

Recent Studies on Gut Microbiome and Antimicrobial Resistance

1. Gut Microbiota Modulation For Multidrug-Resistant Organism Decolonization: Present And Future Perspectives

This study shows that the emergence of antimicrobial resistance (AMR) is of great concern to global public health. Treatment of multi-drug resistant (MDR) infections is a major clinical challenge: the increase in antibiotic resistance leads to a greater risk of therapeutic failure, relapses, longer hospitalizations, and worse clinical outcomes.

Scientists have found that microbiota-based strategies need to be considered in the prevention and treatment of MDRO. Further, FMT (fecal microbiota transplantation) is a promising tool which is effective and safe, especially in cases where conventional therapies have not proven effective. Randomized clinical trials (RCTs) are needed to standardize the methodology and set regulatory boundaries in order to include FMT in MDR clinical management.

Source: Lorenza Putignani, Human Microbiome Unit and Parasitology Unit, Bambino Gesù Children's Hospital, IRCCS, Italy. Gut Microbiota Modulation for Multidrug-Resistant Organism Decolonization: Present and Future Perspectives. Front Microbiol. 2019; 10: 1704. <https://doi.org/10.3389/fmicb.2019.01704>

2. Metagenomics: Aid To Combat Antimicrobial Resistance In Diarrhea

Antimicrobial resistance (AMR) has emerged as an obstacle in the supply administration of antimicrobial agents to critical diarrheal patients. This review shows that metagenomics is one such next-generation technique that has proved to be a monumental advancement in the area of molecular taxonomy. The current understanding of structure, function and dysbiosis of microbiota associated with antimicrobial resistance is realized due to its conception. Researchers have described the major milestones achieved due to the advent and implementation of this new technique in the context of antimicrobial resistance. These achievements Source: span a wide panorama from the discovery of novel microorganisms to invention of translational value.

Source: Rituparna De, Division of Bacteriology, National Institute of Cholera and Enteric Diseases, Kolkata, India. Metagenomics: aid to combat antimicrobial resistance in diarrhea. Gut Pathog 11, 47 (2019). <https://doi.org/10.1186/s13099-019-0331-8>

3. Microbiome As A Tool And A Target In The Effort To Address Antimicrobial Resistance

This article describes the intersections of immunity, microbiome and antimicrobial exposure, and the use of vaccines and other alternative strategies for the control and management of antimicrobial resistance.

Source: David A. Relman, Department of Medicine and Department of Microbiology and Immunology, Stanford University School of Medicine, Stanford and Infectious Diseases Section, Veterans Affairs Palo Alto Health Care System, Palo Alto. Microbiome as a tool and a target in the effort to address antimicrobial resistance. PNAS December 18, 2018 115 (51) 12902-12910. <https://doi.org/10.1073/pnas.1717163115>

4. Early-Life Gut Microbiome Modulation Reduces The Abundance Of Antibiotic-Resistant Bacteria

This study shows that how the infant gut microbiome can be modified, resulting in a significant reduction of Antibiotic Resistant Genes (ARGs) and the potentially pathogenic bacteria that harbor them.

Scientists have found that infants fed *B. infantis* EVC001 exhibited a change to the gut microbiome, resulting in a 90% lower level of ARGs compared to controls. ARGs that differed significantly between groups were predicted to confer resistance to **beta lactams**, **fluoroquinolones**, or **multiple drug classes**, the majority of which belonged to **Escherichia**, **Clostridium**, and **Staphylococcus**. Minimal inhibitory concentration assays confirmed the resistance phenotypes among isolates with these genes. Further, they have also found extended-spectrum beta lactamases among healthy, vaginally delivered breastfed infants who had never been exposed to antibiotics. This study highlights the importance of developing novel approaches to limit the spread of these genes among clinically relevant bacteria. Future studies are needed to determine whether colonization with *B. infantis* EVC001 decreases the incidence of AR infections in breastfed infants.

Source: Mark A. Underwood, Foods for Health Institute, University of California and Department of Pediatrics, UC Davis Children's Hospital, Sacramento, USA. Early-life gut microbiome modulation reduces the abundance of antibiotic-resistant bacteria. Antimicrob Resist Infect Control 8, 131 (2019). <https://doi.org/10.1186/s13756-019-0583-6>

5. Isolation And Characterization Of *L. Parafarraginis* (Ku495926) Inhibiting Multidrug-Resistant And Extended Spectrum **Beta**-Lactamase Gram-Negative Bacteria

This study shows that a *Lactobacillus* isolate from commercial yogurt, identified as *Lactobacillus parafarraginis*, inhibits the growth of several multidrug-resistant/extended spectrum **β -lactamase bacteria**. Researcher found that the inhibitory substance is a unique, bacteriocin-like peptide which is heat stable up to 121°C and these antimicrobial peptides produced by bacteria are released to kill other related bacteria that are not immune to their action. Findings from the study may hold promise for possible therapeutic application.

Source: Rachele Allen-Mcfarlane, Howard University, Department of Biology, Washington D.C. Isolation and characterization of L. parafarraginis (ku495926) inhibiting multidrug-resistant and extended spectrum beta-lactamase gram-negative bacteria. Journal of Microbiology, Biotechnology and Food Sciences, February - March, 2019, VOL. 8, NO. 4, Pages 970-978. DOI: 10.15414/jmbfs.2019.8.4.970-978

6. Intestinal Microbiota And Antibiotic Resistance: Perspectives And Solutions

The increasing number of hospital-acquired infections caused by MDR bacteria indicates a large and uncontrolled reservoir of these microorganisms, which seamlessly transit between hosts and the immediate environment. The value of FMT in the elimination of MDR bacteria has become more evident in recent years with an increasing number of reports which shows that FMT can re-establish colonisation resistance as well as other functions associated with a normal intestinal microbiota. Further, the promising results on the potential use of FMT to control the resistome warrant novel and specifically designed large scale studies to gauge the impact of this intervention. Hence FMT may change the way we manage patients infected or colonised by MDR bacteria and the control of MDR bacteria in the community.

Source: Jordi Vila, Department of Clinical Microbiology, Center of Biomedical Diagnosis, Hospital Clinic, Barcelona, Spain. Intestinal microbiota and antibiotic resistance: Perspectives and solutions. Human Microbiome Journal, Volume 9, August 2018, Pages 11-15. <https://doi.org/10.1016/j.humic.2018.05.002>

7. The Intestinal Microbiota As A Reservoir And A Therapeutic Target To Fight Multi-Drug-Resistant Bacteria: A Narrative Review Of The Literature

The exposure to antibiotics significantly reduces the bacterial density of intestinal microbiota leaving an ecologic void that can be occupied by potentially pathogenic and/or resistant bacteria frequently present in hospital settings. Consequently, the intestinal microbiota of inpatients acts as a major reservoir and plays a critical role in perpetuating the spread of resistant bacteria. There are novel innovative methods to protect the host microbiota during antibiotic treatment, but they do not offer a solution for already established colonization by resistant microorganisms. Fecal microbiota transfer (FMT) is a promising intervention to achieve this goal; however, controlled trials report lower success rates than initial retrospective studies, especially in case of gram negatives.

The aim of the present article is to highlight the importance of the intestinal microbiota in the global spread of multi-drug-resistant (MDR) microorganisms and to review the recent advances to protect the human microbiota from the action of antibiotics as well as a critical discussion about the evidence of decolonization of MDR microorganisms by FMT.

Source: Jordi Vila, Department of Clinical Microbiology, Center of Biomedical Diagnosis, Hospital Clinic, Barcelona, Spain. The Intestinal Microbiota as a Reservoir and a Therapeutic Target to Fight Multi-Drug-Resistant Bacteria: A Narrative Review of the Literature. Human Microbiome Journal, Volume 9, August 2018, Pages 11-15. <https://doi.org/10.1016/j.humic.2018.05.002>

8. Human Milk Microbiota: Transferring The Antibiotic Resistome To Infants

Commensal bacterial population is believed to be a reservoir for antibiotic resistance genes (ARGs). The infant gut microbiota has relatively higher abundance of ARGs than the adults. These genes can get transferred from commensals to pathogens by horizontal gene transfer, which magnifies the spectrum of antibiotic resistance in the environment. Breast milk microbiota that is responsible for the initial seeding of infant gut microbiota has also been found to harbour a vast array of ARGs. This review discusses the recent findings that indicate the potential of breast milk microbiota to act as a vehicle for transmission of ARGs to infants.

Source: Lahari Das, Department of Zoology, University of Delhi. Human Milk Microbiota: Transferring the Antibiotic Resistome to Infants. Indian J Microbiol 59, 410-416 (2019). <https://doi.org/10.1007/s12088-019-00824->

9. Characterizing The Antimicrobial Function Of A Dairy-Originated Probiotic, *Propionibacterium Freudenreichii*, Against Multidrug-Resistant *Salmonella Enterica* Serovar Heidelberg In Turkey Poults

Antimicrobial potential of dairy-origin probiotic bacteria, *Propionibacterium freudenreichii*, against multidrug-resistant *Salmonella Heidelberg* (SH) in turkey poults was determined in the current study. *In vitro* experiments, two strains (subsp.) of *P. freudenreichii*: *P. freudenreichii freudenreichii* B3523 (PF) and *P. freudenreichii shermanii* B4327 (PS) were tested for their ability to resist low pH (2.5) and bile salts (0.3%). Researchers have found that both PF and PS resisted pH = 2.5 and 0.3% bile salts with surviving populations comparable to the control and adhered well onto the avian epithelial cell lines. The strains were susceptible to antibiotics and did not invade the epithelial cells or exhibit hemolytic properties. The CFCSs were highly bactericidal against all tested pathogens. In turkey poults, PF significantly reduced cecal colonization of SH and the dissemination of the pathogen to the liver, compared to the SH challenge controls ($P < 0.05$). Further, study result reveals that PF, a non-host gastrointestinal tract-derived probiotic, could be an antibiotic alternative to prevent the early colonization of SH in poults, improving the pre-harvest safety of turkeys.

Source: Divek V. T. Nair and Anup Kollanoor Johny, Department of Animal Science, University of Minnesota, United States. Characterizing the Antimicrobial Function of a Dairy-Originated Probiotic, *Propionibacterium freudenreichii*, Against Multidrug-Resistant *Salmonella enterica* Serovar Heidelberg in Turkey Poults. *Front Microbiol.* 2018; 9: 1475. <https://doi.org/10.3389/fmicb.2018.01475>

10. Cell Free Preparations Of Probiotics Exerted Antibacterial And Antibiofilm Activities Against Multidrug Resistant *E. Coli*

Scientists have evaluated the efficacy of probiotics to control multidrug-resistant *E. coli* and reduce their ability to form biofilms. In this study six *E. coli* resistant to at least five antibiotics i.e. **Ceftazidime, Ampicillin, Clarithromycin, Amoxicillin+Clavulanic Acid and Ceftriaxone** were isolated.

In this study they observed that preparations of cell-free spent media (CFSM) of six probiotics belonging to the genus *Bifidobacterium* and *Lactobacillus* which were grown in Man-Rogosa-Sharpe (MRS) broth exhibited strong antibacterial activity against all *E. coli* isolates. Two *E. coli* isolates, namely *E. coli* WW1 and IC2, which were most resistant to all antibiotics, were subjected to antibiofilm experiments. Further, CFSM of MRS fermented by all probiotics results in inhibition of biofilm formation while *B. longum* caused highest inhibition i.e 57.94% in case of *E. coli* IC2 biofilms and *L. plantarum* was responsible for 64.57% reduction of *E. coli* WW1 biofilms whereas in case of CFSM of skim milk fermented by *L. helveticus* and *L. rhamnosus* exhibited a slight inhibitory activity against IC2 isolate (inhibition percentage of 31.52 and 17.68, respectively) while WW1 isolate biofilms was reduced by CFSM of milk fermented by *B. longum* and *L. helveticus* (70.81 and 69.49 reduction percentage, respectively). These results support the effective use of probiotics as antimicrobial alternatives and to eradicate biofilms formed by multidrug-resistant *E. coli*.

Source: Ahmed G. Abdelhamid, Botany Department, Faculty of Science, Benha University, Benha, Egypt. Cell Free Preparations Of Probiotics Exerted Antibacterial And Antibiofilm Activities Against Multidrug Resistant *E. coli*. *Saudi Pharmaceutical Journal*, Volume 26, Issue 5, July 2018, Pages 603-607. <https://doi.org/10.1016/j.jsps.2018.03.004>

11. Multidrug Resistant Pathogens Respond Differently To The Presence Of Co-Pathogen, Commensal, Probiotic And Host Cells

In this study multidrug resistant organisms (MDROs) were co-cultured in pair wise combinations either with: (1) another MDRO, (2) skin commensals (*Staphylococcus epidermidis* and *Corynebacterium jeikeium*), (3) the common probiotic *Lactobacillus reuteri*, and (4) human fibroblasts. RNA-Seq analysis shows that distinct regulation of virulence and antimicrobial resistance gene responses across different combinations of MDROs, commensals, and human cells. Co-culture assays demonstrates that microbial interactions can modulate gene responses of both the target and pathogen/commensal species, and that the responses are specific to the identity of the pathogen/commensal species. Moreover, bacteria have mechanisms to distinguish between friends, foe and host cells. Further, these results provide foundational data and insight into the possibility of manipulating the local microbiome when treating complicated polymicrobial wound, intra-abdominal, or respiratory infections.

Source: Agnes P. Chan, J. Craig Venter Institute (JCVI), Medical Center Drive, United States. Multidrug resistant pathogens respond differently to the presence of co-pathogen, commensal, probiotic and host cells. *Sci Rep* 8, 8656 (2018). <https://doi.org/10.1038/s41598-018-26738-1>

12. Marine Actinomycetes With Probiotic Potential And Bioactivity Against Multidrug-Resistant Bacteria

In this study a total of 21 marine **actinomycetes** isolated from the Caspian Sea have been screened out. The nucleotide sequence of the 16S rRNA gene (1.5 kb) shows that the potent strains belong to the genus **Streptomyces**. Scientists have found that disk diffusion method indicates among the 3 potent isolates, MN39 and MN2 produce biomolecules with antibacterial activity against MDR bacteria specially **methicillin-resistant Staphylococcus aureus** (MRSA) and **vancomycin-resistant Enterococcus** (VRE). In addition, potent strains show that remarkable anti-vibrio activity as well as extracellular enzyme production including amylase and protease. The results of this study reveals that the marine actinomycetes isolated from the sediments of Caspian Sea produce biomolecules that are effective against MDR bacteria, and suggests that these strains deserve to be studied as potential probiotics due to their anti-vibrio activity besides exoenzyme production.

Source: Hamed Norouzi, Department of Biology, University of Isfahan, Iran. Marine Actinomycetes with Probiotic Potential and Bioactivity Against Multidrug-resistant Bacteria. Int J Mol Cell Med. 2018; 7 (1) :44-52. <http://ijmcmcd.org/article-1-794-en.html>

13. Synergistic or Antagonistic Effects of Probiotics and Antibiotics- Alone or in Combination- on Antimicrobial-Resistant Pseudomonas aeruginosa Isolated from Burn Wounds

The current study explains that probiotics had a useful potential inhibitory effect on the growth of the pathogens. This study result reveals that the effect of inhibitory zone in combination with use of tetracycline + a probiotic strain - are more than using the antibiotic and probiotic alone. Also, in the current study they have found that among the probiotics, **Lactobacillus plantarum** 299v had the highest effect, although not significant, on resistant P. aeruginosa. The inhibitory effect of **L. plantarum** 299v were significantly higher than that of ciprofloxacin and in addition, antibacterial activity of **gentamicin + L. salivarius** (ES1) were significantly higher compared with that of **gentamicin + L. routeri**. Further studies are needed to describe different results. Therefore, it seems that the type of antibiotics and probiotics are important to create the synergistic or antagonistic effects.

Source: Tahereh Mousavi Shabestari, Antimicrobial Resistance Research Center, Institute of Immunology and Infectious Diseases, Iran University of Medical Sciences, Tehran, Iran. Synergistic or Antagonistic Effects of Probiotics and Antibiotics- Alone or in Combination- on Antimicrobial-Resistant Pseudomonas aeruginosa Isolated from Burn Wounds. Arch Clin Infect Dis. 2018 ; 13(3):e63121. doi: 10.5812/archcid.63121. <http://archcid.com/articles/63121.html>

14. Post-Antibiotic Gut Mucosal Microbiome Reconstitution Is Impaired by Probiotics and Improved by Autologous FMT

Probiotics are widely prescribed for prevention of antibiotics-associated dysbiosis and related adverse effects. Researchers invasively examined the effects of multi-strain probiotics or autologous fecal microbiome transplantation (aFMT) on post-antibiotic reconstitution of the murine and human mucosal microbiome niche.

This study reveals that antibiotic perturbation enhances probiotics colonization in the human mucosa but improves mild colonization in mice. Compared to spontaneous post-antibiotic recovery, probiotics induced a marked delay and persistently incomplete indigenous stool/mucosal microbiome reconstitution and host transcriptome recovery toward homeostatic configuration, while aFMT induced a rapid and near-complete recovery within days of administration. In vitro, Lactobacillus-secreted soluble factors contributed to probiotics-induced microbiome inhibition. Further, potential post-antibiotic probiotic benefits may be offset by a compromised gut mucosal recovery, highlighting a need for developing aFMT or personalized probiotic approaches achieving mucosal protection without compromising microbiome recolonization in the antibiotics-perturbed host.

Source: Eran Elinav, Immunology Department, Weizmann Institute of Science, Israel. Post-Antibiotic Gut Mucosal Microbiome Reconstitution Is Impaired by Probiotics and Improved by Autologous FMT. Cell, Volume 174, Issue 6, P1406-1423.E16, September 06, 2018. <https://doi.org/10.1016/j.cell.2018.08.047>

15. The Role of Fecal Microbiota Transplantation in Reducing Intestinal Colonization With Antibiotic-Resistant Organisms: The Current Landscape and Future Directions

The intestinal tract is a recognized reservoir of antibiotic-resistant organisms (ARO), and a potential target for strategies to reduce ARO colonization. Microbiome therapies such as fecal microbiota transplantation (FMT) have been established as an effective treatment for recurrent **Clostridioides difficile** infection and may be an effective approach for reducing intestinal ARO colonization. This study review the current published literature on the role of FMT for eradication of intestinal ARO colonization, the potential benefit and limitations of the use of FMT and outline a research agenda for the future study of FMT for intestinal ARO colonization.

Source: Jennie H Kwon, Division of Infectious Diseases, John T. Milliken Department of Internal Medicine, Washington University School of Medicine, St Louis, Missouri. The Role of Fecal Microbiota Transplantation in Reducing Intestinal Colonization With Antibiotic-Resistant Organisms: The Current Landscape and Future Directions, Open Forum Infectious Diseases, Volume 6, Issue 7, July 2019. <https://doi.org/10.1093/ofid/ofz288>

16. A Practical Guide For Probiotics Applied To The Case Of Antibiotic-Associated Diarrhea In The Netherlands

Antibiotic-associated diarrhea (AAD) is a side-effect frequently associated with the use of broad spectrum antibiotics. In this study a workflow for the assessment of the efficacy of probiotics for the prevention of antibiotic-associated diarrhea is presented. The workflow consists of a series of steps which includes both systematic review of available literature and meta-analysis of relevant clinical trials, inventory of available products and formulation of evidence-based recommendations. Scientists have found that there is sufficient evidence to make a recommendation for the use of specific probiotic products for the prevention of antibiotic associated diarrhea. According to the study results the probiotic strain **Lactobacillus rhamnosus GG** with a minimal daily dose of 2×10^9 CFU is most effective in treatment of AAD.

Source: Remco Kort, Microbiology and Systems Biology, Netherlands Organization for Applied Scientific Research (TNO), The Netherlands. A practical guide for probiotics applied to the case of antibiotic-associated diarrhea in The Netherlands. BMC Gastroenterol 18, 103 (2018). <https://doi.org/10.1186/s12876-018-0831-x>

17. Antibacterial Effectiveness of Fecal Water and in Vitro Activity of a Multi-Strain Probiotic Formulation against Multi-Drug Resistant Microorganisms

Intestinal colonization with multi-drug resistant (MDR) microorganisms is a consequence of antimicrobial-induced gut dysbiosis. Scientists have investigated whether the ingestion of high concentration multi-strain probiotic formulation would change the antibacterial activity of the feces against clinical strains of MDR microorganisms. The corresponding in vitro antibacterial activity is also investigated.

This study demonstrates that a 7-day probiotic supplementation increases the fecal activity against MDR microorganisms. A multi-strain probiotic formulation exhibits high in vitro antibacterial activity against MDR microorganisms of clinical concern and the higher activity of the whole formulation than the cell-free supernatant might be due to the interaction between live microorganisms rather than only to the production of antibacterial substances exclusively present in the cell-free supernatant.

The results of the present investigation support the potential use of this specific multi-strain probiotic formulation as an antimicrobial strategy for the treatment of intestinal colonization caused by MDR microorganisms.

Source: Alessandra Oliva, Department of Public Health and Infectious Diseases, Sapienza University of Rome, Italy. Antibacterial Effectiveness of Fecal Water and in Vitro Activity of a Multi-Strain Probiotic Formulation against Multi-Drug Resistant Microorganisms. Microorganisms 2020, 8(3), 332. <https://doi.org/10.3390/microorganisms8030332>

18. Beneficial Microbes: Role In The Era Of Antimicrobial Resistance

This article demonstrates that one of the most effective ways to reduce the abundance of multi-drug resistant pathogens is with the use of beneficial microorganisms and/or their metabolites, analogous to the effective environmentally-friendly biological method of eliminating stubborn pests in farmlands by agriculturalists. The benefits of the gut microbiota are being constantly unraveled as advanced next-generation sequencing techniques arise. The field of microbio-therapeutics is steadily growing. Further, harnessing the potentials of these microbes is paramount to making the world a healthier and better place to live.

Source: Ayorinde O. Afolayan, Adewale Adetoye and Funmilola A. Ayeni. Beneficial Microbes: Role In The Era Of Antimicrobial Resistance. Book on Antimicrobial resistance: A global threat. Peer reviewed chapter, November, 2018. DOI: 10.5772/intechopen.79635.

<https://www.intechopen.com/books/antimicrobial-resistance-a-global-threat/beneficial-microbes-roles-in-the-era-of-antimicrobial-resistance>

19. Faecal Microbiota Transplantation For The Decolonization Of Antibiotic-Resistant Bacteria In The Gut: A Systematic Review And Meta-Analysis

A systematic review was performed by undertaking a comprehensive search on MEDLINE, Embase, CENTRAL, PubMed and CINAHL databases for evidence up until May 2018. Quality of reporting is assessed using PROCESS and CARE checklists. Evidence of low quality shows that decolonization was achieved in half of the cases one month after FMT with higher response noted in **Pseudomonas aeruginosa**, and lower response in **Klebsiella pneumoniae** with **New Delhi metallo-beta-lactamase 1 (NDM-1)** and **extended-spectrum beta-lactamase (ESBL)** mechanisms of resistance. In successful cases, 70% of decolonization cases occurred within the first week after FMT. This review indicates a potential benefit of FMT as a decolonization intervention, which can only be confirmed by future well-designed RCTs.

Source: V. Tavoukjian, Florence Nightingale Faculty of Nursing, Midwifery and Palliative Care, King's College London. Faecal Microbiota Transplantation For The Decolonization Of Antibiotic-Resistant Bacteria In The Gut: A Systematic Review And Meta-Analysis. The Journal of Hospital Infection, June 2019 Volume 102, Issue 2, Pages 174-188.

<https://doi.org/10.1016/j.jhin.2019.03.010>

20. The Use of Microbiome Restoration Therapeutics to Eliminate Intestinal Colonization With Multidrug-Resistant Organisms

The intestinal tract is an important reservoir for many multidrug-resistant organisms (MDROs), and next-generation sequencing has expanded understanding of the resistome, defined as the comprehensive sum of genetic determinants of AR. Intestinal decolonization has been explored as a strategy to eradicate MDROs with selective digestive tract decontamination and probiotics being notable examples with mixed results. This review focuses on fecal microbiota transplantation and the early evidence supporting its efficacy in decolonizing MDROs and potential mechanisms of action to reduce AR genes. Current evidence suggests that fecal microbiota transplantation may have promise in restoring healthy microbial diversity and reducing AR, and clinical trials are underway to better characterize its safety and efficacy.

Source: Colleen S. Kraft, Division of Infectious Diseases and Department of Pathology and Laboratory Medicine, Emory University, Atlanta, Georgia. The Use of Microbiome Restoration Therapeutics to Eliminate Intestinal Colonization With Multidrug-Resistant Organisms. The American journal of The Medical Sciences November 2018 Volume 356, Issue 5, Pages 433-440. <https://doi.org/10.1016/j.amjms.2018.08.015>

21. Human Microbiomes And Antibiotic Resistance

Human microbiomes are complex ecosystems involving bacteria, viruses, archaea or eukaryotes that are co-evolving in an environment subject to various selective pressures, such as antibiotic administration, diet and/or lifestyle. In this sympatric lifestyle, competition is hard and the synthesis of antibiotic molecules and/or antibiotic resistance genes (ARGs) is one solution that is developed by the organisms to survive. This environment becomes a large source of ARGs for pathogenic bacteria, leading to the risk of infection due to multidrug resistant bacteria. Culture and metagenomics are two complementary methods developed to study these microbiomes in order to better understand the type of bacteria and ARGs present in the human body, as well as the factors that modulate the abundance and variety of these ARGs. They have found that our knowledge about antibiotic resistance is still poor and only partially understood at present. This lack of knowledge also applies to factors involved in transfer between bacteria, especially in the incompletely known complex ecosystem, and limits our understanding of the exchange and communication that exists between bacteria. Further studies are warranted to identify both the putative ARGs present in the human microbiome, as well as the dynamics of their acquisition/exchange in the human microbiome.

Source: Jean-Marc Rolain, Aix-Marseille Univ., France. Human microbiomes and antibiotic resistance. Human microbiome journal, Volume 10, December 2018, Pages 43-52. <https://doi.org/10.1016/j.humic.2018.08.005>

22. Abundance And Diversity Of Resistomes Differ Between Healthy Human Oral Cavities And Gut

The global threat of antimicrobial resistance has driven the use of high-throughput sequencing techniques to monitor the profile of resistance genes, known as the resistome, in microbial populations. The human oral cavity contains a poorly explored reservoir of these genes.

In this study researchers analyzed and compare the resistome profiles of 788 oral cavities worldwide with paired stool metagenomes. Researchers have found country and body site-specific differences in the prevalence of antimicrobial resistance genes, classes and mechanisms in oral and stool samples. Within individuals, the highest abundances of antimicrobial resistance genes are found in the oral cavity, but the oral cavity contains a lower diversity of resistance genes compared to the gut. Additionally, co-occurrence analysis shows contrasting ARG-species associations between saliva and stool samples. Maintenance and persistence of antimicrobial resistance is likely to vary across different body sites. Further, study highlights the importance of characterizing the resistome across body sites to uncover the antimicrobial resistance potential in the human body.

Source: Victoria R. Carr, Centre for Host-Microbiome Interactions, Faculty of Dentistry, Oral and Craniofacial Sciences, King's College London, London, UK. Abundance and diversity of resistomes differ between healthy human oral cavities and gut. Nat Commun 11, 693 (2020). <https://doi.org/10.1038/s41467-020-14422-w>

23. Antibiotic Resistome In A Large-Scale Healthy Human Gut Microbiota Deciphered By Metagenomic And Network Analyses

The human gut microbiota is an important reservoir of antibiotic resistance genes (ARGs). In this study a metagenomic approach and network analysis were used to establish a comprehensive antibiotic resistome catalog and to obtain co-occurrence patterns between ARGs (Antibiotic Resistance Genes) and microbial taxa in fecal samples from 180 healthy individuals from 11 different countries. In total, 507 ARG subtypes belonging to 20 ARG types were detected with abundances ranging from 7.12×10^{-7} to 2.72×10^{-1} copy of ARG/copy of 16S-rRNA gene. Tetracycline, multidrug, macrolide-lincosamide-streptogramin, bacitracin, vancomycin, beta-lactam and aminoglycoside resistance genes were the top seven most abundant ARG types. The multidrug ABC transporter, aadE, bacA, acrB, tetM, tetW, vanR and vanS were shared by all 180 individuals, suggesting their common occurrence in the human gut. Compared to populations from the other 10 countries, the Chinese population harboured the most abundant ARGs. Moreover, LEfSe analysis suggested that the MLS resistance type and its subtype 'ermF' were representative ARGs of the Chinese population. Antibiotic inactivation, antibiotic target alteration and antibiotic efflux were the dominant resistance mechanism categories in all populations. Procrustes analysis revealed that microbial phylogeny structured the antibiotic resistome. Co-occurrence patterns obtained via network analysis implied that 12 species might be potential hosts of 58 ARG subtypes.

Source: Bing Li, Division of Energy & Environment, Graduate School at Shenzhen, Tsinghua University, China. Antibiotic resistome in a large-scale healthy human gut microbiota deciphered by metagenomic and network analyses. Environ. Microbiol. 20, 355-368 (2018). <https://doi.org/10.1111/1462-2920.14009>

24. Maternal Gut And Breast Milk Microbiota Affect Infant Gut Antibiotic Resistome And Mobile Genetic Elements

The infant gut microbiota has a high abundance of antibiotic resistance genes (ARGs) compared to adults, even in the absence of antibiotic exposure. Researchers have studied the potential sources of infant gut ARGs by performing metagenomic sequencing of breast milk, as well as infant and maternal gut microbiomes. In this study they found that fecal ARG and mobile genetic element (MGE) profiles of infants are more similar to those of their own mothers than to those of unrelated mothers. MGEs in mothers' breast milk are also shared with their own infants. Termination of breastfeeding and intrapartum antibiotic prophylaxis of mothers, which have the potential to affect microbial community composition, are associated with higher abundances of specific ARGs, the composition of which is largely shaped by bacterial phylogeny in the infant gut. Further, study result suggest that infants inherit the legacy of past antibiotic consumption of their mothers via transmission of genes, but microbiota composition still strongly impacts the overall resistance load.

Source: Katariina Parnanen, Department of Microbiology, University of Helsinki, Finland. Maternal gut and breast milk microbiota affect infant gut antibiotic resistome and mobile genetic elements. Nat Commun 9, 3891 (2018). <https://doi.org/10.1038/s41467-018-06393-w>

25. Recovery Of Gut Microbiota Of Healthy Adults Following Antibiotic Exposure

In this study researchers investigated how to minimize the impact of antibiotics. Gut microorganisms harbour and exchange antibiotics resistance genes, collectively called their resistome. Using shotgun sequencing-based metagenomics, the partial eradication and subsequent regrowth of the gut microbiota in 12 healthy men was analyzed over a 6-month period following a 4-day intervention with a cocktail of 3 last-resort antibiotics: **meropenem**, **gentamicin** and **vancomycin**. Initial changes included blooms of **enterobacteria** and other pathobionts, such as **Enterococcus faecalis** and **Fusobacterium nucleatum**, and the depletion of **Bifidobacterium species** and butyrate producers. The gut microbiota of the subjects recovered to near-baseline composition within 1.5 months, although 9 common species, which were present in all subjects before the treatment, remained undetectable in most of the subjects after 180 days. Species that harbour β -lactam resistance genes were positively selected for during and after the intervention. Harbouring glycopeptide or aminoglycoside resistance genes increased the odds of de novo colonization; however, the former also decreased the odds of survival. Compositional changes under antibiotic intervention in vivo matched results from in vitro susceptibility tests. The study showed that despite a mild yet long-lasting imprint following antibiotics exposure, the gut microbiota of healthy young adults are resilient to a short-term broad-spectrum antibiotics intervention and their antibiotics resistance gene carriage modulates their recovery processes.

Source: Filip K. Knop, Novo Nordisk Foundation Center for Basic Metabolic Research, Faculty of Health and Medical Sciences; Center for Diabetes Research, Gentofte Hospital and Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Denmark. Recovery of gut microbiota of healthy adults following antibiotic exposure. Nat Microbiol 3, 1255-1265 (2018). <https://doi.org/10.1038/s41564-018-0257-9>

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