FAIRMONT CHATEAU LAURIER, OTTAWA | APRIL 5, 2017

THE MICROBIOME IN HUMAN HEALTH
ABOUT CIFAR

Established in 1982, CIFAR is a Canadian-based, global organization, comprised of over 400 fellows, scholars and advisors from more than 130 institutions in 17 countries. CIFAR brings together outstanding researchers to work in global networks that address some of the most important questions our world faces today. Our research is focused on improving human health, transforming technology, building strong societies and sustaining the Earth. Our networks help support the growth of research leaders and are catalysts for change in business, government and society.

Support for Ideas Exchange:

Support for the CIFAR Humans & the Microbiome program

The CIFAR Humans & the Microbiome program is generously supported by Brain Canada Foundation through the Canada Brain Research Foundation, FRQ Santé, Genome British Columbia, Genome Canada, the Jon and Nancy Love Foundation at Toronto Foundation, Manulife, and the Trottier Family Foundation.
On April 5, 2017, Fellows of CIFAR’s program in Humans & the Microbiome held a roundtable discussion with funding partners and key individuals in the public health sector on the role of the microbiome in human health. The roundtable highlighted the program’s current understanding and gaps in knowledge about how microbes affect human health, development and cultural evolution, and their plans for how to they aim to shed new insights on these areas over the next few years. Discussions with participants explored where the program’s research intersect with core issues and areas of interest of their organizations, of which water, public health, antibiotics, nutrition and relevance to the brain were key themes of the conversation. This report summarizes the key discussion points from that roundtable.

INTRODUCTION TO HUMANS & THE MICROBIOME PROGRAM - JANET ROSSANT

- All animals are colonized by large numbers of microorganisms on surfaces such as skin, mucosal membranes, teeth, and in GI tract. These microbes are collectively referred to as the microbiota. These microbes are numerous, outnumbering human cells by 10 times.
- Microbes play an important role in our health, social behaviour and evolution. For example, gut microbes help us digest food, educate our immune system, influence the development and functioning of our nervous system. Disturbing the microbiota then by antibiotics and lifestyle changes can lead to poor health outcomes. In terms of behavior and evolution, good microbes can help humans adapt to new environments.
- A major benefit of the microbiota is to provide “colonization resistance” against incoming pathogens and there is mounting evidence that the microbiota plays an active role in this type of protection.
- Over the past 50 years, we have seen a dramatic drop in the rates of infectious diseases including measles, mumps, hepatitis A, rheumatic fever and tuberculosis. At the same time, we have seen surges in immune disorders such as Crohn’s disease, multiple sclerosis, asthma and type 1 diabetes. This disappearing microbial diversity begs the question if we are living too cleanly and the need to better understand the role for microbes in human disease.
- To date, the microbiota has been associated with many conditions include type 1 diabetes, autism, allergies, obesity, cancer, and asthma to name a few. The complex interactions between the microbiota and humans is being actively explored and striking correlations are being found for particular disease states. There is however a need for research to move beyond correlative studies to ones that go to causality in order to understand the impact of the microbiome.
- Researchers are discovering that many previous unsuspected areas of human health, such as childhood development, are being influenced by the microbes living within us. For example, the maternal microbiome has been shown to affect baby before and after birth with long-term consequences.
- The Humans & the Microbiome program is probing the role of the microbiota in areas of human development, evolution and society (e.g. socio-cultural relations and change). The integration of health and anthropology makes this program particularly unique amongst other major international microbiome-based initiatives, giving it the potential to be truly transformative as a result. The broad range of funders is a reflection of the program’s reach and its importance to various stakeholders.
- This multidisciplinary nature of the program is allowing the program to explore the role of the microbiome beyond just human health and disease. Non health-related questions being tackled include what is the history of the human microbiome and how does it change across generations, geographies and ethnicities? How has it co-evolved with humans to help us adjust to changing food supplies and new diseases? Has it actually guided human behaviour and cultural practices? Should we consider humans as ‘superorganisms’ or ‘holobionts’, inseparable from our microbes and our environment? And what does this mean to our understanding of what it is to be human?
- The program currently has 19 Fellows & Advisors, spanning a variety of disciplines and geographic areas. Expertise in the program to date is provided in the areas of Microbiology, developmental and stem cell biology, metabolism and human physiology, evolutionary biology, history and social science, and anthropology.
DISCUSSION AROUND DRINKING WATER AND FOOD:

- There needs to be a shift in our conceptions of bacteria related to food and water consumption. For example, despite the perspective by the public that our drinking water is sterile, it actually contains many non-threatening microorganisms rather than being “pure” in the sterile sense. It is curious to think of how we might alter our language when speaking about these organisms to the public, for example, using the term “opportunistic pathogens” when describing drinking water.
- People are more willing to accept a certain amount of “xyz” in their food, but there is an apparent lower tolerance for such risk in drinking water. The anti-fluoride movement in drinking water was cited as a key example.
- Water treatment plants often want to eradicate microbes as it is easier and cheaper. But the question was raised as to how genomics and microbiome research could help direct the nature and specificity of that treatment, ensuring certain microorganisms that might be highly beneficial to our health remain intact.
- It could be envisioned that water treatment systems become personalized. With an understanding of which microorganisms are beneficial for our health and the regional microbial compositions of drinking water, spiking water with different microbes as a probiotic treatment for a specific population could be considered. It was noted that such water delivery would have its challenges though as each distribution system (i.e. pipes) harbours different microbial communities.

DISCUSSION ON ANTIBIOTICS AND PROBIOTICS:

- The microbiome is critical during the first full year of life and up to years three and four. Antibiotics taken during this time period can therefore have profound long term impacts.
- The same bacteria or probiotic that may be good for one person is not necessarily good for another given our unique genomes. With this complexity, we need to consider a precision/personalized medicine approach to probiotics.
- The concept of food probiotics is challenged by the public’s desire to have food sterile.
- There is a need for the public to better understand the role of antibiotics, highlighting that when taken properly and with justified reasons, it can have positive benefits. That said, we need to also rethink the use of antibiotics and the understand the consequences of prolonged exposure. For example, studies have shown that increased antibiotic use can lead to higher rates of depression.

DISCUSSION ON PUBLIC HEALTH & PUBLIC ENGAGEMENT:

- The need to effectively communicate with the public regarding public health issues of which the microbiome is well linked is critical. Give current knowledge, there was a desire to see a role in Public Health in re-educating the public, moving away from messaging that they are helping to keep us sterile. For example, it was once thought that the lung and breast milk were sterile however they have since been shown to be filled with microbes.
- From a public health perspective, the microbiome poses challenges as it is harder to prove things are safe than to prove things aren’t dangerous.
- E.coli was discussed as a key example of how messaging about the microbiome needs to shift as there are various strains of the bacteria, some acting as commensal organism, others as pathogenic. This underlying complexity of interactions with the human body needs to be considered in our thinking and messaging of the microbiome.
• The anthropological connection is crucial when studying and discussing the microbiome, particularly in the context of public health. We need to know understand our ancestral microbiome and how our relationship with microbes has changed over time before making specific health interventions. It was noted that the San Diego architecture school is embedding the microbiome into its curriculum.

• In work by Humans & the Microbiome program member Eran Elinav on the impact of food and microbiome on blood sugar levels, studies showed that the response to the same food was highly individualized, illustrating the need for personalized approaches (e.g. diets). However, it was noted that there could be challenges that would come from personalized public health (e.g. standard recommendations).

HOW CLOSE ARE WE TO BEING ABLE TO TELL THE MESSAGE AND INTERVENE BASED ON STUDIES ON THE MICROBIOME?

• The microbiome has the advantage that it is easily communicated and a topic that the public has a strong appetite for, perhaps because it is naturally occurring. However, the microbiome is a frontier science and research in this area is still in its infancy which poses obvious communication challenges. It was questioned where society’s appetite and openness for dialogue around the microbiome present an opportunity for more action.

• It was perceived that the public is more receptive than biomedical community to microbiome-based interventions given the sense that it has been challenging to implement change until the public demands it. To address the conservative approach of the medical community to microbiome-based interventions, it was felt that focus should be placed on how to educate and inform them on the importance of the microbiome to health and disease. Thinking of how to do so in a global context should also be examined.

• The public is ahead of the biomedical community in adapting microbiome-based interventions. This is seen for example on the explosion of the probiotic industry. However, while there is strong interest by the public in the probiotic world, such interventions have still not gone through sufficient studies with the necessary scientific rigour.

• The innate immune system and the host-microbiome system are well-connected. Immune cells can sense microbes and their metabolic products and translate the signals into various responses. Such responses have been well noted in the brain, illustrating a brain-gut-immune system connection. It is possible to think then about how we could use the microbiome to influence the immune system as well (e.g. in inflammatory bowel disease).

• Currently, personalized medicine is focused on 1/15th of the genome. There is an opportunity to create more room for personalized medicine to focus on the microbe sequences.

• There is a need to better understand the role of the microbiome in disease treatment. For example, how might the microbiome might impact a person’s response to treatment given its role in the metabolism of pharmaceuticals? How the microbiome impacted by drug treatment to ensure it remains intact to prevent disease? This last question was discussed in the context of antibiotic delivery, particularly in hospital settings, and whether IV versus orally could be less disruptive to the microbiome as it would bypass the gut.

• There still needs to be a fuller understanding of the microbiome of a “built environment” or rather the microbiome of the indoors. Studies have shown that hospital patients do better with open windows yet it was uncertain what a healthy indoor microbiome look like.

• In relation to maternal-child health, even through caesarian delivery, a baby will eventually develop microbiome, though the rate is slower compared to vaginally born babies. Vaginal swabbing, though shown to be effective in restoring the microbiome of caesarian born babies to those of vaginally born babies, was noted as getting pushback in the US given some of associated risks (e.g. potential for transfer of sexually transmitted diseases).
PARTNER/STAKEHOLDER PRIORITIES:

- Genome Canada noted an interest in the microbiome’s impact beyond human health (e.g. livestock), though health maintains a focus for them. They noted antimicrobial resistance is a key area of study, including how to manage it.

- Brain Canada noted an interest in the microbiome on brain and also development. It was commented that there is a strong connection between the microbiome and the brain, particularly given the evidence that germfree animals show brain development issues. The microbiome was also mentioned to have strong connections to autism and other neuropsychiatric disorders. It was noted that there is also compelling data linking the microbiome to neurodegenerative disorders (e.g. Multiple sclerosis, Parkinson’s and Alzheimer’s). Strong correlations have also been shown between stress/anxiety/depression and anorexia with malnutrition. That said, while data is increasing on the connections between the microbiome and health, research still needs to examine the question of correlation vs. causation.

- Public Health: There is an interest in researchers from academia, private sector and public health agencies to come together regularly to explore the technological aspects of the microbiome (e.g. bioinformatics, sequencing and metabolomics). There was also a desire to engage Health Canada more broadly on conversations about the microbiome.

NEXT STEPS:

- With the public’s push to probiotics and antibiotics, public education on the microbiome was seen as an important area where synergies across sectors (academia, public health, government) could be found to create meaningful impact.

- Engaging the regulatory sector in these conversations was viewed as important given the number of probiotic products and biologics/therapeutics on and emerging in the market.

- Discussion explored whether there would be benefit to making the microbiome as a social determinant of health. For example, should a child exhibit an impoverished microbiome, this could translate to poor health which if the microbial determinants of health were known, could provide opportunities for intervention.

APPENDIX 1: PARTICIPANTS

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<tr>
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