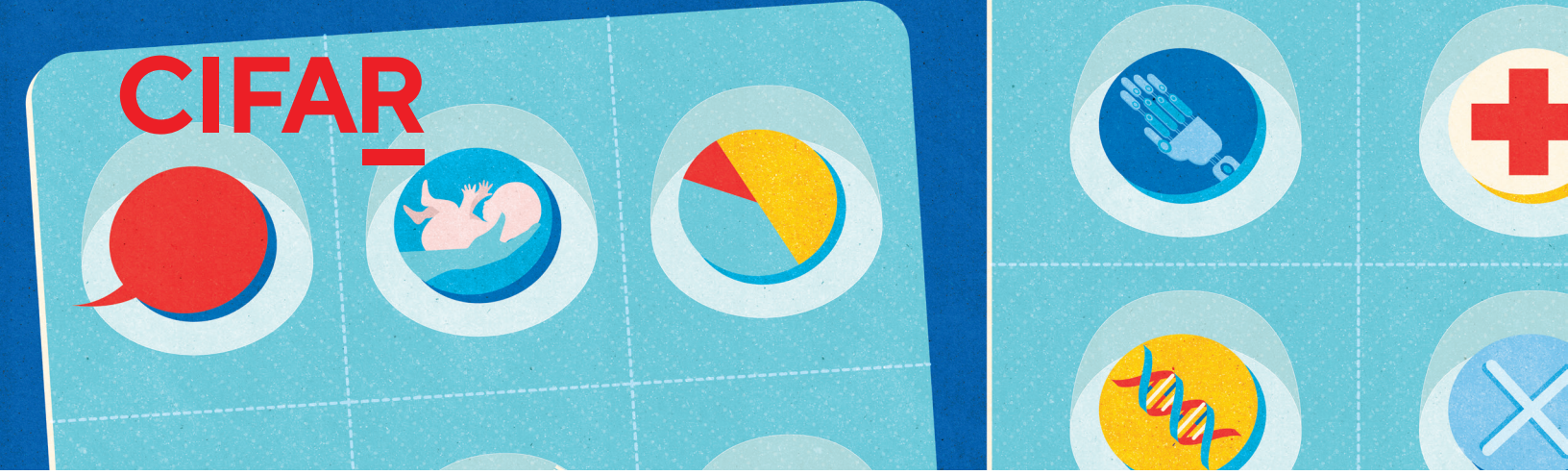

CIFAR Exchange Engagement in Health & Well-being

The Human Microbiome & Public Health: Supporting Healthy Development and Aging

September 25, 2018, Toronto, ON, Canada

We are gradually uncovering the world of the human microbiome, seeing our microbial selves for the first time. What are we learning about the relationship between microbes and healthy development and aging - and how can policymakers and practitioners use emerging insights to drive change?

On September 25, 2018 CIFAR's program in Humans & the Microbiome and the Dalla Lana School of Public Health co-hosted a roundtable discussion exploring the relationship between the microbiome, healthy development and aging, and our built environments. Together, CIFAR fellows and participants from the public health community examined the opportunities and challenges posed by communicating emerging knowledge from microbiome research and adopting these insights into public health priorities.

This brief highlights key discussion points and proposed next steps for further intersectoral collaboration in this area.

BACKGROUND: CURRENT UNDERSTANDING OF THE HUMAN MICROBIOME

Brett Finlay, CIFAR Senior Fellow & Co-director, Humans & the Microbiome; University of British Columbia

- We are more microbial than human; the human microbiome contains around 100 times the genes of the human genome. Trillions of microorganisms reside on and throughout the human body, and recent scientific advancements have enabled researchers to sequence and analyze their genomic content and function.
- Microbes have largely been studied and viewed from the perspective of pathology, often considered to be germs associated with disease. In some aspects this perspective is accurate. Lifesaving antibiotics and improved hygienic practices have significantly

decreased the incidence of formerly common infectious diseases, such as rheumatic fever, tuberculosis, measles and hepatitis.

- However, the vast majority of microbes in the human microbiome are beneficial, extending human digestive, immune, and neurological function. The "hygiene hypothesis" posits that decades of over-sanitization (such as hyper-cleanliness and antibiotic overuse) have reduced our microbial exposure, impairing both the diversity of the human microbiome and our early immune development. In contrast to the benefits of hygiene in managing infectious diseases, alterations in the gut microbiota have been linked to multiple chronic and neurological conditions, including obesity, diabetes, asthma, autism, Alzheimer's and Parkinson's diseases, and multiple sclerosis. Ongoing societal changes in hygiene and medicine have driven increases in the prevalence of these chronic diseases.
- Researchers have observed developmental "critical windows" for the human microbiome. Alterations during the formation and establishment of the gut microbiota in early childhood are linked to long-term health consequences. For example, babies born via caesarean section exhibit distinct gut microbial communities compared to children born vaginally as the latter are exposed to vaginal/fecal microbes. C-section and antibiotic use alter early microbiome formation and are associated with an increased risk of asthma, while early exposure to protective microbes may reduce asthma risk.

ROUNDTABLE DISCUSSION

At the intersections of research and practice, what challenges and opportunities exist for future research and the development and evolution of public health programs/policies education?

Aging and the Microbiome

- Aging influences the composition and function of the human microbiome. Microbial imbalance contributes to chronic, low-grade inflammation, which accelerates aging and contributes to age-related diseases - a phenomenon known as "inflammaging". For example, altered microbial populations have been reported in populations with neurodegenerative disease - such as gastrointestinal comorbidities that proceed and co-occur with Parkinson's disease, and gum disease that is associated with dementia progression.
- Researchers are just beginning to explore the mechanisms linking microbes to aging processes, such as assessing whether microbial-targeted therapies improve age-related disease. Lifestyle recommendations supporting diet, physical activity, and dental hygiene have been shown to improve cognitive functions, decrease the risk of neurodegenerative disease, and modulate gut and oral microbes.
- To date, it is established that interactions between the human microbiome and the surrounding environment are important, as the surrounding environment modifies the human microbiome and subsequently influences health. Built environments in later life such as long-term care homes act as mini-communities to which individuals'

microbiomes adjust, shaped by policies (e.g. design standards) and practices (e.g. medication use, hygiene/sanitization).

- Ongoing studies are examining the microbial communities found within the built environment, such as whether the microbes within a long-term care home protect or exacerbate aging processes. The "One Health" concept examines health through human-environment-animal interactions, and could provide a structure to examine the human microbiome.

Linking Research to Public Health Policy

- Public health recommendations (such as official dietary guidelines) are based on an established evidence foundation that includes large-scale clinical trials and analyses of systematic reviews. As the evidence base for the microbiome is still developing, such public health policy changes incorporating microbiome findings may require additional discussion and time. However, core areas of microbiome research are advancing rapidly. Many associative links have been established between the microbiome and health, and the field is starting to shift focus towards discovering microbial mechanisms and establishing causal links.

- Those driving change in policy and practice (both in government and in areas such as medicine, dentistry, gynecology and midwifery, pediatrics, geriatrics) should anticipate a growing knowledge base in the microbiome in the years to come as the field is on the edge of a new era of health - both in research and practice. Decision-makers that shape policy and practice should engage with emerging insights into the relationship between the microbiome and healthy aging to open opportunities for positive change in the near-term - such as furthering efforts to reduce improper use of antibiotics and other medications, and oversanitation practices in vulnerable populations.

Linking Research to Practice

- Simply sharing information about the microbiome's role in health is insufficient to achieve change. Cultural factors, such as worldviews based in human exceptionalism and health campaigns presenting microbes as germs, influence reactions to and uptake of scientific findings about the human microbiome. Further, the uptake of microbiome information and behaviours has been more rapid in highly educated populations.

- Establishing credibility and trust across the public is paramount. Microbiome findings should be responsibly integrated into existing health messages and public health initiatives - e.g vaginal birth and breastfeeding - that can be promoted equitably across the population.

- Health practitioners can serve as key sources of timely information on the microbiome for patients - including those already looking to popular media for health recommendations. Despite the surge of microbiome research, microbiology prerequisites are absent from many healthcare curriculums. To properly support healthy development and aging through the microbiome, education and promotion of microbiome research is needed within the biomedical field - particularly in degree programs teaching public health, medicine, and dentistry.

PRIORITIES & NEXT STEPS

The precise function of the microbiome on human health requires more study.

Roundtable participants support: (1) ongoing intersectoral collaboration between researchers and public health, and; (2) promotion of the microbiome as a promising therapeutic target.

Priority Considerations

- **Fact vs Fiction**: Segments of the public have rapidly embraced microbial-targeted therapies and interventions (e.g. pro/prebiotics, fecal microbiota transplants), despite limited and mixed scientific evidence. To inform the use of such products already on the market, studies are needed that examine their efficacy and therapeutic value.
- **Evidence-based Policy**: Public health and policy officials face barriers to incorporating promising microbiome studies into policy, as this body of evidence is still newly emerging. To gain traction, researchers should focus on the most promising areas of microbiome research. Continued studies focused on microbial mechanisms and the efficacy of microbial-targeted therapeutics are needed.
- **Microbiome Diversity at the Individual Level**: Despite evidence that microbial diversity is good for health, the view of microbes as germs to be eradicated prevails. The resulting "anti-microbial" hygiene practices reduce microbial diversity and likely have serious implications for health. Promotion of practices supporting a healthy microbiome needs to meaningfully engage the entire population.
- **Microbiome Preservation at the Population Level**: There are opportunities that could halt or reverse loss of microbiome diversity, such as "biobanking" — storing endangered microbial species. However, the built and natural environments of the future will be different from today; preservation attempts may face future efficacy challenges.
- **Ethical Considerations**: The use of microbial markers to stratify, predict, or diagnose human disease is one of the most rapidly advancing and promising areas in microbiome research. However, there are ethical implications posed by diagnosing disease without addressing or providing treatments, similar to the ethical concerns following the rise of genomics and personalized medicine.

Next Steps

- **Public Outreach**: Communicating microbiome messages that consider the existing context of microbiome-related knowledge and behaviours is critical to long-term credibility and efficacy. For example, it will be valuable to simultaneously remain vigilant within academia to resist hype and urge caution (e.g. conservative antibiotic use), while promoting the positive benefits of a diverse microbiome. We also need to better understand how the public perceives the terms "microbiome" or "metaorganism" and its connections to health. CIFAR's Humans & the Microbiome research program is striking this balance by undertaking a study with the FrameWorks Institute to explore how best to develop effective public health messaging on the microbiome.

- **Influencing Public Health Education**: Microbiome case studies should be developed and incorporated into public health curricula to highlight where changes today can impact on health in the future. Educating the next generation of health practitioners may be most effective in promoting evidence-based practices.
- **Interdisciplinary Collaboration**: Ongoing engagement between leaders in basic sciences and public health is needed. Collaborative, multidisciplinary research like CIFAR's Humans & the Microbiome research program will provide critical and transformative insights for the future of human microbiome studies. Examples of collaborative projects between the public health sector and microbiome researchers could include:
    - exploring how microbiome profiles change across the life cycle;
    - examining public attitudes to the microbiome across different public health professions and population demographics;
    - understanding what the key messages are from a research perspective and how to connect to the public's interests;
    - exploring the impacts on the microbiome caused by occupational health practices (e.g. shift work);
    - examining the influence of social and environmental perturbations on individual and community microbiomes (e.g. mass migration, urbanization);
    - understanding the equitable impact of products and interventions;
    - studying the microbiome and antimicrobial resistance;
    - focusing microbiome studies at the level of populations and in different settings (e.g. socio-economics groups) and;
    - developing improved FMTs (fecal microbiota transplant) for gastrointestinal diseases.

Kylynda C. Bauer was the primary writer of this report.

KNOWLEDGE PARTNERS

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CIFAR's program in Humans & the Microbiome examines how the microorganisms that live within us, collectively termed the microbiome, influence human evolution, development, health, and anthropology. CIFAR fellows in this program explore the profound capacities of the human microbiome through a multidisciplinary lens. The program currently has 19 fellows and advisors comprising a range of disciplines, including microbiology, evolutionary biology, ecology, developmental and stem cell biology, and social sciences. For more information, visit: https://www.cifar.ca/research/programs/humans-the-microbiome.

Dalla Lana School of Public Health, University of Toronto investigates global health discoveries, notably the influence of tobacco on health, air pollution, inner city and Indigenous health, and occupational disease and disability. The largest public health school in Canada, Dalla Lana has more than 850 faculty, 1,000 students, and diverse research collaborations and training partnerships in Toronto and worldwide.
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