fetuses. *Toxicologic Pathology*, 32, 2004. Available from: <http://dx.doi.org/10.1080/01926230490520269>, doi:10.1080/01926230490520269.
- [48] Satoshi Furukawa, Koji Usuda, Masayoshi Abe, Seigo Hayashi, and Izumi Ogawa. Indole-3-acetic acid induces microencephaly in mouse fetuses. *Experimental and Toxicologic Pathology*, 59(1):43–52, 2007. Available from: <https://www.sciencedirect.com/science/article/pii/S0940299307000024>, doi:https://doi.org/10.1016/j.etp.2006.12.001.
- [49] Kan Gao, Chun-long Mu, Aitak Farzi, and Wei-yun Zhu. Tryptophan metabolism: A link between the gut microbiota and brain. *Advances in Nutrition*, pages 709–23, 12 2019. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7231603/>, doi:10.1093/advances/nmz127.
- [50] Mauro Giuffrè, Michele Campigotto, Giuseppina Campisciano, Manola Comar, and Lory Saveria Crocè. A story of liver and gut microbes: how does the intestinal flora affect liver disease? a review of the literature. *American Journal of Physiology-Gastrointestinal and Liver Physiology*, 318, 05 2020. Available from: <http://dx.doi.org/10.1152/ajpgi.00161.2019>, doi:10.1152/ajpgi.00161.2019.
- [51] Lorena Jacqueline Gómez-Godínez, José Luis Aguirre-Noyola, Esperanza Martínez-Romero, Ramón Ignacio Arteaga-Garibay, Javier Ireta-Moreno, and José Martín Ruvalcaba-Gómez. A look at plant-growth-promoting bacteria. *Plants*, 12, 2023. Available from: <http://dx.doi.org/10.3390/plants12081668>, doi:10.3390/plants12081668.
- [52] Emmanuel Gonzalez, Nicholas B. Brereton, Chen Li, Lilian Lopez Leyva, Noel W. Solomons, Luis B. Agellon, Marilyn E. Scott, and Kristine G. Koski. Distinct changes occur in the human breast milk microbiome between early and established lactation in breastfeeding guatemalan mothers. *Frontiers in Microbiology*, 02 2021. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7907006/>, doi:10.3389/fmicb.2021.557180.
- [53] Vinicius GoularteSilva and Luciana Campos Paulino. Ketoconazole beyond antifungal activity: Bioinformaticsbased hypothesis on lipid metabolism in dandruff and seborrheic dermatitis. *Experimental Dermatology*, 31, 2022. Available from: <http://dx.doi.org/10.1111/exd.14505>, doi:10.1111/exd.14505.
- [54] Stefanie Grabrucker, Moira Marizzoni, Edina SilajdUx017e[bad char vv=382]iUx0107[bad char vv=263], Nicola Lopizzo, Elisa Mombelli, Sarah Nicolas, Sebastian Dohm-Hansen, Catia Scassellati, Davide Vito Moretti, Melissa Rosa, Karina Hoffmann, John F Cryan, Olivia F O’Leary, Jane A English, Aonghus Lavelle, Cora O’Neill, Sandrine Thuret, Annamaria Cattaneo, and Yvonne M Nolan. Microbiota from Alzheimer’s patients induce deficits in cognition and hippocampal neurogenesis. *Brain*, page awad303, 10 2023. Available from: <https://doi.org/10.1093/brain/awad303>, arXiv: <https://academic.oup.com/brain/advance-article-pdf/doi/10.1093/brain/awad303/52031863/awad303.pdf>, doi:10.1093/brain/awad303.
- [55] Giacomo Gravina, Maryam Ardalan, Tetyana Chumak, Halfdan Rydbeck, Xiaoyang Wang, Carl Joakim Ek, and Carina Mallard. Transcriptome network analysis links perinatal *staphylococcus epidermidis* infection to microglia reprogramming in the immature hippocampus. *Glia*, 71, 2023. Available from: <http://dx.doi.org/10.1002/glia.24389>, doi:10.1002/glia.24389.
- [56] George T Grossberg. Cholinesterase inhibitors for the treatment of alzheimer’s disease:: Getting on and staying on. *Current Therapeutic Research, Clinical and Experimental*, pages 216–35, Apr 2003. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4052996/>, doi:10.1016/S0011-393X(03)00059-6.
- [57] Sevag Hamamah, Armin Aghazarian, Anthony Nazaryan, Andras Hajnal, and Mihai Covasa. Role of microbiota-gut-brain axis in regulating dopaminergic signaling. *Biomedicines*, 10, 2022. Available from: <http://dx.doi.org/10.3390/biomedicines10020436>, doi:10.3390/biomedicines10020436.
- [58] Susse Kerkelund Hansen, Janus J. Haagensen, Morten Gjermansen, Thomas Martini Jrgensen, Tim Tolker-Nielsen, and Sren Molin. Characterization of a pseudomonas putida rough variant evolved in a mixed-species biofilm with acinetobacter sp. strain c6. *Journal of Bacteriology*, pages 4932–43, 04 2007. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1913468/>, doi:10.1128/JB.00041-07.
- [59] Jae-Hyeok Heo, Dong-Gyu Im, Seung-Hyeon Lee, and Jin-Young Ahn. The clinical significance of brain microbleeds in patients with alzheimer’s disease: Preliminary study. *Annals of Indian Academy of Neurology*, pages 495–8, Oct-Dec 2016. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5144472/>, doi:10.4103/0972-2327.194426.
- [60] Jonathan R. Humphreys, Skyler D. Hebdon, Holly Rohrer, Lauren Magnusson, Chris Urban, Yi-Pei Chen, and Jonathan Lo. Establishing *butyribacterium methylotrophicum* as a platform organism for the production of biocommodities from liquid c<sub>1</sub> metabolites. *Applied and Environmental Microbiology*, 88, 03 2022. Available from: <http://dx.doi.org/10.1128/AEM.01111.2022>, doi:10.1128/AEM.01111.2022.



- 1128/aem.02393-21, doi:10.1128/aem.02393-21.
- [61] Vassilena Iankova, Ivan Karin, Thomas Klopstock, and Susanne A. Schneider. Emerging disease-modifying therapies in neurodegeneration with brain iron accumulation (nbia) disorders. *Frontiers in Neurology*, 12, 2021. Available from: <https://www.frontiersin.org/articles/10.3389/fneur.2021.629414>, doi:10.3389/fneur.2021.629414.
  - [62] Vojtechova Iveta, Machacek Tomas, Kristofikova Zdenka, Stuchlik Ales, and Tomas Petrasek. Infectious origin of alzheimer's disease: Amyloid beta as a component of brain antimicrobial immunity. *PLOS Pathogens*, 18(11):1–25, 11 2022. Available from: <https://doi.org/10.1371/journal.ppat.1010929>, doi:10.1371/journal.ppat.1010929.
  - [63] Ru Jia, Dongqing Yang, Dake Xu, and Tingyue Gu. Mitigation of a nitrate reducing pseudomonas aeruginosa biofilm and anaerobic biocorrosion using ciprofloxacin enhanced by d-tyrosine. *Scientific Reports*, 7, 07 2017. Available from: <https://www.nature.com/articles/s41598-017-07312-7>, doi:10.1038/s41598-017-07312-7.
  - [64] Xiaoyan Jia, Chang He, Weibo Jiang, Chuang Wen, Fan Gao, Guangzhen Jiang, Xiangfei Li, Cheng Chi, Wenbin Liu, and Dingdong Zhang. Identification of potential pathways whereby dietary l-tryptophan ameliorates the glucose metabolic disorder of blunt snout bream through long non-coding rnas. *Aquaculture*, 545:737256, 2021. Available from: <https://www.sciencedirect.com/science/article/pii/S0044848621009194>, doi:https://doi.org/10.1016/j.aquaculture.2021.737256.
  - [65] Shams Tabrez Khan and Akira Hiraishi. Diaphorobacter nitroreducens> gen. nov., sp. nov., a poly(3hydroxybutyrate) degrading denitrifying bacterium isolated from activated sludge. *The Journal of General and Applied Microbiology*, 48(6):299–308, 2002. Available from: [https://www.jstage.jst.go.jp/article/jgam/48/6/48\\_6\\_299/\\_pdf/-char/en](https://www.jstage.jst.go.jp/article/jgam/48/6/48_6_299/_pdf/-char/en), doi:10.2323/jgam.48.299.
  - [66] Thilo Khler, Lasta Kocjancic Curty, Francisco Barja, Christian van Delden, and Jean-Claude Pechre. Swarming of pseudomonas aeruginosa is dependent on cell-to-cell signaling and requires flagella and pili. *Journal of Bacteriology*, pages 5990–6, Nov 2000. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC94731/>.
  - [67] Mia Kim, Seong-Yun Jeong, Su Jeong Yoon, Sun Ja Cho, Young Hun Kim, Min Ju Kim, Eun Yoen Ryu, and Sang-Joon Lee. Aerobic denitrification of pseudomonas putida ad-21 at different c/n ratios. *Journal of bioscience and bioengineering*, pages 498–502, Nov 2008. Available from: <https://pubmed.ncbi.nlm.nih.gov/19111647/>, doi:10.1263/jbb.106.498.
  - [68] Minseo Kim, Sun Jae Park, Seulggie Choi, Jooyoung Chang, Sung Min Kim, Seongsong Jeong, Young Jun Park, Gyeongsil Lee, Joung Sik Son, Joseph C. Ahn, and Sang Min Park. Association between antibiotics and dementia risk: A retrospective cohort study. *Frontiers in Pharmacology*, 13, 2022. Available from: <https://www.frontiersin.org/articles/10.3389/fphar.2022.888333>, doi:10.3389/fphar.2022.888333.
  - [69] Sudarsan Kollimuttathuillam, Nyan Bethel, and Hamid Shaaban. A case of acinetobacter junii cavitary pneumonia with bacteremia in a patient with systemic lupus erythematosus. *Cureus*, 11 2021. Available from: <http://dx.doi.org/10.7759/cureus.19711>, doi:10.7759/cureus.19711.
  - [70] Kairi Koort, Kristiina Sõsa, Silver Türk, Eleri Lapp, Elle Talving, Peeter Karits, Karin Rosenstein, Madis Jaagura, Aire Sekavin, Deniss Sõritsa, Kai Haldre, Helle Karro, Paul Korrovits, Andres Salumets, and Reet Mändar. <i>lactobacillus crispatus</i>-dominated vaginal microbiome and <i>acinetobacter</i>-dominated seminal microbiome support beneficial <sc>art</sc> outcome. *Acta Obstetricia et Gynecologica Scandinavica*, 102, 2023. Available from: <http://dx.doi.org/10.1111/aogs.14598>, doi:10.1111/aogs.14598.
  - [71] Scott J. Kramer and Mark B. Pochapin. Gastric phytobezoar dissolution with ingestion of diet coke and cellulase. *Gastroenterology & Hepatology*, pages 770–2, Nov 2012. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3966177/>.
  - [72] MANJU A KURIAN, ALASDAIR MCNEILL, JEAN-PIERRE LIN, and EAMONN R MAHER. Childhood disorders of neurodegeneration with brain iron accumulation (nbia). *Developmental Medicine & Child Neurology*, 53, 2011. Available from: <http://dx.doi.org/10.1111/j.1469-8749.2011.03955.x>, doi:10.1111/j.1469-8749.2011.03955.x.
  - [73] Anamika Kushwaha, Radha Rani, Sanjay Kumar, Tarence Thomas, Arun Alfred David, and Meraz Ahmed. A new insight to adsorption and accumulation of high lead concentration by exopolymer and whole cells of lead-resistant bacterium acinetobacter junii l. pb1 isolated from coal mine dump. *Environmental Science and Pollution Research*, 24(11):10652–10661, Apr 2017. Available from: <https://doi.org/10.1007/s11356-017-8752-8>, doi:10.1007/s11356-017-8752-8.
  - [74] Mamoru Kyogashima. *Contradictory Functions of The Sulfatide in the Blood Coagulation System*, pages 343–350. Springer US, Boston, MA, 2001. Available from: [https://doi.org/10.1007/978-1-4615-1267-7\\_22](https://doi.org/10.1007/978-1-4615-1267-7_22), doi:10.1007/978-1-4615-1267-7\_22.
  - [75] Lidia La Barbera, Federica Macaluso, Serena Fasano, Giulia Grasso, Francesco Ciccica, and Giuliana Guggino. Microbiome changes in connective tissue diseases and vasculitis: Focus on metabolism and inflammation. *International Journal of Molecular Sciences*, 06 2022. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9224234/>, doi:10.3390/ijms23126532.
  - [76] Richard Lathe, Nikki M. Schultek, Brian J. Balin, Garth D. Ehrlich, Lavinia Alberi Auber, George Perry, Edward B. Breitschwerdt, David B. Corry, Richard L. Doty, Robert A. Rissman, Peter L. Nara, Ruth Itzhaki, William A. Eimer, and Rudolph E. Tanzi. Establishment of a consensus protocol to explore the brain pathobiome in patients with mild cognitive impairment and alzheimer's disease. *Alzheimer's & Dementia*, 06 2023. Available from: <http://dx.doi.org/10.1002/alz.13076>, doi:10.1002/alz.13076.
  - [77] Eun-Sook Lee, Hongtao Chen, Chadwick Hardman, Anthony Simm, and Clivel Charlton. Excessive s-adenosyl-l-methionine-dependent methylation increases levels of methanol, formaldehyde and formic acid in rat brain striatal homogenates: Possible role in s-adenosyl-l-methionine-induced parkinsons disease-like disorders. *Life sciences*, pages 821–7, 10 2008. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2885904/>, doi:10.1016/j.lfs.2008.09.020.

- [78] Jae-Hyeok Lee, Ji Young Yun, Allison Gregory, Penelope Hogarth, and Susan J. Hayflick. Brain mri pattern recognition in neurodegeneration with brain iron accumulation. *Frontiers in Neurology*, 11, 2020. Available from: <https://www.frontiersin.org/articles/10.3389/fneur.2020.01024>, doi:10.3389/fneur.2020.01024.
- [79] Nicholas Leonard, Steven Krueger, and Mehdi Rashighi. Successful treatment of progressive macular hypomelanosis. *Dermatology Reports*, 10 2020. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7772758/>, doi:10.4081/dr.2020.8509.
- [80] Asaf Levy, Isai Salas Gonzalez, Maximilian Mittelviehhaus, Scott Clingenpeel, Sur Herrera Paredes, Jiamin Miao, Kunru Wang, Giulia Devescovi, Kyra Stillman, Freddy Monteiro, Bryan Rangel Alvarez, Derek S. Lundberg, Tse-Yuan Lu, Sarah Lebeis, Zhao Jin, Meredith McDonald, Andrew P. Klein, Meghan E. Feltcher, Tijana Glavina Rio, Sarah R. Grant, Sharon L. Doty, Ruth E. Ley, Bingyu Zhao, Vittorio Venturi, Dale A. Pelletier, Julia A. Vorholt, Susannah G. Tringe, Tanja Woyke, and Jeffery L. Dangl. Genomic features of bacterial adaptation to plants. *Nature Genetics*, 50, 2018. Available from: <http://dx.doi.org/10.1038/s41588-017-0012-9>, doi:10.1038/s41588-017-0012-9.
- [81] Jie Li and Jian Cheng. Apolipoprotein e4 exacerbates ethanol-induced neurotoxicity through augmentation of oxidative stress and apoptosis in n2a-app cells. *Neuroscience Letters*, 665:1–6, 2018. Available from: <https://www.sciencedirect.com/science/article/pii/S0304394017309473>, doi:https://doi.org/10.1016/j.neulet.2017.11.038.
- [82] Zhuo Li, Hua Zhu, Ling Zhang, and Chuan Qin. The intestinal microbiome and alzheimer’s disease: A review. *Animal Models and Experimental Medicine*, 1, 2018. Available from: <http://dx.doi.org/10.1002/ame2.12033>, doi:10.1002/ame2.12033.
- [83] Ailing Lin, Ting Wang, Chenxi Li, Fan Pu, Zeinab Abdelrahman, Mengqi Jin, Zhenqing Yang, Liming Zhang, Xingqi Cao, Kaili Sun, Tongyao Hou, Zuyun Liu, Liying Chen, and Zuobing Chen. Association of sarcopenia with cognitive function and dementia risk score: A national prospective cohort study. *Metabolites*, 02 2023. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9965467/>, doi:10.3390/metabo13020245.
- [84] Chieh-Hsin Lin, Ping-Kun Chen, Shi-Heng Wang, and Hsien-Yuan Lane. Effect of sodium benzoate on cognitive function among patients with behavioral and psychological symptoms of dementia. *JAMA Network Open*, 4, 04 2021. Available from: <http://dx.doi.org/10.1001/jamanetworkopen.2021.6156>, doi:10.1001/jamanetworkopen.2021.6156.
- [85] Shih-Yao Lin, Asif Hameed, A. B. Arun, You-Cheng Liu, Yi-Han Hsu, Wei-An Lai, P. D. Rekha, and Chiu-Chung Young. Description of noviherbaspirillum malthae gen. nov., sp. nov., isolated from an oil-contaminated soil, and proposal to reclassify herbaspirillum soli , herbaspirillum aurantiacum , herbaspirillum canariense and herbaspirillum psychrotolerans as noviherbaspirillum soli comb. nov., noviherbaspirillum aurantiacum comb. nov., noviherbaspirillum canariense comb. nov. and noviherbaspirillum psychrotolerans comb. nov. based on polyphasic analysis. *International Journal of Systematic and Evolutionary Microbiology*, 63, 11 2013. Available from: <http://dx.doi.org/10.1099/ijls.0.048231-0>, doi:10.1099/ijls.0.048231-0.
- [86] Yi-Ting Lin, Ping-Hsun Wu, Hei-Hwa Lee, Mwenya Mubanga, Cheng-Sheng Chen, Mei-Chuan Kuo, Yi-Wen Chiu, Po-Lin Kuo, and Shang-Jyh Hwang. Indole-3 acetic acid increased risk of impaired cognitive function in patients receiving hemodialysis. *NeuroToxicology*, 73:85–91, 2019. Available from: <https://www.sciencedirect.com/science/article/pii/S0161813X18302389>, doi:https://doi.org/10.1016/j.neuro.2019.02.019.
- [87] Hans-Jrg Linde, Joachim Hahn, Ernst Holler, Udo Reischl, and Norbert Lehn. Septicemia due to acinetobacter junii. *Journal of Clinical Microbiology*, pages 2696–7, Jul 2002. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC120562/>, doi:10.1128/JCM.40.7.2696-2697.2002.
- [88] Jinping Liu, Lirong Chang, Yizhi Song, Hui Li, and Yan Wu. The role of nmda receptors in alzheimers disease. *Frontiers in Neuroscience*, 02 2019. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6375899/>, doi:10.3389/fnins.2019.00043.
- [89] Zachery R. Lonergan, Lauren D. Palmer, and Eric P. Skaar. Histidine utilization is a critical determinant of acinetobacter pathogenesis. *Infection and Immunity*, 88, 06 2020. Available from: <http://dx.doi.org/10.1128/iai.00118-20>, doi:10.1128/iai.00118-20.
- [90] Lilian Lopez Leyva, Emmanuel Gonzalez, Noel W. Solomons, and Kristine G. Koski. Human milk microbiome is shaped by breastfeeding practices. *Frontiers in Microbiology*, 13, 2022. Available from: <https://www.frontiersin.org/articles/10.3389/fmicb.2022.885588>, doi:10.3389/fmicb.2022.885588.
- [91] C. M. Manaia. Pseudomonas thermotolerans sp. nov., a thermotolerant species of the genus pseudomonas sensu stricto. *INTERNATIONAL JOURNAL OF SYSTEMATIC AND EVOLUTIONARY MICROBIOLOGY*, 52, 11 2002. Available from: <http://dx.doi.org/10.1099/ijls.0.02059-0>, doi:10.1099/ijls.0.02059-0.
- [92] Célia M Manaia and Edward R B Moore. Pseudomonas thermotolerans sp. nov., a thermotolerant species of the genus pseudomonas sensu stricto. *International Journal of Systematic and Evolutionary Microbiology*, 52, 11 2002. Available from: <http://dx.doi.org/10.1099/00207713-52-6-2203>, doi:10.1099/00207713-52-6-2203.
- [93] Mike J Marchywka. Update to covid-19 age distribution notes. Technical Report MJM-2021-007, not institutionalized , independent, 306 Charles Cox , Canton GA 30115, 8 2021. Version .1, may change significantly if less than 1.00. Available from: [https://www.researchgate.net/publication/353946686\\_Draft\\_table\\_comparing\\_expectations\\_to\\_recent\\_results\\_with\\_covid-19](https://www.researchgate.net/publication/353946686_Draft_table_comparing_expectations_to_recent_results_with_covid-19).
- [94] Mike J Marchywka. Wetting tryptophan with calcium pantothenate. techreport MJM-2021-014, not institutionalized, independent, 306 Charles Cox , Canton GA 30115, 12 2021. Available from: [https://www.researchgate.net/publication/356785163\\_Wetting\\_Tryptophan\\_With\\_Calcium\\_Pantothenate](https://www.researchgate.net/publication/356785163_Wetting_Tryptophan_With_Calcium_Pantothenate).
- [95] Mike J Marchywka. Clinical and microbiological improvement in dog after metal and benzoate containing supplement mix. techreport MJM-2022-013, not institutionalized, independent, 44 Crosscreek Trail, Jasper GA 30143, 11 2022. Available from: [https://zenodo.org/record/7293723#\\_Y2WaP3XMLCI](https://zenodo.org/record/7293723#_Y2WaP3XMLCI), doi:10.5281/zenodo.7293723.



- [96] Mike J Marchywka. Experiences with a family of science based kitchen snacks for dogs. techreport MJM-2021-018, not institutionalized, independent, 306 Charles Cox , Canton GA 30115, 1 2022. Available from: [https://www.researchgate.net/publication/357517852\\_Experiences\\_with\\_a\\_Family\\_of\\_Science\\_Based\\_Kitchen\\_Snacks\\_for\\_Dogs](https://www.researchgate.net/publication/357517852_Experiences_with_a_Family_of_Science_Based_Kitchen_Snacks_for_Dogs).
- [97] Mike J Marchywka. Happy again : Possible canine riboflavin deficiency. techreport MJM-2022-009, not institutionalized, independent, 306 Charles Cox , Canton GA 30115, 3 2022. Available from: [https://www.researchgate.net/publication/359504498\\_Happy\\_Again\\_Possible\\_Canine\\_Riboflavin\\_Deficiency](https://www.researchgate.net/publication/359504498_Happy_Again_Possible_Canine_Riboflavin_Deficiency).
- [98] Mike J Marchywka. Recent vitamin k literature in the conext of a non-monotonic response curve : Local vs global optima and other speculation. techreport MJM-2022-015, not institutionalized, independent, 44 Crosscreek Trail Jasper GA 30143, 1 2023. Available from: [https://www.researchgate.net/publication/366642398\\_Recent\\_Vitamin\\_K\\_Literature\\_in\\_the\\_Conext\\_of\\_a\\_non-Monotonic\\_Response\\_Curve\\_Local\\_vs\\_Global\\_Optima\\_and\\_other\\_Speculation](https://www.researchgate.net/publication/366642398_Recent_Vitamin_K_Literature_in_the_Conext_of_a_non-Monotonic_Response_Curve_Local_vs_Global_Optima_and_other_Speculation), doi:10.13140/RG.2.2.34218.29124.
- [99] M.J. Marchywka. On the age distribution of sars-cov-2 patients. Technical Report MJM-2020-002-0.10, not institutionalized , independent, 306 Charles Cox , Canton GA 30115, 7 2020. Version 0.10 , may change significantly if less than 1.00. Available from: [https://www.linkedin.com/posts/marchywka\\_notes-on-aging-as-it-relates-to-covid19-activity-6684083706170265601-JMnN](https://www.linkedin.com/posts/marchywka_notes-on-aging-as-it-relates-to-covid19-activity-6684083706170265601-JMnN).
- [100] M.J. Marchywka. Impromptu bibtex find and merge tool. Technical Report MJM-2021-002, not institutionalized , independent, 306 Charles Cox , Canton GA 30115, 01 2021. Version 0.1.1 , may change significantly if less than 1.00. Available from: [https://www.researchgate.net/publication/350608962\\_toobib](https://www.researchgate.net/publication/350608962_toobib).
- [101] M.J. Marchywka. On the age distribution of sars-cov-2 patients. Technical Report MJM-2020-002-0.12, not institutionalized , independent, 306 Charles Cox , Canton GA 30115, 3 2021. Version 0.10 , may change significantly if less than 1.00. Available from: [https://www.researchgate.net/publication/350021196\\_On\\_the\\_age\\_distribution\\_of\\_covid-19\\_patients](https://www.researchgate.net/publication/350021196_On_the_age_distribution_of_covid-19_patients).
- [102] M.J. Marchywka. Supplement usage including vitamin k by a heartworm positive pregnant pit bull and her puppies. Technical Report MJM-2021-003, not institutionalized , independent, 306 Charles Cox , Canton GA 30115, 05 2021. Version 0.50 , may change significantly if less than 1.00. Available from: [https://www.researchgate.net/publication/354924460\\_Supplement\\_Usage\\_Including\\_Vitamin\\_K\\_by\\_a\\_Heartworm\\_Positive\\_Pregnant\\_Pit\\_Bull\\_and\\_Her\\_Puppies](https://www.researchgate.net/publication/354924460_Supplement_Usage_Including_Vitamin_K_by_a_Heartworm_Positive_Pregnant_Pit_Bull_and_Her_Puppies).
- [103] N. Marwa, N. Singh, S. Srivastava, G. Saxena, V. Pandey, and N. Singh. Characterizing the hypertolerance potential of two indigenous bacterial strains (*Bacillus flexus* and *Acinetobacter junii*) and their efficacy in arsenic bioremediation. *Journal of Applied Microbiology*, 126(4):1117–1127, 04 2019. Available from: <https://doi.org/10.1111/jam.14179>, arXiv: <https://academic.oup.com/jambio/article-pdf/126/4/1117/47337021/jambio1117.pdf>, doi:10.1111/jam.14179.
- [104] Chisa Matsumoto, Shigeru Shibata, Takuya Kishi, Satoshi Morimoto, Masaki Mogi, Koichi Yamamoto, Kazuo Kobayashi, Masami Tanaka, Kei Asayama, Eiichiro Yamamoto, Hironori Nakagami, Satoshi Hoshide, Masashi Mukoyama, Kazuomi Kario, Koichi Node, and Hiromi Rakugi. Long covid and hypertension-related disorders: a report from the japanese society of hypertension project team on covid-19. *Hypertension Research*, 46, 2023. Available from: <https://www.nature.com/articles/s41440-022-01145-2>, doi:10.1038/s41440-022-01145-2.
- [105] Dina Medina-Vera, Emma N Zambrana-Infantes, Antonio J Lopez-Gamero, Julia Verheul-Campos, Luis J Santin, Elena Baixeras, Juan Suarez, Francisco J Pavon, Cristina Rosell-Valle, and Fernando Rodriguez de Fonseca. Transcending the amyloid-beta dominance paradigm in alzheimer’s disease: An exploration of behavioural, metabolic, and gut microbiota phenotypes in 5xfad mice. *Neurobiology of disease*, page 106295, 09 2023. Available from: <https://pubmed.ncbi.nlm.nih.gov/37717663/>, doi:10.1016/j.nbd.2023.106295.
- [106] Nishila Mehta, Fernando Martinez Guasch, Corey Kamen, Sumesh Shah, Lisa D. Burry, Christine Soong, and Sangeeta Mehta. Proton pump inhibitors in the elderly hospitalized patient: Evaluating appropriate use and deprescribing. *Journal of Pharmacy Technology*, 36, 2020. Available from: <http://dx.doi.org/10.1177/8755122519894953>, doi:10.1177/8755122519894953.
- [107] Xiao Jun Meng, Yu Xiu Zhang, Rong Jia, Xia Li, Tuan Yao Chai, and Yun He Wang. Isolation and characterization of the phenol degradation bacterium <i>diaphorobacter</i> p2 strain from coking wastewater. *Advanced Materials Research*, 550-553, 2012. Available from: <http://dx.doi.org/10.4028/www.scientific.net/amr.550-553.2296>, doi:10.4028/www.scientific.net/amr.550-553.2296.
- [108] Judith Miklosy. Historic evidence to support a causal relationship between spirochetal infections and alzheimers disease. *Frontiers in Aging Neuroscience*, 04 2015. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4399390/>, doi:10.3389/fnagi.2015.00046.
- [109] Pablo Mohaupt, Jerome Vialaret, Christophe Hirtz, and Sylvain Lehmann. Readthrough isoform of aquaporin-4 (aqp4) as a therapeutic target for alzheimer’s disease and other proteinopathies. *Alzheimer’s research & therapy*, page 170, 10 2023. Available from: <https://pubmed.ncbi.nlm.nih.gov/37821965/>, doi:10.1186/s13195-023-01318-2.
- [110] Lázaro Molina, Ruggero La Rosa, Juan Nogales, and Fernando Rojo. <i>pseudomonas putida</i> kt2440 metabolism undergoes sequential modifications during exponential growth in a complete medium as compounds are gradually consumed. *Environmental Microbiology*, 21, 2019. Available from: <http://dx.doi.org/10.1111/1462-2920.14622>, doi:10.1111/1462-2920.14622.
- [111] Yves Moné, Joshua P. Earl, JarosUx0142[bad E. Król, Azad Ahmed, Bhaswati Sen, Garth D. Ehrlich, and Jeffrey R. Lapidés. Evidence supportive of a bacterial component in the etiology for alzheimer’s disease and for a temporal-spatial development of a pathogenic microbiome in the brain. *Frontiers in Cellular and Infection Microbiology*, 13, 2023. Available from: <https://www.frontiersin.org/articles/10.3389/fcimb.2023.1123228>, doi:10.3389/fcimb.2023.1123228.
- [112] Emilia Morawiec, MichaUx0142[bad vv=322] CzerwiUx0144[bad char vv=324]ski, Anna Bednarska Czer-

- wiUx0144[bad char vv=324]ska, and Andrzej Wiczowski. Semen dysbiosis just a male problem? *Frontiers in Cellular and Infection Microbiology*, 12, 2022. Available from: <https://www.frontiersin.org/articles/10.3389/fcimb.2022.815786>, doi:10.3389/fcimb.2022.815786.
- [113] F. Moroni, P. Russi, V. Carlà, G. De Luca, and V. Politi. *The Regulation of Brain Kynurenine Acid Content: Focus on Indole-3-Pyruvic Acid*, pages 299–308. Springer New York, Boston, MA, 1991. Available from: [https://doi.org/10.1007/978-1-4684-5952-4\\_27](https://doi.org/10.1007/978-1-4684-5952-4_27), doi:10.1007/978-1-4684-5952-4\_27.
- [114] Amritpal Mudher and Simon Lovestone. Alzheimer’s disease-do tauists and baptists finally shake hands? *Trends in neurosciences*, pages 22–6, Jan 2002. Available from: <https://pubmed.ncbi.nlm.nih.gov/11801334/>, doi:10.1016/S0166-2236(00)02031-2.
- [115] Shilpa Mujumdar, Jayshree Bhojar, Anuja Akkar, Shailja Hundekar, Neha Agnihotri, Pratiksha Jaybhay, and Smita Bhuyan. Chapter 15 - acinetobacter: A versatile plant growth-promoting rhizobacteria (pgpr). In Prashant Swapnil, Mukesh Meena, Harish, Avinash Marwal, Selvakumar Vijayalakshmi, and Andleeb Zehra, editors, *Plant-Microbe Interaction - Recent Advances in Molecular and Biochemical Approaches*, pages 327–362. Academic Press, 2023. Available from: <https://www.sciencedirect.com/science/article/pii/B9780323918756000098>, doi:https://doi.org/10.1016/B978-0-323-91875-6.00009-8.
- [116] Koji Narui, Norihisa Noguchi, Aya Saito, Kazuhiro Kakimi, Noboru Motomura, Kinya Kubo, Shinichi Takamoto, and Masanori Sasatsu. Anti-infectious activity of tryptophan metabolites in the <small>l</small>-tryptophan&ndash;<small>l</small>-kynurenine pathway. *Biological and Pharmaceutical Bulletin*, 32(1):41–44, 2009. Available from: [https://www.jstage.jst.go.jp/article/bpb/32/1/32\\_1\\_41/\\_article/-char/ja/](https://www.jstage.jst.go.jp/article/bpb/32/1/32_1_41/_article/-char/ja/), doi:10.1248/bpb.32.41.
- [117] Asfa Nazish, Fozia, Baharullah Khattak, Taj Ali Khan, Ijaz Ahmad, Riaz Ullah, Ahmed Bari, Majid M. Asmari, Hafiz M. Mahmood, Muhammad Sohaib, Ahmad El Askary, Attalla F. El-kott, and Mohamed M. Abdel-Daim. Antinematode activity of abomasum bacterial culture filtrates against haemonchus contortus in small ruminants. *Animals*, 11, 2021. Available from: <http://dx.doi.org/10.3390/ani11061843>, doi:10.3390/ani11061843.
- [118] S. Nishanth Kumar, C. Mohandas, and Bala Nambisan. Purification, structural elucidation and bioactivity of tryptophan containing diketopiperazines, from comamonas testosteroni associated with a rhabditid entomopathogenic nematode against major human-pathogenic bacteria. *Peptides*, 53:48–58, 2014. Invertebrate Neuropeptides XIV. Available from: <https://www.sciencedirect.com/science/article/pii/S019697811300332X>, doi:https://doi.org/10.1016/j.peptides.2013.09.019.
- [119] Carin Northuis, Elizabeth Bell, Pamela Lutsey, Kristen M George, Rebecca F. Gottesman, Tom H. Mosley, Eric A Whitsel, and Kamakshi Lakshminarayan. Cumulative use of proton pump inhibitors and risk of dementia: The atherosclerosis risk in communities study. *Neurology*, 2023. Available from: <https://n.neurology.org/content/early/2023/08/09/WNL.0000000000207747>, arXiv:https://n.neurology.org/content/early/2023/08/09/WNL.0000000000207747.full.pdf, doi:10.1212/WNL.0000000000207747.
- [120] Mutsumi Ogawa, Fumiko Shimizu, Yukie Ishii, Tetsuya Takao, and Akikazu Takada. Uniqueness of tryptophan in the transport system in the brain and peripheral tissues. *Food and Nutrition Sciences*, 14, 2023. Available from: <http://dx.doi.org/10.4236/fns.2023.145026>, doi:10.4236/fns.2023.145026.
- [121] S M O’Mahony, G Clarke, Y E Borre, T G Dinan, and J F Cryan. Serotonin, tryptophan metabolism and the brain-gut-microbiome axis. *Behavioural brain research*, pages 32–48, 07 2014. Available from: <https://pubmed.ncbi.nlm.nih.gov/25078296/>, doi:10.1016/j.bbr.2014.07.027.
- [122] Omid Omrani, Anna Krepelova, Seyed Mahdi Rasa, Dovydas Syrvinskas, Jing Lu, Francesco Annunziata, George Garside, Seerat Bajwa, Susanne Reinhardt, Lisa Adam, Sandra Käppel, Nadia Ducano, Daniela Donna, Alessandro Ori, Salvatore Oliviero, Karl Lenhard Rudolph, and Francesco Neri. Ifnugamma-stat1 axis drives aging-associated loss of intestinal tissue homeostasis and regeneration. *Nature Communications*, 14, 09 2023. Available from: <https://www.nature.com/articles/s41467-023-41683-y>, doi:10.1038/s41467-023-41683-y.
- [123] Chihiro Ono, Manabu Yoshida, Natsuko Kawano, Kenji Miyado, and Akihiro Umezawa. Staphylococcus epidermidis is involved in a mechanism for female reproduction in mice. *Regenerative Therapy*, 1:11–17, 2015. Available from: <https://www.sciencedirect.com/science/article/pii/S2352320415000073>, doi:https://doi.org/10.1016/j.reth.2014.12.003.
- [124] Michael Otto. Staphylococcus epidermidis the accidental pathogen. *Nature reviews. Microbiology*, pages 555–67, Aug 2009. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2807625/>, doi:10.1038/nrmicro2182.
- [125] Diana Pacheco-Alvarez, R. Sergio Solórzano-Vargas, Roy A. Gravel, Rafael Cervantes-Roldán, Antonio Velázquez, and Alfonso León-Del-Río. Paradoxical regulation of biotin utilization in brain and liver and implications for inherited multiple carboxylase deficiency. *Journal of Biological Chemistry*, 279, 2004. Available from: <http://dx.doi.org/10.1074/jbc.M407056200>, doi:10.1074/jbc.M407056200.
- [126] T. Padmavathi, R. Dikshit, and S. Seshagiri. Effect of rhizophagus spp. and plant growth-promoting acinetobacter junii on solanum lycopersicum and capsicum annum. *Brazilian Journal of Botany*, 38(2):273–280, Jun 2015. Available from: <https://doi.org/10.1007/s40415-015-0144-z>, doi:10.1007/s40415-015-0144-z.
- [127] Elena L Paley, Galina Denisova, Olga Sokolova, Natalia Posternak, Xukui Wang, and Anna-Liisa Brownell. Tryptamine induces tryptophanyl-trna synthetase-mediated neurodegeneration with neurofibrillary tangles in human cell and mouse models. *Neuromolecular medicine*, pages 55–82, 2007. Available from: <https://pubmed.ncbi.nlm.nih.gov/17114825/>, doi:10.1385/nmm.9:1:55.
- [128] Gregory C. Palmer, Kelli L. Palmer, Peter A. Jorth, and Marvin Whiteley. Characterization of the pseudomonas aeruginosa transcriptional response to phenylalanine and tyrosine. *Journal of Bacteriology*, pages 2722–8, 03 2010. Available

- from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2876504/>, doi:10.1128/JB.00112-10.
- [129] Prashant Kumar Pandey, Pankaj Verma, Himanshu Kumar, Ashish Bavdekar, Milind S. Patole, and Yogesh S. Shouche. Comparative analysis of fecal microflora of healthy full-term indian infants born with different methods of delivery (vaginal vs cesarean): *Acinetobacter* sp. prevalence in vaginally born infants. *Journal of Biosciences*, 37(1):989–998, Dec 2012. Available from: <https://doi.org/10.1007/s12038-012-9268-5>, doi:10.1007/s12038-012-9268-5.
  - [130] Claudia Pantke, Martin Obst, Karim Benzerara, Guillaume Morin, Georges Ona-Nguema, Urs Dippon, and Andreas Kappler. Green rust formation during fe(ii) oxidation by the nitrate-reducing *acidovorax* sp. strain bofen1. *Environmental Science & Technology*, 46, 02 2012. Available from: <http://dx.doi.org/10.1021/es2016457>, doi:10.1021/es2016457.
  - [131] Santosh K. Patnaik, Eduardo G. Cortes, Eric D. Kannisto, Achamaporn Punnanitont, Samjot S. Dhillon, Song Liu, and Sai Yendamuri. Lower airway bacterial microbiome may influence recurrence after resection of early-stage non-small cell lung cancer. *The Journal of Thoracic and Cardiovascular Surgery*, 161, 2021. Available from: <http://dx.doi.org/10.1016/j.jtcvs.2020.01.104>, doi:10.1016/j.jtcvs.2020.01.104.
  - [132] Kamlesh Pawar, Carlos Hanisch, Sergio Eliseo Palma Vera, Ralf Einspanier, and Soroush Sharbati. Down regulated lncrna meg3 eliminates mycobacteria in macrophages via autophagy. *Scientific Reports*, 6, 01 2016. Available from: <https://www.nature.com/articles/srep19416>, doi:10.1038/srep19416.
  - [133] Luc Pellerin. Lactate as a pivotal element in neuron-glia metabolic cooperation. *Neurochemistry international*, pages 331–8, Sep-Oct 2003. Available from: <https://pubmed.ncbi.nlm.nih.gov/12742077/>, doi:10.1016/s0197-0186(03)00020-2.
  - [134] Rémi Peyraud, Patrick Kiefer, Philipp Christen, Jean-Charles Portais, and Julia A. Vorholt. Co-consumption of methanol and succinate by *methylobacterium extorquens* am1. *PLoS ONE*, 7, 11 2012. Available from: <http://dx.doi.org/10.1371/journal.pone.0048271>, doi:10.1371/journal.pone.0048271.
  - [135] V. Politi, G. De Luca, V. Gallai, Puca, and M. Comin. *Clinical Experiences with the Use of Indole-3-Pyruvic Acid*, pages 227–232. Springer US, Boston, MA, 1999. Available from: [https://doi.org/10.1007/978-1-4615-4709-9\\_29](https://doi.org/10.1007/978-1-4615-4709-9_29), doi:10.1007/978-1-4615-4709-9\_29.
  - [136] Daniela C. Popescu, He Huang, Naveen K. Singhal, Leah Shriver, Jennifer McDonough, Robert J. Clements, and Ernest J. Freeman. Vitamin k enhances the production of brain sulfatides during remyelination. *PLoS ONE*, 08 2018. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6110503/#:~:text=Vitamin%20K%20increases%20the%20synthesis,a%20C24%3A1%20fatty%20acid.>, doi:10.1371/journal.pone.0203057.
  - [137] R. J. Porter. Cognitive deficit induced by acute tryptophan depletion in patients with alzheimers disease. *American Journal of Psychiatry*, 157, 04 2000. Available from: <http://dx.doi.org/10.1176/appi.ajp.157.4.638>, doi:10.1176/appi.ajp.157.4.638.
  - [138] R. J. PORTER, B. S. LUNN, and J. T. O'BRIEN. Effects of acute tryptophan depletion on cognitive function in alzheimer's disease and in the healthy elderly. *Psychological Medicine*, 33, 2003. Available from: <http://dx.doi.org/10.1017/s0033291702006906>, doi:10.1017/s0033291702006906.
  - [139] Birgit M. Pr, Kevin P. Francis, Felix von Stetten, and Siegfried Scherer. Correlation of 16s ribosomal dna signature sequences with temperature-dependent growth rates of mesophilic and psychrotolerant strains of the *bacillus cereus* group. *Journal of Bacteriology*, pages 2624–30, Apr 1999. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC93692/>.
  - [140] Steven T. Proulx and Britta Engelhardt. Central nervous system zoning: How brain barriers establish subdivisions for cns immune privilege and immune surveillance. *Journal of Internal Medicine*, 292, 2022. Available from: <http://dx.doi.org/10.1111/joim.13469>, doi:10.1111/joim.13469.
  - [141] Yaoyu Pu, Lijia Chang, Youge Qu, Siming Wang, Kai Zhang, and Kenji Hashimoto. Antibiotic-induced microbiome depletion protects against mptp-induced dopaminergic neurotoxicity in the brain. *Aging (Albany NY)*, pages 6915–29, 09 2019. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6756889/>, doi:10.18632/aging.102221.
  - [142] Medha Rao, Katherine Young, Ladonya Jackson-Cowan, Arianne Kourosch, and Nicholas Theodosakis. Post-inflammatory hypopigmentation: Review of the etiology, clinical manifestations, and treatment options. *Journal of Clinical Medicine*, 12, 2023. Available from: <http://dx.doi.org/10.3390/jcm12031243>, doi:10.3390/jcm12031243.
  - [143] Giorgia Renga, Fiorella D'Onofrio, Marilena Pariano, Roberta Galarini, Carolina Barola, Claudia Stincardini, Marina M. Bellet, Helmut Ellemunter, Cornelia Lass-Flörl, Claudio Costantini, Valerio Napolioni, Allison K. Ehrlich, Cinzia Antognelli, Massimo Fini, Enrico Garaci, Emilia Nunzi, and Luigina Romani. Bridging of host-microbiota tryptophan partitioning by the serotonin pathway in fungal pneumonia. *Nature Communications*, 14, 09 2023. Available from: <https://www.nature.com/articles/s41467-023-41536-8>, doi:10.1038/s41467-023-41536-8.
  - [144] N. Rodríguez-Berbel, R. Ortega, M.E. Lucas-Borja, A. Solé-Benet, and I. Miralles. Long-term effects of two organic amendments on bacterial communities of calcareous mediterranean soils degraded by mining. *Journal of Environmental Management*, 271:110920, 2020. Available from: <https://www.sciencedirect.com/science/article/pii/S0301479720308495>, doi:<https://doi.org/10.1016/j.jenvman.2020.110920>.
  - [145] Kymberleigh A. Romano, Eugenio I. Vivas, Daniel Amador-Noguez, and Federico E. Rey. Intestinal microbiota composition modulates choline bioavailability from diet and accumulation of the proatherogenic metabolite trimethylamine-<i>n</i>-oxide. *mBio*, 6, 2015. Available from: <http://dx.doi.org/10.1128/mbio.02481-14>, doi:10.1128/mbio.02481-14.
  - [146] Michael P. Ryan, Ludmila Sevjahova, Rachel Gorman, and Sandra White. The emergence of the genus *comamonas* as important opportunistic pathogens. *Pathogens*, 09 2022. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9504711/>, doi:10.3390/pathogens11091032.



- [147] Santonu Kumar Sanyal, Jeremiah Shuster, and Frank Reith. Cycling of biogenic elements drives biogeochemical gold cycling. *Earth-Science Reviews*, 190, 2019. Available from: <http://dx.doi.org/10.1016/j.earscirev.2018.12.010>, doi:10.1016/j.earscirev.2018.12.010.
- [148] Karl Savonije and Donald F. Weaver. The role of tryptophan metabolism in alzheimer's disease. *Brain Sciences*, 13, 2023. Available from: <http://dx.doi.org/10.3390/brainsci13020292>, doi:10.3390/brainsci13020292.
- [149] Roni Scherzer-Attali, Riccardo Pellarin, Marino Convertino, Anat Frydman-Marom, Nirit Egoz-Matia, Sivan Peled, Michal Levy-Sakin, Deborah E. Shalev, Amedeo Cafilisch, Ehud Gazit, and Daniel Segal. Complete phenotypic recovery of an alzheimer's disease model by a quinone-tryptophan hybrid aggregation inhibitor. *PLoS ONE*, 5, 06 2010. Available from: <http://dx.doi.org/10.1371/journal.pone.0011101>, doi:10.1371/journal.pone.0011101.
- [150] Matthias Schmidt, Allison N. Pearson, Matthew R. Incha, Mitchell G. Thompson, Edward K. Baidoo, Ramu Kaku-manu, Aindrila Mukhopadhyay, Patrick M. Shih, Adam M. Deutschbauer, Lars M. Blank, and Jay D. Keasling. Nitrogen metabolism in pseudomonas putida: Functional analysis using random barcode transposon sequencing. *Applied and Environmental Microbiology*. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9004399/>, doi:10.1128/aem.02430-21.
- [151] Nikki Schultek. Nikki schultek on linkedin: Could a breakdown in the brains networks allow infections to contribute tounicodeellipsis. 09 2023. Available from: [https://www.linkedin.com/feed/update/urn:li:activity:7108409998031941632/?commentUrn=urn%3A%3Acomment%3A\(activity%3A7108409998031941632%2C7108889485295157248\)&dashCommentUrn=urn%3A%3Acomment%3A\(7108889485295157248%2Curn%3A%3Aactivity%3A7108409998031941632\)](https://www.linkedin.com/feed/update/urn:li:activity:7108409998031941632/?commentUrn=urn%3A%3Acomment%3A(activity%3A7108409998031941632%2C7108889485295157248)&dashCommentUrn=urn%3A%3Acomment%3A(7108889485295157248%2Curn%3A%3Aactivity%3A7108409998031941632)).
- [152] Julie Schulthess, Sumeet Pandey, Melania Capitani, Kevin C. Rue-Albrecht, Isabelle Arnold, Fanny Franchini, Agnieszka Chomka, Nicholas E. Ilott, Daniel G.W. Johnston, Elisabete Pires, James McCullagh, Stephen N. Sansom, Carolina V. Arancibia-Crcamo, Holm H. Uhlig, and Fiona Powrie. The short chain fatty acid butyrate imprints an antimicrobial program in macrophages. *Immunity*, pages 432–445.e7, Feb 2019. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6382411/>, doi:10.1016/j.immuni.2018.12.018.
- [153] M. Shehzadi, K. Fatima, A. Imran, M. S. Mirza, Q. M. Khan, and M. Afzal. Ecology of bacterial endophytes associated with wetland plants growing in textile effluent for pollutant-degradation and plant growth-promotion potentials. *Plant Biosystems - An International Journal Dealing with all Aspects of Plant Biology*, 150, 11 2016. Available from: <http://dx.doi.org/10.1080/11263504.2015.1022238>, doi:10.1080/11263504.2015.1022238.
- [154] Roberto Siani, Georg Stabl, Caroline Gutjahr, Michael Schlöter, and Viviane Radl. Acidovorax pan-genome reveals specific functional traits for plant beneficial and pathogenic plant-associations. *Microbial Genomics*, 12 2021. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8767351/>, doi:10.1099/mgen.0.000666.
- [155] Min Sub Sim, Connor T. Skennerton, and Victoria J. Orphan. Physiological, genomic, and sulfur isotopic characterization of methanol metabolism by desulfovibrio carbinolicus. *PLOS ONE*, 16, 01 2021. Available from: <http://dx.doi.org/10.1371/journal.pone.0245069>, doi:10.1371/journal.pone.0245069.
- [156] Purushottam Kumar Singh, Anamika Kushwaha, Nidhi Hans, Aishvarya Gautam, and Radha Rani. Evaluation of the cytotoxicity and interaction of lead with lead resistant bacterium acinetobacter junii pb1. *Brazilian Journal of Microbiology*, pages 223–30, 01 2019. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6863301/>, doi:10.1007/s42770-019-00041-1.
- [157] David R. Singleton, Janice Lee, Allison N. Dickey, Aaron Stroud, Elizabeth H. Scholl, Fred A. Wright, and Michael D. Aitken. Polyphasic characterization of four soil-derived phenanthrene-degrading acidovorax strains and proposal of acidovorax carolinensis sp. nov. *Systematic and applied microbiology*, pages 460–72, 06 2018. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6361392/>, doi:10.1016/j.syapm.2018.06.001.
- [158] Gwenn S Smith, Hiroto Kuwabara, Haijuan Yan, Najilla Nassery, Mark Yoon, Vidya Kamath, Michael Kraut, Neda F Gould, Alena Savonenko, Jennifer Coughlin, Martin Lodge, Martin Pomper, Ayon Nandi, Daniel Holt, Robert F Dannals, and Jeannie M Leoutsakos. Serotonin degeneration and amyloid-beta deposition in mild cognitive impairment: Relationship to cognitive deficits. *Journal of Alzheimer's disease : JAD*, 09 2023. Available from: <https://pubmed.ncbi.nlm.nih.gov/37718818/>, doi:10.3233/JAD-230570.
- [159] Pablo Suárez Pérez. Bacterial gene diversity related to tryptophan metabolism and indole-3-acetic acid (iaa) production in the rhizosphere. *Universitat Oberta de Catalunya (UOC)*, 01 2020. Available from: <https://openaccess.uoc.edu/bitstream/10609/108066/6/psuarezpeTFM0120memory.pdf>.
- [160] Suresh Sudarsan, Lars M. Blank, Alexander Dietrich, Oliver Vielhauer, Ralf Takors, Andreas Schmid, and Matthias Reuss. Dynamics of benzoate metabolism in pseudomonas putida kt2440. *Metabolic Engineering Communications*, pages 97–110, 03 2016. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5779716/>, doi:10.1016/j.meten.2016.03.005.
- [161] Li-Na Sun, Jun Zhang, Qing Chen, Jian He, Qin-Fen Li, and Shun-Peng Li. Comamonas jiangduensis sp. nov., a biosurfactant-producing bacterium isolated from agricultural soil. *International Journal of Systematic and Evolutionary Microbiology*, 63, 06 2013. Available from: <http://dx.doi.org/10.1099/ijs.0.045716-0>, doi:10.1099/ijs.0.045716-0.
- [162] Nan Sun, Yuxin Wang, Jianhua Chen, Pingzhi Wang, Weitang Song, Peifang Ma, Yabin Duan, Ziyuan Jiao, and Yixiao Li. Colonization and interaction of bacteria associated with chinese chives affected by ecological compartments and growth conditions. *Frontiers in Microbiology*, 02 2022. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8883035/>, doi:10.3389/fmicb.2022.775002.
- [163] K S Sundaram, J H Fan, J A Engelke, A L Foley, J W Suttie, and M Lev. Vitamin k status influences brain sulfatide metabolism in young mice and rats. *The Journal of nutrition*, pages 2746–51, Nov 1996. Available from: <https://pubmed.ncbi.nlm.nih.gov/8888888/>.

- [//pubmed.ncbi.nlm.nih.gov/8914944/](https://pubmed.ncbi.nlm.nih.gov/8914944/), doi:10.1093/jn/126.11.2746.
- [164] Abdoulaye Sy, Antonius J. Timmers, Claudia Knief, and Julia A. Vorholt. Methylobacterium extorquens during colonization of medicago truncatula under competitive conditions. *Applied and Environmental Microbiology*, pages 7245–52, Nov 2005. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1287603/>, doi:10.1128/AEM.71.11.7245-7252.2005.
- [165] Marta Talaveron-Rey, Monica Alvarez-Cordoba, Irene Villalon-Garcia, Suleva Povea-Cabello, Juan M Suarez-Rivero, David Gomez-Fernandez, Ana Romero-Gonzalez, Alejandra Suarez-Carrillo, Manuel Munuera-Cabeza, Paula Cilleros-Holgado, Diana Reche-Lopez, Rocio Pinero-Perez, and Jose A Sanchez-Alcazar. Alpha-lipoic acid supplementation corrects pathological alterations in cellular models of pantothenate kinase-associated neurodegeneration with residual pank2 expression levels. *Orphanet journal of rare diseases*, page 80, 04 2023. Available from: <https://pubmed.ncbi.nlm.nih.gov/37046296/>, doi:10.1186/s13023-023-02687-5.
- [166] Rajesh R Tampi, Brent P Forester, and Marc Agronin. Aducanumab: evidence from clinical trial data and controversies. *Drugs in Context*, 10 2021. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8491638/>, doi:10.7573/dic.2021-7-3.
- [167] Cheril Tapia-Rojas, Carolina B. Lindsay, Carla Montecinos-Oliva, Macarena S. Arrazola, Rocio M. Retamales, Daniel Bunout, Sandra Hirsch, and Nibaldo C. Inestrosa. Is l-methionine a trigger factor for alzheimer’s-like neurodegeneration?: Changes in aubeta oligomers, tau phosphorylation, synaptic proteins, wnt signaling and behavioral impairment in wild-type mice. *Molecular Neurodegeneration*, 10, 2015. Available from: <http://dx.doi.org/10.1186/s13024-015-0057-0>, doi:10.1186/s13024-015-0057-0.
- [168] Florence Thirion, Helene Speyer, Tue Haldor Hansen, Trine Nielsen, Yong Fan, Emmanuelle Le Chatelier, Sébastien Fromentin, Magali Berland, Florian Plaza Oñate, Nicolas Pons, Nathalie Galleron, Florence Levenez, Lajos Mark’o, Till Birkner, Torben Jorgensen, Sofia K. Forslund, Henrik Vestergaard, Torben Hansen, Merete Nordentoft, Ole Mors, Michael E. Benros, Oluf Pedersen, and Stanislav D. Ehrlich. Alteration of gut microbiome in patients with schizophrenia indicates links between bacterial tyrosine biosynthesis and cognitive dysfunction. *Biological Psychiatry Global Open Science*, 3(2):283–291, 2023. Available from: <https://www.sciencedirect.com/science/article/pii/S2667174322000143>, doi:<https://doi.org/10.1016/j.bpsgos.2022.01.009>.
- [169] Ping Tong, Qing-Hua Peng, Li-Min Gu, Wei-Wei Xie, and Wen-Jie Li. Lncrna-meg3 alleviates high glucose induced inflammation and apoptosis of retina epithelial cells via regulating mir-34a/sirt1 axis. *Experimental and Molecular Pathology*, 107, 2019. Available from: <http://dx.doi.org/10.1016/j.yexmp.2018.12.003>, doi:10.1016/j.yexmp.2018.12.003.
- [170] Francisco Torres-Bondia, Farida Dakterzada, Leonardo Galván, Miquel Buti, Gaston Besanson, Eric Gill, Roman Buil, Jordi de Batlle, and Gerard Piñol Ripoll. Proton pump inhibitors and the risk of alzheimer’s disease and non-alzheimer’s dementias. *Scientific Reports*, 10, 12 2020. Available from: <https://www.nature.com/articles/s41598-020-78199-0>, doi:10.1038/s41598-020-78199-0.
- [171] Komarova Tatiana V., Petrunia Igor V., Shindyapina Anastasia V., Silachev Denis N., Sheshukova Ekaterina V., Kiryanov Gleb I., and Yuri L. Dorokhov. Endogenous methanol regulates mammalian gene activity. *PLOS ONE*, 9(2):1–9, 02 2014. Available from: <https://doi.org/10.1371/journal.pone.0090239>, doi:10.1371/journal.pone.0090239.
- [172] Ado Van Assche. Phd ado van assche. *Open Science Framework*. Available from: <https://osf.io/w7mk3/>, doi:10.17605/osf.io/w7mk3.
- [173] Marlous C. M. van der Weijden, Peter Jan van Laar, Roald A. Lambrechts, Dineke S. Verbeek, and Marina A. J. Tijssen. Cortical pencil lining on swi mri in nbia and healthy aging. *BMC Neurology*, 19, 2019. Available from: <http://dx.doi.org/10.1186/s12883-019-1471-7>, doi:10.1186/s12883-019-1471-7.
- [174] Christopher H. van Dyck, Chad J. Swanson, Paul Aisen, Randall J. Bateman, Christopher Chen, Michelle Gee, Michio Kanekiyo, David Li, Larisa Reyderman, Sharon Cohen, Lutz Froelich, Sadao Katayama, Marwan Sabbagh, Bruno Vellas, David Watson, Shobha Dhadha, Michael Irizarry, Lynn D. Kramer, and Takeshi Iwatsubo. Lecanemab in early alzheimer’s disease. *New England Journal of Medicine*, 388, 01 2023. Available from: <http://dx.doi.org/10.1056/nejmoa2212948>, doi:10.1056/nejmoa2212948.
- [175] G van Hall, J S Raaymakers, W H Saris, and A J Wagenmakers. Ingestion of branched-chain amino acids and tryptophan during sustained exercise in man: failure to affect performance. *The Journal of Physiology*, pages 789–94, Aug 1995. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1156566/>.
- [176] Sebastiaan P. van Kessel, Alexandra K. Frye, Ahmed O. El-Gendy, Maria Castejon, Ali Keshavarzian, Gertjan van Dijk, and Sahar El Aidy. Gut bacterial tyrosine decarboxylases restrict levels of levodopa in the treatment of parkinson’s disease. *Nature Communications*, 10, 2019. Available from: <http://dx.doi.org/10.1038/s41467-019-08294-y>, doi:10.1038/s41467-019-08294-y.
- [177] Mario Vanechoutte, Alexandr Nemec, Peter Kämpfer, Piet Cools, and Georges Wauters. *Acinetobacter* , *Chryseobacterium* , and other nonfermentative gram-negative rods, 05 2015. Available from: <http://dx.doi.org/10.1128/9781555817381.ch44>, doi:10.1128/9781555817381.ch44.
- [178] Manuel T. Velasquez, Ali Ramezani, Alotaibi Manal, and Dominic S. Raj. Trimethylamine n-oxide: The good, the bad and the unknown. *Toxins*, 11 2016. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5127123/>, doi:10.3390/toxins8110326.
- [179] Ramon Velazquez, Wendy Winslow, and Marc A. Mifflin. Choline as a prevention for alzheimers disease. *Aging (Albany NY)*, pages 2026–7, 02 2020. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7041773/>, doi:10.18632/aging.102849.
- [180] Antoine Verger, Igor Yakushev, Nathalie L. Albert, Bart van Berckel, Matthias Brendel, Diego Cecchin, Pablo Aguiar Fer-



- andez, Francesco Fraioli, Eric Guedj, Silvia Morbelli, Nelleke Tolboom, Tatjana Traub-Weidinger, Donatienne Van Weehaeghe, and Henryk Barthel. Fda approval of lecanemab: the real start of widespread amyloid pet use? the eanm neuroimaging committee perspective. *European Journal of Nuclear Medicine and Molecular Imaging*, pages 1553–5, 03 2023. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10119064/>, doi:10.1007/s00259-023-06177-5.
- [181] Nicholas M. Vogt, Robert L. Kerby, Kimberly A. Dill-McFarland, Sandra J. Harding, Andrew P. Merluzzi, Sterling C. Johnson, Cynthia M. Carlsson, Sanjay Asthana, Henrik Zetterberg, Kaj Blennow, Barbara B. Bendlin, and Federico E. Rey. Gut microbiome alterations in alzheimer’s disease. *Scientific Reports*, 7, 10 2017. Available from: <https://www.nature.com/articles/s41598-017-13601-y>, doi:10.1038/s41598-017-13601-y.
- [182] Alyssa Walker and Daniel M. Czyz. Oh my gut! is the microbial origin of neurodegenerative diseases real? *Infection and Immunity*, 09 2023. Available from: <http://dx.doi.org/10.1128/iai.00437-22>, doi:10.1128/iai.00437-22.
- [183] Hai Wang, Xingyu Rong, Gan Zhao, Yifan Zhou, Yi Xiao, Ding Ma, Xi Jin, Yonglin Wu, Yuchen Yan, Hao Yang, Yuan Zhou, Manning Qian, Chen Niu, Xin Hu, Da-Qiang Li, Qingyun Liu, Yumei Wen, Yi-Zhou Jiang, Chao Zhao, and Zhi-Ming Shao. The microbial metabolite trimethylamine n-oxide promotes antitumor immunity in triple-negative breast cancer. *Cell Metabolism*, 34, 2022. Available from: <http://dx.doi.org/10.1016/j.cmet.2022.02.010>, doi:10.1016/j.cmet.2022.02.010.
- [184] Yilin Wang, Lei Li, Xiaodong Zhao, Shaomei Sui, Qi Wang, Guizhi Shi, Huilian Xu, Xiujuan Zhang, Yan He, and Jinsong Gu. Intestinal microflora changes in patients with mild alzheimer’s disease in a chinese cohort. *Journal of Alzheimer’s Disease*, 88, 07 2022. Available from: <http://dx.doi.org/10.3233/jad-220076>, doi:10.3233/jad-220076.
- [185] Zhi-Bin Wang, Jun-Yan Liu, Xiao-Jing Xu, Xiao-Yuan Mao, Wei Zhang, Hong-Hao Zhou, and Zhao-Qian Liu. Neurodegeneration with brain iron accumulation: Insights into the mitochondria dysregulation. *Biomedicine & Pharmacotherapy*, 118:109068, 2019. Available from: <https://www.sciencedirect.com/science/article/pii/S0753332219304858>, doi:<https://doi.org/10.1016/j.biopha.2019.109068>.
- [186] Zhiqiang Wang, Lili Ding, Jun Zhu, Yinxia Su, Li Wang, Lina Liu, Qi Ma, and Hua Yao. Long non-coding rna meg3 mediates high glucose-induced endothelial cell dysfunction. *International Journal of Clinical and Experimental Pathology*, pages 1088–100, 03 2018. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6958101/>.
- [187] Lingyu Wen, Yiqun Huang, Weiwei Wang, Lige Zhang, Jijun Xu, Zhao Li, Ping Xu, and Hongzhi Tang. A novel diaphorobacter sp. strain isolated from saponification wastewater shows highly efficient phenanthrene degradation. *Environmental Research*, 214:114047, 2022. Available from: <https://www.sciencedirect.com/science/article/pii/S0013935122013743>, doi:<https://doi.org/10.1016/j.envres.2022.114047>.
- [188] B. Widner, F. Leblhuber, J. Walli, G. P. Tilz, U. Demel, and D. Fuchs. Tryptophan degradation and immune activation in alzheimer’s disease. *Journal of Neural Transmission*, 107(3):343–353, Mar 2000. Available from: <https://doi.org/10.1007/s007020050029>, doi:10.1007/s007020050029.
- [189] Andrew D. Winters, Roberto Romero, Maria Teresa Gervasi, Nardhy Gomez-Lopez, Maria Rosa Tran, Valeria Garcia-Flores, Percy Pacora, Eunjung Jung, Sonia S. Hassan, Chaur-Dong Hsu, and Kevin R. Theis. Does the endometrial cavity have a molecular microbial signature? *Scientific Reports*, 9, 07 2019. Available from: <https://www.nature.com/articles/s41598-019-46173-0>, doi:10.1038/s41598-019-46173-0.
- [190] Andrea C Wong, Ashwarya S Devason, Iboro C Umana, Timothy O Cox, Lenka Dohnalova, Lev Litichevskiy, Jonathan Perla, Patrick Lundgren, Zienab Etwebi, Luke T Izzo, Jihee Kim, Monika Tetlak, Helene C Descamps, Simone L Park, Stephen Wisser, Aaron D McKnight, Ryan D Pardy, Junwon Kim, Niklas Blank, Shaan Patel, Katharina Thum, Sydney Mason, Jean-Christophe Beltra, Michael F Michieletto, Shin Foong Ngiew, Brittany M Miller, Megan J Liou, Bhoomi Madhu, Oxana Dmitrieva-Posocco, Alex S Huber, Peter Hewins, Christopher Petucci, Candice P Chu, Gwen Baraniecki-Zwil, Leila B Giron, Amy E Baxter, Allison R Greenplate, Charlotte Kearns, Kathleen Montone, Leslie A Litzky, Michael Feldman, Jorge Henao-Mejia, Boris Striepen, Holly Ramage, Kellie A Jurado, Kathryn E Wellen, Una O’Doherty, Mohamed Abdel-Mohsen, Alan L Landay, Ali Keshavarzian, Timothy J Henrich, Steven G Deeks, Michael J Peluso, Nuala J Meyer, E John Wherry, Benjamin A Abramoff, Sara Cherry, Christoph A Thaiss, and Maayan Levy. Serotonin reduction in post-acute sequelae of viral infection. *Cell*, 10 2023. Available from: <https://pubmed.ncbi.nlm.nih.gov/37848036/>, doi:10.1016/j.cell.2023.09.013.
- [191] Wenjie Xu, Ziyi Yang, Hao Tang, Chen Wang, and Zhengfang Ye. Response of immobilized denitrifying bacterial consortium to tetracycline exposure. *Ecotoxicology and Environmental Safety*, 239:113652, 2022. Available from: <https://www.sciencedirect.com/science/article/pii/S0147651322004924>, doi:<https://doi.org/10.1016/j.ecoenv.2022.113652>.
- [192] Xiao Xu, Wei Cheng, Xin Liu, Heng You, Guitai Wu, Kunming Ding, Xiuliang Tu, Lanfang Yang, Youpin Wang, Yadong Li, Haoshuang Gu, and Xingguo Wang. Selenate reduction and selenium enrichment of tea by the endophytic herbaspirillum sp. strain wt00c. *Current Microbiology*, pages 588–601, 04 2019. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7075828/>, doi:10.1007/s00284-019-01682-z.
- [193] Xiaoxiao Yan, Haibo Jia, and Junbo Zhao. Lncrna meg3 attenuates the malignancy of retinoblastoma cells through inactivating pi3k /akt/mtor signaling pathway. *Experimental Eye Research*, 226:109340, 2023. Available from: <https://www.sciencedirect.com/science/article/pii/S0014483522004213>, doi:<https://doi.org/10.1016/j.exer.2022.109340>.
- [194] Meifeng Yang, Jing Lu, Junye Miao, Joshua Rizak, Jianzhen Yang, Rongwei Zhai, Jun Zhou, Jiagui Qu, Jianhong Wang, Shangchuan Yang, Yuanye Ma, Xintian Hu, and Rongqiao He. Alzheimer’s disease and methanol toxicity (part 1): chronic methanol feeding led to memory impairments and tau hyperphosphorylation in mice. *Journal of Alzheimer’s disease : JAD*, pages 1117–29, 2014. Available from: <https://pubmed.ncbi.nlm.nih.gov/24787915/>, doi:10.3233/JAD-131529.
- [195] Meifeng Yang, Junye Miao, Joshua Rizak, Rongwei Zhai, Zhengbo Wang, Tanzeel Huma, Ting Li, Na Zheng, Shihao Wu, Yingwei Zheng, Xiaona Fan, Jianzhen Yang, Jianhong Wang, Shangchuan Yang, Yuanye Ma, Longbao Lu, Rongqiao

- He, and Xintian Hu. Alzheimer's disease and methanol toxicity (part 2): lessons from four rhesus macaques (macaca mulatta) chronically fed methanol. *Journal of Alzheimer's disease : JAD*, pages 1131–47, 2014. Available from: <https://pubmed.ncbi.nlm.nih.gov/24787917/>, doi:10.3233/JAD-131532.
- [196] Mon Oo Yee, Joerg Deutzmann, Alfred Spormann, and Amelia-Elena Rotaru. Cultivating electroactive microbes from field to bench. *Nanotechnology*, 31. Available from: <http://dx.doi.org/10.1088/1361-6528/ab6ab5>, doi:10.1088/1361-6528/ab6ab5.
- [197] Hung YT, Lee YT, Huang LJ, Chen TL, Yu KW, Fung CP, Cho WL, and Liu CY. Clinical characteristics of patients with acinetobacter junii infection. *Journal of Microbiology, Immunology, and Infection = Wei Mian yu gan ran za zhi*, 42:47–53, 02 2009. Available from: [https://europepmc.org/article/med/19424558?utm\\_medium=email&utm\\_source=transaction&client=bot](https://europepmc.org/article/med/19424558?utm_medium=email&utm_source=transaction&client=bot).
- [198] Nayela Zeba, Timothy D. Berry, Monika S. Fischer, Matthew F. Traxler, and Thea Whitman. Soil carbon mineralization and microbial community dynamics in response to pyom addition. *Cold Spring Harbor Laboratory*, 06 2023. Available from: <http://dx.doi.org/10.1101/2023.06.21.545992>, doi:10.1101/2023.06.21.545992.
- [199] Binbin Zhang, Minjie Jiang, Jianan Zhao, Yu Song, Weidong Du, and Junping Shi. The mechanism underlying the influence of indole-3-propionic acid: A relevance to metabolic disorders. *Frontiers in Endocrinology*, 03 2022. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8972051/>, doi:10.3389/fendo.2022.841703.
- [200] Jun Zhang, Jian Chen, Yi-Fei Wu, Xia Liu, Charles Packianathan, Venkadesh S. Nadar, Barry P. Rosen, and Fang-Jie Zhao. Functional characterization of the methylarsenite-inducible arsm operon from noviherspirillum denitrificans hc18. *Environmental microbiology*, pages 772–83, 01 2022. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8881391/>, doi:10.1111/1462-2920.15909.
- [201] Manman Zhang, Zhaoqi Kang, Xiaoting Guo, Shiting Guo, Dan Xiao, Yidong Liu, Cuiqing Ma, Ping Xu, and Chao Gao. Regulation of glutarate catabolism by gntR family regulator csir and lysR family regulator gcdr in pseudomonas putida kt2440. *mBio*, 10, 08 2019. Available from: <http://dx.doi.org/10.1128/mbio.01570-19>, doi:10.1128/mbio.01570-19.
- [202] Peidong Zhang, Zhihao Li, Peiliang Chen, Ao Zhang, Yu Zeng, Xiru Zhang, Qingmei Huang, Dan Liu, Songtao Qi, and Chen Mao. Regular proton pump inhibitor use and incident dementia: population-based cohort study. *BMC Medicine*, 20, 2022. Available from: <http://dx.doi.org/10.1186/s12916-022-02478-y>, doi:10.1186/s12916-022-02478-y.
- [203] Shusong Zhang, Xingbin Sun, Yueting Fan, Tianlei Qiu, Min Gao, and Xuming Wang. Heterotrophic nitrification and aerobic denitrification by diaphorobacter polyhydroxybutyrativorans sl-205 using poly(3-hydroxybutyrate-co-3-hydroxyvalerate) as the sole carbon source. *Bioresource Technology*, 241, 2017. Available from: <http://dx.doi.org/10.1016/j.biortech.2017.05.185>, doi:10.1016/j.biortech.2017.05.185.
- [204] Ting Zhang and Houjin Zhang. Microbial consortia are needed to degrade soil pollutants. *Microorganisms*, 01 2022. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8874626/>, doi:10.3390/microorganisms10020261.
- [205] Jian-Ying Zhao, Juan Chen, Zhong-Ting Hu, Juan Li, Hua-Ying Fu, Philippe C. Rott, and San-Ji Gao. Genetic and morphological variants of acidovorax avenae subsp. avenae cause red stripe of sugarcane in china. *Frontiers in Plant Science*, 14, 2023. Available from: <https://www.frontiersin.org/articles/10.3389/fpls.2023.1127928>, doi:10.3389/fpls.2023.1127928.
- [206] Guo-Wei Zhou, Xiao-Ru Yang, Regin Ronn, Jian-Qiang Su, Li Cui, Bang-Xiao Zheng, and Yong-Guan Zhu. Metabolic inactivity and re-awakening of a nitrate reduction dependent iron(ii)-oxidizing bacterium bacillus ferrooxidans. *Frontiers in Microbiology*, 10, 2019. Available from: <https://www.frontiersin.org/articles/10.3389/fmicb.2019.01494>, doi:10.3389/fmicb.2019.01494.
- [207] Lepeng Zhou, Wen Qiu, Jie Wang, Aihua Zhao, Chuhui Zhou, Tao Sun, Ziyu Xiong, Peihua Cao, Wei Shen, Jingfen Chen, Xiaolu Lai, Liu-hong Zhao, Yue Wu, Meng Li, Feng Qiu, Yanhong Yu, Zhenjiang Zech Xu, Hongwei Zhou, Wei Jia, Yan Liao, Ravi Retnakaran, Daniel Krewski, Shi Wu Wen, Jose C. Clemente, Tianlu Chen, Ri-hua Xie, and Yan He. Effects of vaginal microbiota transfer on the neurodevelopment and microbiome of cesarean-born infants: A blinded randomized controlled trial. *Cell Host & Microbe*, 31, 2023. Available from: <http://dx.doi.org/10.1016/j.chom.2023.05.022>, doi:10.1016/j.chom.2023.05.022.

### Acknowledgments

1. Nikki Schultek for brining this work [151] as well as the infectious hypothesis to my attention.
2. Pubmed eutils facilities and the basic research it provides.
3. Free software including Linux, R, LaTeX etc.
4. Thanks everyone who contributed incidental support.
5. I have to credit my own software such as bash scripts and of course TooBib[100] for facilitating citation discovery.

**Appendix A: Statement of Conflicts**

No specific funding was used in this effort and there are no financial relationships with others that could create a conflict of interest.

**Appendix B: About the Authors**

This work was performed at a dog rescue run by Barbara Cade and housed in rural Georgia. The author of this report ,Mike Marchywka, has a background in electrical engineering and has done extensive research using free online literature sources. I hope to find additional people interested in critically examining the results.

**Appendix C: Interpretation Issues- General and Specific**

While trying to generate hypotheses about cause and effect in order to ultimately design a useful intervention, its important to remember some caveats specific to these data and ambient nutrient levels. The features and citations picked out for this work may be influenced by literature skew towards trendy topics and selection bias. The data are all relative abundances so no real inferences about absolute amounts can be made and all the processing steps employed by the original authors have not been explored. Much of the analysis will now depend on reasoning such as "nutrient X favors organism Y" but the available amount of "X" could itself be due to many factors. Ideally a rate equation should be written to account for all sources and sinks of "X" but even in that case both are likely to be controlled by feedback mechanisms.

The relationship between microbe relative abundance, nutrient status, and brain health could be quite complicated even if fitness could be easily related to nutrient concentration. The limiting nutrient could exist in amounts determined by various feedback signals from functioning brain or be limited by supply and vascular function. High concentration could even reflect low uptake by neurons in some diseased states. A rate equation with the right control terms could show the complexity of causal inference.

For example, increased abundance simply indicates comparative fitness increase. Assuming histidine is limiting, that may be due to increased supply due to host signalling or a virulent organism releasing it or failure of senescent neurons to compete. All fitness arguments and static levels need to be carefully considered with rate equations that include feedback for source control.

**Appendix D: Symbols, Abbreviations and Colloquialisms**

TERM definition and meaning

**Appendix E: General caveats and disclaimer**

This document was created in the hope it will be interesting to someone including me by providing information about some topic that may include personal experience or a literature review or description of a speculative theory or idea. There is no assurance that the content of this work will be useful for any particular purpose.

All statements in this document were true to the best of my knowledge at the time they were made and every attempt is made to assure they are not misleading or confusing. However, information provided by others and observations that can be manipulated by unknown causes ( "gaslighting" ) may be misleading. Any use of this information should be preceded by validation including replication where feasible. Errors may enter into the final work at every step from conception and research to final editing.

Documents labelled "NOTES" or "not public" contain substantial informal or speculative content that may be terse and poorly edited or even sarcastic or profane. Documents labelled as "public" have generally been edited to be more coherent but probably have not been reviewed or proof read.

Generally non-public documents are labelled as such to avoid confusion and embarrassment and should be read with that understanding.

**Appendix F: A baseline nutrient outline****Appendix G: Citing this as a tech report or white paper**

Note: This is mostly manually entered and not assured to be error free.  
This is tech report MJM-2023-008.

Version	Date	Comments
0.01	2023-09-17	Create from empty.tex template
-	October 24, 2023	version 0.30 MJM-2023-008
0.3	2023-10-24	first draft done for now.
1.0	20xx-xx-xx	First revision for distribution

Released versions,  
build script needs to include empty releases.tex

Version	Date	URL
.3	2023-10-25	<a href="https://www.linkedin.com/posts/marchywka_brain-bacteria-as-nutrient-diagnostic-activity-712274532401">https://www.linkedin.com/posts/marchywka_brain-bacteria-as-nutrient-diagnostic-activity-712274532401</a>
.3	2023-10-25	<a href="https://www.researchgate.net/publication/374946157_potuse-2023-10-24-v3">https://www.researchgate.net/publication/374946157_potuse-2023-10-24-v3</a>
.3	2023-10-25	<a href="https://www.academia.edu/108555399/Brain_Microbiome_Make_Your_Garden_Grow_Feed_Your_Head">https://www.academia.edu/108555399/Brain_Microbiome_Make_Your_Garden_Grow_Feed_Your_Head</a>
.3	2023-10-25	<a href="https://zenodo.org/records/10038912">https://zenodo.org/records/10038912</a>
.3	2023-10-25	

```
@techreport{marchywka-MJM-2023-008-0.30 ,
filename={potuse} ,
run-date={October 24, 2023} ,
title={Brain Microbiome : Make Your Garden Grow? Feed Your Head } ,
author={Mike J Marchywka } ,
type={techreport} ,
name={marchywka-MJM-2023-008-0.30 } ,
number={MJM-2023-008} ,
version={0.30 } ,
institution={not institutionalized, independent } ,
address={ 44 Crosscreek Trail, Jasper GA 30143} ,
date={October 24, 2023} ,
startdate={2023-09-17} ,
day={24} ,
month={10} ,
year={2023} ,
author1email={marchywka@hotmail.com} ,
contact={marchywka@hotmail.com} ,
author1id={orcid.org/0000-0001-9237-455X} ,
pages={ 28}
}
```

Supporting files. Note that some dates,sizes, and md5's will change as this is rebuilt.

This really needs to include the data analysis code but right now it is auto generated picking up things from prior build in many cases

```
106509 Sep 25 15:05 dailysnapx.bib b7eb45640d2a9f3424f3f26126405444
45700 Jan 10 2023 /home/documents/latex/bib/releases.bib e563ee01d21db5cead662baa64a3947f
7331 Jan 24 2019 /home/documents/latex/pkg/fltpage.sty 73b3a2493ca297ef0d59d6c1b921684b
7434 Oct 21 1999 /home/documents/latex/pkg/lgrind.sty ea74beead1aa2b711ec2669ba60562c3
1069 Oct 15 2021 /home/documents/latex/share/includes/disclaimer-gaslight.tex 94142
b0e063984d082bff3b400abe0fb
425 Oct 11 2020 /home/documents/latex/share/includes/disclaimer-status.tex b276f09e06a3a9114f927e4199f379f7
3717 Aug 18 18:59 /home/documents/latex/share/includes/mjmaddbib.tex 3715beeb1216a8e9c3178477af732808
```

```

117 Oct 16 15:35 /home/documents/latex/share/includes/mjmlistings.tex c1c3bd564b7fb321b4d8f223c7d3cde3
4250 Mar 22 2023 /home/documents/latex/share/includes/mycommands.tex ee611f5c0a8bcd0c6a5453a0521ddc8e
2883 Oct 16 16:01 /home/documents/latex/share/includes/myskeletonpackages.tex
    ba7541965f073c211dc9e8fbd3231afd
29313 Jan 27 2019 /home/documents/latex/share/includes/plainurl.bst dfacbf66df173afc674ca07e6b8dad42
1538 Aug 14 2021 /home/documents/latex/share/includes/recent_template.tex 49763d2c29f74e4b54fa53b25c2cc439
7217 May 15 17:54 /home/documents/latex/share/overrides/mol2chemfig.sty 5aa81c197d462c2153a794ccee9881ef
77690 May 20 18:35 /home/marchywka/.texlive2019/texmf-var/luatex-cache/generic-dev/fonts/otl/lmmono9-
    regular.luc 96acce07e21c918c677d94556d7a487
124213 May 20 18:35 /home/marchywka/.texlive2019/texmf-var/luatex-cache/generic-dev/fonts/otl/lmroman10-
    bold.luc be24eb5b757919758e60aa4f6d6aeb1d
132135 Oct 12 07:42 /home/marchywka/.texlive2019/texmf-var/luatex-cache/generic-dev/fonts/otl/lmroman10-
    italic.luc 48267fd5932c239fb4bad361e29a6f1e
123142 May 20 18:35 /home/marchywka/.texlive2019/texmf-var/luatex-cache/generic-dev/fonts/otl/lmroman10-
    regular.luc d3b29489a8ffc91cd4e03357f67b2fc5
124110 May 20 18:35 /home/marchywka/.texlive2019/texmf-var/luatex-cache/generic-dev/fonts/otl/lmroman12-
    bold.luc 8287c14a46bbf501cc26dc995afe5943
123481 May 20 18:35 /home/marchywka/.texlive2019/texmf-var/luatex-cache/generic-dev/fonts/otl/lmroman12-
    regular.luc 43b95c7579b49c47160ac0c030902624
121774 Sep 15 07:11 /home/marchywka/.texlive2019/texmf-var/luatex-cache/generic-dev/fonts/otl/lmroman5-
    regular.luc c99e387d782447967e8d270ff980a91f
124323 May 20 18:35 /home/marchywka/.texlive2019/texmf-var/luatex-cache/generic-dev/fonts/otl/lmroman6-
    regular.luc 6f24b27a1b5aa4b0cc9bac3053577dc4
124198 May 20 18:35 /home/marchywka/.texlive2019/texmf-var/luatex-cache/generic-dev/fonts/otl/lmroman7-
    regular.luc 86fe133d3cae7b679738c113e6f1abb9
123949 May 20 18:35 /home/marchywka/.texlive2019/texmf-var/luatex-cache/generic-dev/fonts/otl/lmroman8-
    regular.luc 4c67e46bb33a79c15e883e91a392459c
124254 May 20 18:35 /home/marchywka/.texlive2019/texmf-var/luatex-cache/generic-dev/fonts/otl/lmroman9-bold
    .luc d65daa4f1bfa8d8116e83ffdb58b835
131665 May 20 18:35 /home/marchywka/.texlive2019/texmf-var/luatex-cache/generic-dev/fonts/otl/lmroman9-
    italic.luc 75ae5c563908ddf015a78b6a6c60e1f7
123771 May 20 18:35 /home/marchywka/.texlive2019/texmf-var/luatex-cache/generic-dev/fonts/otl/lmroman9-
    regular.luc 389c904e3ac3a14fd699c9e66e0cad24
531926 Oct 24 13:46 non_pmc_potuse.bib 7e85320d759de2b1dbc50ae6cc682603
229954 Oct 24 19:11 pmc_potuse.bib 11a0492c3c9e81299edec598c05219f5
27686 Oct 24 20:36 potuse.aux 17fe1ba786fe543982d183736587cec5
107545 Oct 24 20:36 potuse.bbl d041b2fa2af9b9b7b2c4574b0fd2dbe5
762281 Oct 24 20:36 potuse.bib cbb70c3fa4fe395f5ef2a00194d5bf
2629 Oct 24 20:36 potuse.blg 5b44b9f431235d7ed091ecadb242d8ee
0 Oct 24 20:37 potuse.bundle_checksums d41d8cd98f00b204e9800998ecf8427e
31413 Oct 24 20:36 potuse.flx d6987a62e7558f1252a0120d40ab909a
3 Oct 24 20:36 potuse.last_page 51a6d96331d5eaa300358c7a0faf168d
56102 Oct 24 20:36 potuse.log 31c2e28941647fe740cf296bd2d05b7e
4720 Oct 24 20:36 potuse.out 7c224597b253832d0d8719ffe9bc70075
328802 Oct 24 20:36 potuse.pdf a623a59e7b2d6877c15695f477fac8fc
90591 Oct 24 20:33 potuse.tex 0779094683f45dd196f0702ce13a4e18
2251 Oct 24 20:36 potuse.toc bdc3f9ffff437c0a4ed46eb2203a16e8
413 Sep 17 16:55 releases.tex 56213b8bd7e164dd6e668b62f5acf868
15 May 20 18:34 /var/lib/texmf/fonts/map/pdftex/updmap/pdftex.map -> pdftex_dl14.map
    f177baa1c39a3ebd62c3096a43521a0d
2639650 May 31 06:05 /var/lib/texmf/web2c/luatex/lualatex.fmt f86507d809f5764fcd9fe4e15658c86c
328802 Oct 24 20:36 potuse.pdf a623a59e7b2d6877c15695f477fac8fc

```