Recent Studies and Publications on Gut Microbiome and Antimicrobial Resistance

STUDIES

1. Bacteroidales Species In The Human Gut Are A Reservoir Of Antibiotic Resistance Genes Regulated By Invertible Promoters

This study assessed the threat posed by Antibiotic Resistance Genes (ARGs) regulated by invertible promoters by systematically searching for ARGs regulated by invertible promoters in the human gut microbiome and examining their origin, prevalence, and distribution.

Researchers have identified ARGs regulated by invertible promoters and categorized them into three classes based on the invertase-regulating phase variation. In the human gut microbiome, ARGs regulated by invertible promoters are exclusively found in ***Bacteroidales species***.

The genomic analysis shows that ARGs regulated by invertible promoters have convergently originated from ARG insertions into glycan-synthesis loci that were regulated by invertible promoters at least three times. Moreover, all three classes of invertible promoters regulating ARGs are located within integrative conjugative elements (ICEs). Therefore, horizontal transfer via ICEs could explain the wide taxonomic distribution of ARGs regulated by invertible promoters. Overall, these findings reveal that glycan-synthesis loci regulated by invertible promoters in Bacteroidales species are an important hotspot for the emergence of clinically-relevant ARGs regulated by invertible promoters.

Source: Xiaofang Jiang, National Library Of Medicine, National Institutes Of Health, Bethesda, Maryland, USA. Bacteroidales Species In The Human Gut Are A Reservoir Of Antibiotic Resistance Genes Regulated By Invertible Promoters. Npj Biofilms Microbiomes 8, 1 (2022). https://doi.org/10.1038/s41522-021-00260-1

2. Antimicrobial Resistance Profiles Of Human Brucella Melitensis Isolates In Three Different Microdilution Broths: The First Multicentre Study In Bosnia And Herzegovina

This study prospectively analyzed the rates of resistance among human ***Brucella melitensis*** strains isolated in Bosnia and Herzegovina.

Study result shows that in 209 patients, ***B. melitensis*** blood cultures were positive for 111 (53.1%). Among the 108 isolates investigated, 91 (84.3%) were resistant to trimethoprim-sulfamethoxazole on Brucella broth (BB), but not on either cation-adjusted Mueller-Hinton broth (CAMHB). Nearly all isolates (>90%) were resistant to azithromycin on BB and both CAMHBs.

Source: Silvio Špičić, Croatian Veterinary Institute, Savska Cesta, Zagreb, Croatia. Antimicrobial Resistance Profiles Of Human Brucella Melitensis Isolates In Three Different Microdilution Broths: The First Multicentre Study In Bosnia And Herzegovina. Journal Of Global Antimicrobial Resistance, Volume 29, June 2022, Pages 99-104. https://doi.org/10.1016/j.jgar.2022.02.005

3. Antibiotic Exposure Prevents Acquisition Of Beneficial Metabolic Functions In The Preterm Infant Gut Microbiome

Study results show that in antibiotic-naïve infants, gestational and postnatal age imparted similar trajectories on maturation of the microbial community and associated metabolic functional capacity, with postnatal age exerting greater contribution. Antibiotic exposure was associated with reversal in maturation trajectory from the first week to the third week of age. Butyrate-producing genera, including ***Clostridium*** and ***Blautia,*** were significantly more abundant in antibiotic-naïve neonates at 3 weeks postnatal age.

Further, metabolic pathways required for short-chain fatty acid synthesis were significantly increased in antibiotic-naïve infants, but not in antibiotic-exposed neonates, at 3 weeks after birth.

Source: David B. Haslam, Division Of Infectious Diseases, Cincinnati Children's Hospital Medical Center And Department Of Pediatrics, University Of Cincinnati, Cincinnati, OH, USA. Antibiotic Exposure Prevents Acquisition Of Beneficial Metabolic Functions In The Preterm Infant Gut Microbiome. Microbiome 10, 103 (2022). https://doi.org/10.1186/s40168-022-01300-4

4. Evidence Of Community-Wide Spread Of Multi-Drug Resistant Escherichia Coli In Young Children In Lusaka And Ndola Districts, Zambia

Researchers have found that all ***E. coli (96.9%)*** were resistant to at least one antimicrobial agent tested. Further, ***700 isolates were Multi-Drug Resistant (MDR), 136 were possibly Extensively-Drug Resistant*** and ***9 were Pan-Drug-Resistant***. ***40% of the isolates were imipenem-resistant***, mostly from healthy children. They have also documented a complex pattern of associations between and within the subgroups of the levels of MDR and socio-demographic characteristics, antibiotic stewardship, and guardians' knowledge of AMR.

This study has revealed the severity of antimicrobial resistance (AMR) in children and the need for a community-specific-risk-based approach to implementing measures to curb the problem.

Source: Flavien Nsoni Bumbangi, School Of Medicine, Eden University And Department Of Disease Control, School Of Veterinary Medicine, University Of Zambia, Zambia. Evidence Of Community-Wide Spread Of Multi-Drug Resistant Escherichia Coli In Young Children In Lusaka And Ndola Districts, Zambia. Microorganisms 2022, 10(8), 1684; https://doi.org/10.3390/microorganisms10081684

5. Prevalence And Risk Factors Of Tet(X4)-Positive Enterobacteriaceae In Human Gut Microbiota

The aim of this study was to investigate the prevalence of tet(X4) in healthy individuals and patients and assess risk factors associated with tet(X4)-positive populations.

Study result shows that the prevalence of tet(X4)-positive Enterobacteriaceae in healthy individuals and patients was substantially higher than previous studies in China. Patients ranging from 19 to 45 years of age had significantly higher odds of tet(X4)-positive bacterial colonization. All tet(X4)-positive Enterobacteriaceae were resistant to tigecycline. In addition, tet(X4)-positive Escherichia coli were highly diverse, with CC10 belonging to the dominant clone. Genome analysis showed that tet(X4) was adjacent to ISVsa3 on the plasmids.

Source: Weidong Zheng, Department Of Laboratory Medicine, Shenzhen University General Hospital, Shenzhen City, China. Prevalence And Risk Factors Of Tet(X4)-Positive Enterobacteriaceae In Human Gut Microbiota. Journal Of Global Antimicrobial Resistance, Volume 31, December 2022, Pages 15-21. https://doi.org/10.1016/j.jgar.2022.07.014

6. First Complete Genome Of A Multidrug-Resistant Strain Of The Novel Human Pathogen Kalamiella Piersonii (GABEKP28) Identified In Human Saliva

This study reports the first complete genome of a multidrug-resistant strain of *K. piersonii (GABEKP28),* isolated from the saliva of a patient with treatment-resistant schizophrenia (TRS), to determine the mobile genetic elements (MGEs), antibiotic resistance genes (ARGs), and virulence factors (VFs) harboured by such a strain of this novel species.

K. piersonii strain GABEKP28 was classified as multidrug-resistant while also carrying plasmidic genetic determinants associated with a hypervirulent phenotype. The complete genome size is 3 881 479 bp and has a guanine-cytosine content of 57.76% while it encodes for 3 525 chromosome coding sequences. The strain was also identified to carry three plasmids of 513 647 bp, 261 771 bp, and 106 029 bp, respectively.

Source: Georgios Miliotis, Antimicrobial Resistance And Microbial Ecology Group, School Of Medicine, University Of Galway And Centre For One Health, Ryan Institute, University Of Galway, Galway, Ireland. First Complete Genome Of A Multidrug-Resistant Strain Of The Novel Human Pathogen Kalamiella Piersonii (GABEKP28) Identified In Human Saliva. Journal Of Global Antimicrobial Resistance, Volume 32, March 2023, Pages 31-34. https://doi.org/10.1016/j.jgar.2022.12.003

7. Antimicrobial Resistance Prevalence Of Escherichia Coli And Staphylococcus Aureus Amongst Bacteremic Patients In Africa: A Systematic Review

This systematic review aims to provide an understanding of the AMR prevalence and trends of common ***bacteremic*** pathogens, namely ***Escherichia coli and Staphylococcus aureus*** in the World Health Organization (WHO) Africa region.

In this review five hundred sixty-two papers were retrieved and out of them 27 papers were included in the final analysis. ***Analysis shows that only 23.4% (11/47) of member states of the WHO African region had reports on AMR in bacteremia***. The Clinical and Laboratory Standards Institute (CLSI) (78.5%) was the most common standard used in the region. ***For E. coli, the pooled resistance was: cefotaxime (42%), imipenem (4%), meropenem (0%), and colistin (0%). For S. aureus, the calculated pooled resistance was cloxacillin (34%), oxacillin (12%), and vancomycin (0%).*** There was a high degree of variation across studies ($I2 > 90\%$).

Source: Erastus Hanganeni Haindongo, School Of Medicine, Faculty Of Health Sciences And Veterinary Medicine, University Of Namibia, Windhoek, Namibia And Institute Of Biomedicine, University Of Turku, Turku, Finland. Antimicrobial Resistance Prevalence Of Escherichia Coli And Staphylococcus Aureus Amongst Bacteremic Patients In Africa: A Systematic Review. Journal Of Global Antimicrobial Resistance, Volume 32, March 2023, Pages 35-43. https://doi.org/10.1016/j.jgar.2022.11.016

Next-Generation and Whole Genome Sequencing

1. Methods To Improve The Accuracy Of Next-Generation Sequencing

This systematic review summarizes the general procedures of ***Next-Generation Sequencing*** (NGS) platforms, highlighting the improvements involved in eliminating errors at each step. Furthermore, the challenges and future development of next-generation sequencing in clinical application is also discussed.

Source: Pengfeng Xiao, State Key Laboratory Of Bioelectronics, School Of Biological Science And Medical Engineering, Southeast University, Nanjing, China. Methods To Improve The Accuracy Of Next-Generation Sequencing. Front. Bioeng. Biotechnol., 20 January 2023, Sec. Biosensors and Biomolecular Electronics, Volume 11 – 2023. https://doi.org/10.3389/fbioe.2023.982111

2. Next-Generation Sequencing: Insights To Advance Clinical Investigations Of The Microbiome

This systematic review described the fundamentals of Next-generation sequencing (NGS), with a focus on 16S rRNA and shotgun metagenomic sequencing. They have discussed pros and cons of each methodology as well as important concepts in data variability, study design, and clinical metadata collection. Moreover, scientists have also share insights as to how NGS might further be integrated into and advance microbiome research and clinical care in the coming years.

Source: Steven L. Salzberg, Department Of Biomedical Engineering; Department Of Computer Science, And Department Of Biostatistics, Johns Hopkins University, Baltimore, Maryland, USA. Next-Generation Sequencing: Insights To Advance Clinical Investigations Of The Microbiome. J Clin Invest. 2022;132(7):e154944. https://doi.org/10.1172/JCI154944

3. Comparison Of Microbial Signatures Between Paired Faecal And Rectal Biopsy Samples From Healthy Volunteers Using Next-Generation Sequencing And Culturomics

This study shows that the bacterial profiles of paired faecal and rectal biopsy wash samples were very similar, validating the use of faecal samples as a convenient surrogate for rectal biopsy-associated microbiota. Anaerobic bacterial culture results show that similar taxonomic patterns to the amplicon sequence analysis disproving the dogma that culture-based methods do not reflect findings of molecular assessments of gut bacterial composition.

Source: Indrani Mukhopadhya, Gut Health Group, Rowett Institute, University Of Aberdeen, Aberdeen, UK. Comparison Of Microbial Signatures Between Paired Faecal And Rectal Biopsy Samples From Healthy Volunteers Using Next-Generation Sequencing And Culturomics. Microbiome 10, 171 (2022). https://doi.org/10.1186/s40168-022-01354-4

Miscellaneous

1. Gut Virome Profiling Identifies A Widespread Bacteriophage Family Associated With Metabolic Syndrome

This study shows **gut virome changes** associated with metabolic syndrome (MetS), a highly prevalent clinical condition preceding cardiometabolic disease, in 196 participants by combined sequencing of bulk whole genome and virus like particle communities.

Researchers found that MetS gut viromes exhibit decreased richness and diversity. They are enriched in phages infecting ***Streptococcaceae*** and ***Bacteroidaceae*** and depleted in those infecting ***Bifidobacteriaceae.*** Differential abundance analysis identifies eighteen viral clusters (VCs) as significantly associated with either MetS or healthy viromes. Among these are a MetS-associated ***Roseburia*** VC that is related to healthy control-associated ***Faecalibacterium*** and ***Oscillibacter*** VCs.

Further analysis of these VCs revealed the ***Candidatus Heliusviridae***, a highly widespread gut phage lineage found in 90+% of participants. The identification of the temperate ***Ca. Heliusviridae*** provides a starting point to studies of phage effects on gut bacteria and the role that this plays in MetS.

Source: Hilde Herrema, Departments Of Internal And Experimental Vascular Medicine, Amsterdam University Medical Centers; Amsterdam Gastroenterology Endocrinology Metabolism, Endocrinology, Metabolism And Nutrition And Amsterdam Cardiovascular Sciences, Diabetes & Metabolism, Amsterdam. 1. Gut Virome Profiling Identifies A Widespread Bacteriophage Family Associated With Metabolic Syndrome. Nat Commun 13, 3594 (2022). https://doi.org/10.1038/s41467-022-31390-5

2. Differential Hydrogen Sulfide Production By A Human Cohort In Response To Animal- And Plant-Based Diet Interventions

The objective of this study was to determine the effect of short-term (1-week) plant- and animal-based eating patterns on ex vivo fecal H2S production in healthy human volunteers.

Study result show that median H2S production was higher following the animal-based diet compared to the plant-based diet (p = 0.02; median difference 29 ppm/g, 95% CI 16–97). However, there was substantial individual variability and 2 of 11 individuals (18%) produced more H2S on the plant-based diet. Using the top and bottom quartiles of H2S percent change between animal- and plant-based diet weeks to define responders and non-responders, significant taxonomic differences were observed between the responder and non-responder cohorts.

Source: Dr. Levi Teigen, Clinical Nutrition, University Of Minnesota Medical School. Differential Hydrogen Sulfide Production By A Human Cohort In Response To Animal- And Plant-Based Diet Interventions. Clinical Nutrition, Volume 41, Issue 6, P1153-1162, June 2022. https://doi.org/10.1016/j.clnu.2022.03.028

3. Systematic Characterization Of Human Gut Microbiome-Secreted Molecules By Integrated Multi-Omics

Researchers have developed a methodological framework which optimizes for the extraction of the microbiome-derived, extracellular biomolecular complement, including nucleic acids, (poly) peptides, and metabolites, from flash-frozen stool samples of healthy human individuals.

Researchers showed the distinctiveness of the different extracellular biomolecular fractions, both in terms of their taxonomic and functional composition. This highlights the challenge of inferring the extracellular biomolecular complement of the gut microbiome based on single-omic data.

Source: Paul Wilmes, Luxembourg Centre For Systems Biomedicine And Department Of Life Sciences And Medicine, Faculty Of Science, Technology And Medicine, University Of Luxembourg, 6 Avenue Du Swing, L-4367, Belvaux, Luxembourg. Systematic Characterization Of Human Gut Microbiome-Secreted Molecules By Integrated Multi-Omics. ISME COMMUN. 1, 82 (2021). https://doi.org/10.1038/s43705-021-00078-0

4. Citizen-Science Reveals Changes In The Oral Microbiome In Spain Through Age And Lifestyle Factors

In this study scientists found oral microbiome changes across age, with middle ages showing a more homogeneous composition, and older ages showing more diverse microbiomes with increased representation of typically low abundance taxa. Chronic health disorders present in the analyzed population were the most impactful factors, followed by smoking and the presence of yeasts in the oral cavity. Further, Multiple intrinsic and extrinsic factors jointly shaped the oral microbiome.

Source: Toni Gabaldón, Centre For Genomic Regulation (CRG), The Barcelona Institute Of Science And Technology, Dr. Aiguader, Barcelona, Spain. Citizen-Science Reveals Changes In The Oral Microbiome In Spain Through Age And Lifestyle Factors. Npj Biofilms Microbiomes 8, 38 (2022). https://doi.org/10.1038/s41522-022-00279-y

Note: Only lead author's names and their affiliations are given. Please see the articles for full details.
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