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INFLUENCE OF GUT RESISTOME ON HUMANS WITH AUTISM SPECTRUM DISORDER

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ABSTRACT: The impact of the gut resistome—genes in the gut microbiota that resist antibiotics—on individuals with autism spectrum disorder (ASD) is investigated in this study. The gut–brain axis, which influences the neurodevelopmental and behavioral effects of ASD, may be influenced by the makeup and activity of gut bacteria, according to recent studies. The immune system, microorganisms, food digestion, and inflammation are all impacted by the gastrointestinal resistome. This could have an indirect impact on ASD symptoms and brain function. Children with ASD may develop dysbiosis as a result of early antibiotic exposure, which can alter the gut microbiota and strengthen resistance genes. ASD may be impacted by dysbiotics because they alter immunological signaling, create neuroactive metabolites, and harm the intestinal barrier. Research on the gut resistome, microbial ecology, and host response can reveal the primary causes of ASD. It also describes how antibiotics, probiotics, and medications that are specifically targeted to the microbiome function.

Keywords: *Gut resistome, Autism Spectrum Disorder, gut microbiota, antibiotic resistance genes, dysbiosis, gut–brain axis, neurodevelopment, immune modulation, microbial metabolites.*

1. INTRODUCTION

The complicated neurological ailment known as autism spectrum disorder (ASD) is characterized by repetitive activities, limited interests, and trouble communicating with others. Along with these main behavioral characteristics, gastrointestinal (GI) issues such diarrhea, constipation, abdominal pain, and irregular bowel habits are common in people with ASD. The gut-brain axis has drawn more attention from researchers in the last ten years. The gastrointestinal tract, gut microbiota, and central nervous system are connected by this two-way communication system. The immune system's operation, human behavior, and brain development have all been found to be significantly influenced by the gut microbiome. The gut resistome, a part of the gut microbiota, has garnered a lot of attention lately. Its possible influence on health outcomes, especially those linked to ASD, is the main reason for this.

The collection of antibiotic resistance genes (ARGs) found in the gut microbiota, regardless of their use or transmission, is referred to as the gut resistome. These genes may have come from commensal bacteria or may have been horizontally transferred from environmental or pathogenic microbes. The resistome is regularly studied in relation to antibiotic resistance and public health. On the other hand, it serves as a genetic reservoir that can change the interactions between hosts, the metabolism of nutrients, and the makeup of microbes.

Numerous factors, especially in the formative years, affect an individual's intestinal resistance. These elements include a person's genetic makeup, birth circumstances, eating habits, exposure to antibiotics, exposure to environmental germs, and genetic constitution. Changes in these traits may have long-term effects on microbial ecology and host physiology. Researchers are particularly interested in the resistome of people with ASD because of their distinct intestinal flora, higher childhood antibiotic exposure, and elevated inflammatory and immunological responses. In many studies, dysbiosis has been observed in people with ASD. This indicates a shift in the proportions of vital bacterial communities that affect the immune system, metabolize neurotransmitters, and create short-chain fatty acids, as well as a decline in microbial diversity. Certain bacterial alterations may be induced or coincident with abnormalities in the gut resistome. Because of their enlarged or unbalanced resistome, only some types of bacteria are able to resist selective pressure. The gut microbiome may be compromised and dysbiosis may worsen as a result.

The influence of the gastrointestinal resistome on ASD may be intensified by a variety of molecular processes. By being near genes that generate toxins, neurotransmitters, or inflammatory signals, ARGs can first change the microbial metabolism of food. Second, antibiotic-resistant bacteria can have their colonization patterns and competitive capacities changed, which may have an impact on the dominant bacterial species in the intestine. Third, modifications to the resistome may have an indirect impact on the host's immune system development. Prolonged contact to populations of resistant bacteria can cause chronic low-grade inflammation, which is commonly seen in people with ASD. Immunological dysregulation throughout crucial stages of neurodevelopment contributes to the pathophysiology of ASD.

One important link between the gastrointestinal resistome and ASD is the use of antibiotics throughout early development. By eradicating beneficial bacteria, encouraging the establishment of resistant species, and strengthening the resistome, antibiotics have the capacity to drastically change the intestinal microbiota. Despite continuous discussions on the underlying processes, numerous epidemiological studies have found links between early antibiotic exposure and an increased risk of neurodevelopmental problems. Frequent administration of antibiotics or a range of antibiotic kinds may worsen microbial and resistome imbalances in those who are predisposed to ASD. Immune system reactions, vagus nerve signal transmission, and changes in bacterial metabolism can all have an impact on brain development.

2. AUTISM SPECTRUM DISORDER (ASD)

The precise causes or molecular mechanisms of autism spectrum disorder (ASD), a significant neurodevelopmental and neuropsychiatric condition, remain unknown. The severity of symptoms and their impact on behavior, communication, and interpersonal interactions can vary significantly among individuals with this illness. These variations illustrate that ASD is not a condition that affects all individuals.

Core Behavioral and Social Impairments: Social interaction, whether verbal or nonverbal, is frequently challenging for individuals on the autism spectrum. Additionally, they establish patterns that are both repetitive and restrictive. These challenges encompass restricted eye

contact, verbal communication difficulties, conversation avoidance, social interaction issues, and repetitive movements that disrupt daily activities.

Associated Comorbid Conditions: Frequently, the mental and physical health of individuals with ASD is adversely affected by the presence of numerous comorbid medical ailments. This spectrum encompasses a variety of challenges, such as delayed speech and language development, reduced intellect, poor abstract reasoning ability, motor coordination, brain development, and information processing. The diagnosis and course of treatment are further complicated by comorbidities.

Sensory Processing Abnormalities: The autism spectrum condition is characterized by the inability to regulate one's senses of scent, touch, or hearing. Numerous children on the autism spectrum exhibit varying degrees of sensitivity to a variety of stimuli, including gustatory, olfactory, visual, and auditory stimuli. These sensory deficiencies can have an impact on an individual's learning, social interactions, and behavior.

Gastrointestinal Symptoms in ASD: Digestive issues are more prevalent among individuals with ASD than in the general population. Acid reflux, dyspepsia, constipation, diarrhea, symptoms similar to irritable bowel syndrome, food intolerances, and inflammatory bowel disease are among the most prevalent symptoms of gastrointestinal problems. As a consequence of these issues, individuals may exhibit inappropriate behavior, experience feelings of sadness, and generally have a reduced quality of life.

Prevalence and Global Distribution: In numerous countries worldwide, the prevalence of autism spectrum disorder (ASD) has recently increased. Although the prevalence is higher in affluent countries and specific Middle Eastern and Gulf states, there are differences in reporting practices, knowledge levels, and diagnostic standards.

Gender Differences in ASD: Autism spectrum disorder is significantly more prevalent in males than in females. There is a possibility that biological, genetic, or hormonal factors may influence the manifestation of symptoms in both sexes, as males are more likely to receive an ASD diagnosis than girls.

Age of Onset and Early Diagnosis: Autism Spectrum Disorder (ASD) is more likely to manifest during the initial three years of life. Doctors can differentiate ASD from other developmental disorders by examining symptoms between 18 and 24 months. It is imperative to promptly diagnose a child in order to initiate treatment and enhance developmental outcomes.

Challenges in Diagnosis: Diagnosing ASD may be difficult due to the potential for its symptoms to be confounded with those of other developmental and mental disorders. A correct diagnosis should be based on a comprehensive evaluation of the patient's developmental history, repetitive behaviors, limited interests, and social communication problems, rather than solely relying on biological indicators.

Genetic Contributions to ASD: The hereditary component of autism spectrum disorder (ASD) has been estimated to be between 60% and 83% in numerous investigations. Scientists have not identified a single gene as the primary offender, despite the significant impact of genetics. This demonstrates the intricacy of the genetic makeup of the disease.

Environmental and Epigenetic Risk Factors: In order to comprehend the causes of ASD, it is necessary to consider factors other than heredity, including environmental and epigenetic factors. The onset and progression of ASD are believed to be influenced by prenatal exposures, gene-environment interactions, and early life events.

Role of Gut Microbiota and Resistome: Recent research indicates that the development of ASD may be influenced by gut flora. The metabolic processes and immunological responses associated with autism spectrum disorder (ASD) may be influenced by changes in the gastrointestinal resistome, which is composed of genes from populations of antibiotic-resistant microorganisms.

Gut–Brain Axis and Immune Involvement: A growing body of research has established a correlation between autism spectrum disorder (ASD) and issues with the gut-brain axis. Neurodevelopmental abnormalities and behavioral symptoms in individuals with autism spectrum disorder (ASD) can be induced by changes in intestinal microbiota that impact immune systems and metabolic pathways.

Gastrointestinal Disorders and Symptom Severity: Compared to their peers who are typically developing, children with ASD are more likely to experience gastrointestinal issues, such as diarrhea and constipation. Individuals who experience these symptoms may observe an enhancement in their overall well-being, discomfort, and behavioral issues.

3. MICROBIOME

THE HUMAN GUT MICROBIOME

- The gastrointestinal tract of humans hosts close to a thousand different microbial species.
- The term gut microbiome describes the community of microorganisms and their genetic material that inhabit the digestive system.
- These microbes are essential for sustaining health and maintaining physiological equilibrium.

Factors Influencing Gut Microbiome Composition

- The makeup of intestinal microbes is influenced by birth method, dietary habits, lifestyle choices, environmental exposures, and genetic background.
- Both external and internal elements continuously reshape microbial diversity and activity across the lifespan.

Functional Role of the Gut Microbiome

The GM contributes to:

- Generating bioactive molecules that impact host physiology
- Supporting and regulating immune system development
- Altering drug metabolism and therapeutic responses
- Controlling gut hormone activity
- Neutralizing and removing toxic compounds
- Because of these roles, microbiome modulation is increasingly viewed as a therapeutic strategy in disease management.

Microbiome and Immune-Mediated Disorders

- Gut microbes strongly affect immune regulation, intestinal barrier integrity, and even distant organ systems.
- Imbalances in microbial communities (dysbiosis) are linked to inflammatory, metabolic, neurological, cardiovascular, and respiratory diseases.
- Environmental triggers such as infections and smoking are key drivers of oral and intestinal dysbiosis.

Gut Microbiome and Rheumatoid Arthritis (RA)

- RA is a long-term autoimmune condition marked by chronic inflammation and progressive joint damage.
- Research shows untreated RA patients have a distinct gut microbial profile compared to healthy individuals.
- Reduced microbial genetic diversity is commonly observed in RA cases.
- Prevotella species, especially Prevotella copri, are often elevated, suggesting microbial imbalance may precede disease onset.
- Lower levels of Faecalibacterium and higher levels of Collinsella have also been associated with RA and irritable bowel syndrome (IBS).

Microbiome and Neurological Disorders

- Growing evidence links gut microbial disturbances to neurological and psychiatric disorders.
- In autism spectrum disorder (ASD), microbial composition differs significantly from that of healthy individuals.
- Studies report reduced Prevotellaceae and Porphyromonadaceae, alongside increased Erysipelotrichaceae, Alcaligenaceae, and Ruminococcaceae.
- Animal experiments reveal that gut microbes can influence social interaction, communication, stress responses, and depressive behaviors.
- Transplanting gut microbiota between animals has even been shown to transfer behavioral traits.

Microbiome and Cancer

- The gut microbiome has been implicated in pancreatic cancer progression.
- Patients with pancreatic cancer often display a more diverse stool microbiome enriched with lipopolysaccharide (LPS)-producing and pathogenic bacteria.
- Elevated levels of genera such as Enterobacter, Veillonella, Hallella, Selenomonas, Prevotella, and Klebsiella have been documented compared to healthy controls.

4. RESISTOME

The antibiotic resistome is the comprehensive collection of antibiotic resistance genes (ARGs) in a specific environment, such as the body. These genes are present in both pathogenic and non-pathogenic microbes and contribute to drug resistance.

Development of the Human Resistome: The resistome typically develops within a few months of birth. Early microbial colonization is essential for the development of the resistome, as the microbiota is a primary source of antibiotic resistance genes (ARGs).

Role of Gut Microbiota and Colonization Resistance: By resisting colonization, indigenous gut organisms prevent the dissemination of hazardous species. Resistance genes are carried by commensal organisms in the stomach, which prevent disease.

Factors Influencing Antibiotic Resistance Genes: A variety of factors influence the diversity and content of ARGs. Factors such as the severity of the illness, hospitalization, live microbial therapy, antibiotic exposure, nursing practices, agriculture, location, and diet are all considered. Across individuals and locations, these components constitute the resistome.

Resistome Analysis Using Metagenomics: The human resistome has been extensively examined in the microbiomes of the intestine, skin, and respiratory tract as a result of the application of metagenomic and next-generation sequencing techniques. These methods

provide a comprehensive understanding of ARG types and propagation without the need for bacterial culturing.

Clinical Significance and ARG Transmission: An comprehension of resistome temporal oscillations is necessary for the regulation of ARG transmission in the domains of agriculture, healthcare, and the environment. ARGs that are therapeutically significant are maintained and dispersed by human microbiome commensals. By transmitting resistance genes to pathobionts or maladies, these commensals enhance their virulence and clinical significance.

Evidence of Gene Transfer from Commensals: Numerous studies have demonstrated that commensal bacteria can provide pathogenic strains with resistance genes. Vancomycin resistance genes, specifically vanB, are present in Eggerthella lenta and Clostridium innocuum. This illustrates the extent to which the gastrointestinal resistome influences clinically significant antibiotic resistance.

5. ANTIBIOTIC RESISTANCE GENES (ARGS)

A resistome is a collection of antibiotic resistance genes (ARGs) that are present in a single bacterium or microbial community. Resistomes have been examined in human digestive systems, soils, marine environments, and animals (Fig. 2). There will be an increase in the number of antibiotic resistance genes identified in the bacterial genomes that are analyzed using metagenomic whole-genome shotgun sequencing (mWGS). As illustrated in Fig. 3, antibiotic resistance genes (ARGs) can be inherited from the producers or acquired from other bacteria.

Resistance genes may be acquired by antibiotic-sensitive bacteria through transformation, transduction, and conjugation, or they may develop resistance as a result of mutations. The primary mechanisms by which bacteria acquire antibiotic resistance are adaptations, ribosomal global protection cell proteins, target replacement, inactivation, and antibiotic alterations (Fig. 4). One method of accomplishing this is to decrease the binding of the antibiotic to the antibiotic target. Pharmacological efflux and target

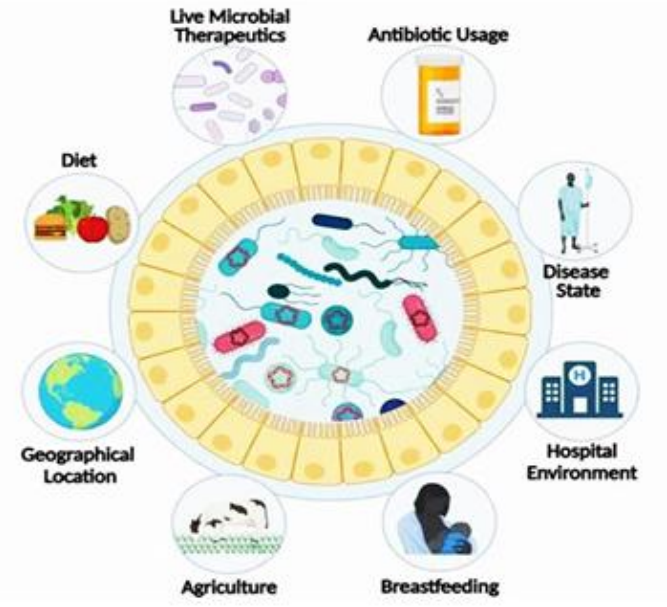

Fig. 1. Collection of environmental antibiotic resistance genes

By altering their structure or losing the efficacy of treatment, bacteria can develop resistance. Natural resistance can be developed by bacteria through neutralization, drug discharge, or

absorption restriction. It is conceivable that this bacterium acquired these techniques from other living organisms.

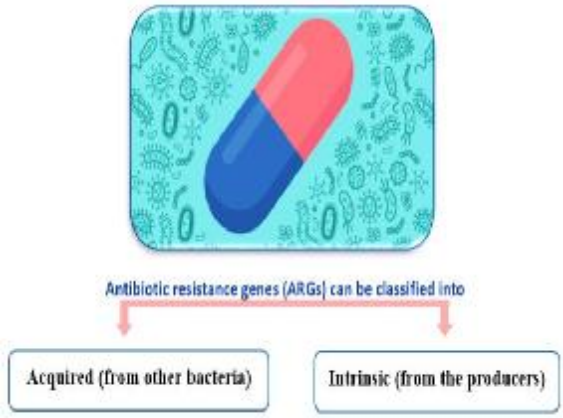

Fig. 2. Description of the reservoir of ARGs. Taken after Cuadrat et al. (2020)

The five primary antimicrobial processes are as follows: influence the formation of cell walls, reduce the synthesis of proteins and nucleic acids, obstruct bacterial routes, and depolarize the cell membrane. Table 1 illustrates antimicrobial group-based procedures. The resistance levels of different bacterial groups can vary significantly. The minimum inhibitory concentration (MIC) is a measure of chemical resistance or susceptibility. Antibiotics exhibit varying minimum inhibitory concentrations. Bacterial antimicrobial susceptibility is the term used to describe the ability of bacteria to respond to a drug. Some individuals believe that the species is inherently resistant, despite the fact that it is in the resistant MIC range. Bacteria's degree of resistance is contingent upon their genetic composition and classification.

Natural resistance may arise from intrinsic genes that are perpetually expressed or from bacterial genes that are activated to resist medications. Inherent resistance is present in all microorganisms, regardless of antibiotic treatment or horizontal gene transfer (Table 2). Antimicrobials are inhibited by the LPS layer, which is composed of numerous compounds and is present in gram-negative bacteria. This elucidates the reason why numerous medications are ineffective against specific bacteria. Mycobacteria cells can be entered by rifampicin and fluoroquinolones through their hydrophobic lipid outer layer. Cellular permeability is diminished by hydrophilic drugs. Additionally, Mycoplasma's resistance renders β-lactams and glycopeptides ineffective against it, as they target the cell wall. Drugs are unable to penetrate the cell due to the presence of Gram-positive bacteria on the cell surface. Polar molecules are present in the cell walls of enterococci, which provide resistance to aminoglycosides and impede the penetration of medications. Gram-positive Staphylococcus aureus bacteria are not susceptible to vancomycin. Vancomycin-resistant S. aureus (VISA) strains are drug-resistant due to their dense cell walls.

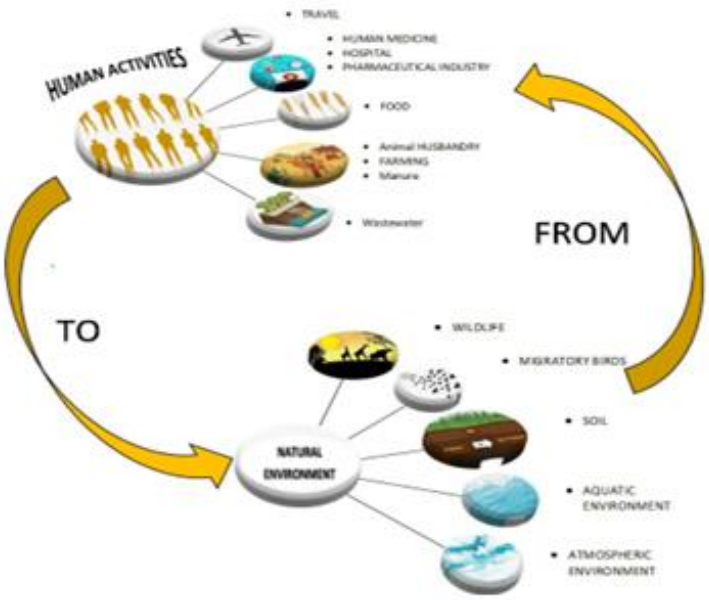

Fig. 3. The classification of ARGs.

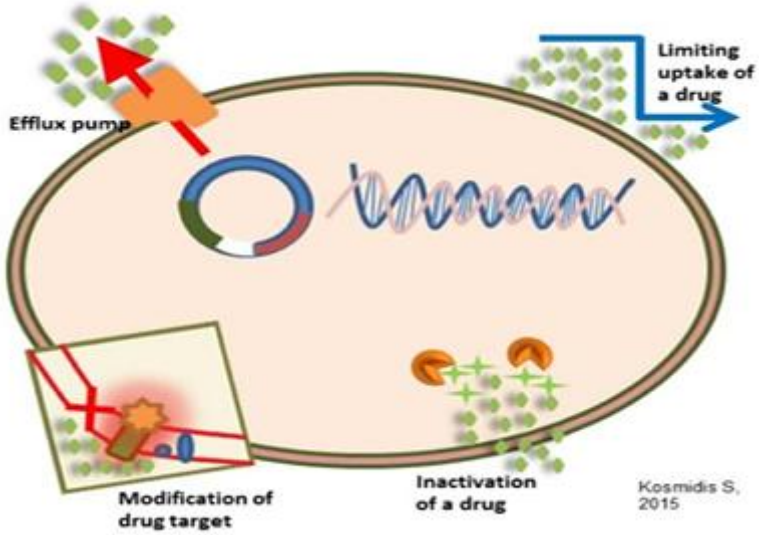

Fig. 4. Types of antimicrobial resistance mechanisms in bacteria.

ARGs may be either permanent or temporary. The primary method for acquiring genetic material from external sources is the plasmid-mediated transfer of resistance genes. The transmission of bacteriophages is very rare. Certain Acinetobacter species are capable of directly absorbing genetic material from their surroundings. Antibiotic resistance in bacteria can also be acquired through the modification of genes that encode drug transporters, enzymes that modify antibiotics, and drug targets. Another factor that diminishes the efficacy of antibiotics is bacteria. S. aureus experiences a gradual increase in size as it acquires resistance to methicillin. Germs may develop resistance to subinhibitory antibacterial medications after prolonged exposure to low concentrations.

6. CONCLUSION

The complex relationship between neurodevelopment, antibiotic resistance, and gut microbial dysbiosis is illustrated by the impact of the gut resistome on autistic spectrum disorder. Changes in the composition of the resistome can lead to dysbiosis, increased inflammation, and an altered gut-brain connection. Individuals with ASD may experience an intensification

of their gastrointestinal and behavioral issues as a result of these modifications. The long-term effects of antibiotics and microbial gene transfer on gastrointestinal health are better understood by understanding the evolution of resistomes. This underscores the ethical application of antibiotics and personalized microbiome-based therapy. The quality of life and therapeutic treatment for ASD may be improved through research on resistome changes caused by diet, probiotics, and specific medications.

REFERENCES

1. De Angelis, M., et al., Autism spectrum disorders and intestinal microbiota. Gut microbes. 2015. 6(3):207-213.
2. Agrawal S et al., Prevalence of autism spectrum disorder in preterm infants: A meta-analysis. Pediatrics, 2018;142(3).
3. Christensen J et al., Prenatal valproate exposure and risk of autism spectrum disorders and childhood autism. Jama. 2013;309(16):1696-1703.
4. Atladóttir HÓ et al., Maternal infection requiring hospitalization during pregnancy and autism spectrum disorders. Journal of autism and developmental disorders. 2010;40(12): 1423-1430.
5. (CDC) Cfdcap. Autism spectrum disorders; 2018. Available:https://www.cdc.gov/
6. Yang X, Zhang N, Schrader P. A study of brain networks for autism spectrum disorder classification using resting-state functional connectivity. Machine Learning with Applications, 2022;8:100290.
7. Hughes HK, Rose D, Ashwood P. The gut microbiota and dysbiosis in autism spectrum disorders. Current neurology and neuroscience reports. 2018;18:1-15.
8. Özcan E, Hsiao EY. Are changes in the gut microbiome a contributor or consequence of autism—why not both? Cell Reports Medicine. 2022;3(1):100505.
9. MacFabe DF, Enteric short-chain fatty acids: microbial messengers of metabolism, mitochondria, and mind: implications in autism spectrum disorders. Microbial ecology in health and disease. 2015;26(1):28177.
10. Fjalstad JW, Esaiassen E, Juvet LK, van den Anker JN, Klingenberg C. Antibiotic therapy in neonates and impact on gut microbiota and antibiotic resistance development: a systematic review. Journal of Antimicrobial Chemotherapy. 2018;73(3):569-80.
11. Gibson MK, Wang B, Ahmadi S, Burnham CA, Tarr PI, Warner BB, Dantas G. Developmental dynamics of the preterm infant gut microbiota and antibiotic resistome. Nature microbiology. 2016;1(4):1-0.
12. Krajmalnik-Brown R, Lozupone C, Kang DW, Adams JB. Gut bacteria in children with autism spectrum disorders: challenges and promise of studying how a complex community influences a complex disease. Microbial Ecology in Health and Disease. 2015;26(1):26914.
13. Schulfer AF, Battaglia T, Alvarez Y, Bijnens L, Ruiz VE, Ho M, Robinson S, Ward T, Cox LM, Rogers AB, Knights D. Intergenerational transfer of antibiotic perturbed microbiota enhances colitis in susceptible mice. Nature microbiology. 2018;3(2):234-42.
14. Kovtun AS, Averina OV, Alekseeva MG, Danilenko VN. Antibiotic resistance genes in the gut microbiota of children with autistic spectrum disorder as possible predictors of the disease. Microbial Drug Resistance. 2020;26(11):1307-20.

15. Collins SM, Kassam Z, Bercik P. The adoptive transfer of behavioral phenotype via the intestinal microbiota: experimental evidence and clinical implications. Current opinion in microbiology. 2013;16(3):240-5.
16. Martinez JL. General principles of antibiotic resistance in bacteria. Drug Discovery Today: Technologies. 2014;11:33-9.
17. Munita JM, Arias CA. Mechanisms of antibiotic resistance. Virulence mechanisms of bacterial pathogens. 2016:481-511.
18. Zhang X-X, Zhang T, Fang HH. Antibiotic resistance genes in water environment. Applied microbiology and biotechnology, 2009;82:397-414.
19. Liu B, Pop M. ARDB—antibiotic resistance genes database. Nucleic acids research. 2009;37(suppl_1):D443-7.
20. Bittker SS, Bell KR. Acetaminophen, antibiotics, ear infection, breastfeeding, vitamin D drops, and autism: an epidemiological study. Neuropsychiatric disease and treatment. 2018:1399-414.
21. Sharma VK, Johnson N, Cizmas L, McDonald TJ, Kim H. A review of the influence of treatment strategies on antibiotic resistant bacteria and antibiotic resistance genes. Chemosphere. 2016;150:702-14.
22. Pulikkan J, Mazumder A, Grace T. Role of the gut microbiome in autism spectrum disorders. Reviews on biomarker studies in psychiatric and neurodegenerative disorders. 2019:253-69.
23. Lord C, Elsabbagh M, Baird G, Veenstra Vanderweele J. Autism spectrum disorder. The lancet. 2018;392(10146):508-20.
24. Forsyth A et al., Autism spectrum disorder in children: Behavioral, Sensory and Gastrointestinal Considerations and Assessment of Oral Health. J Dent Oral Biol. 2018;3(4):1138.
25. Floris DL, Wolfers T, Zabihi M, Holz NE, Zwiers MP, Charman T, Tillmann J, Ecker C, Dell'Acqua F, Banaschewski T, Moessnang C. Atypical brain asymmetry in autism—a candidate for clinically meaningful stratification. Biological Psychiatry: Cognitive Neuroscience and Neuroimaging. 2021;6(8):802-12.