Lec 5 The gut microbiome and metabolic syndrome

<u>The gut microbiome is extraordinarily diverse</u>

- 10^14 bacteria (0.2 – 1.7 kg) primarily within our gut but also our genital tracts, mouth and skin, as well as fungi, protists and viruses.
- 500-1000 different strains of bacteria/person (each person unique)
- More bacterial cells than homo sapiens cells
- 150 x more genes in microbiome than in human genome.
- 10,000 x more genes collectively
- Bacterial colonisation varies in our gut--- the abundance of bacteria within our gastrointestinal tract changes along the gut. The colon and large bowel regions have the greatest number of bacteria (10^12)

<u>The gut microbiota is a self-sustaining ecosystem involved in food digestion</u>

- **Primary function of gut microbiota is to digest our food.**

Muffin -> homogenize -> acidify -> intestinal flora -> mix and transfer -> poo!

<u>Multiple factors influence the gut microbiome</u>

The gut microbiome is extremely variable and the microbiome of each individual is very different. It is dependent on a number of influences which occur during life, and it changes throughout our life.

- We get some of our early microbiota in utero from our mother (maternal transfer) and then we get additional microbiota post-delivery depending on the mode of delivery (either through natural birth or caesarean), mode of feeding and maternal health. Our gut microbiome changes and can have a big impact in the first few years.
- Over the years, there are lifestyle influences such as diet, hygiene and the number of drugs or antibiotics that we take which strongly influence the gut microbiome. There are also physiological influences such as diet and sex hormones. Our gut microbiome changes in old age, partly because the immune system is changing and our dietary diversity also becomes more limited in old age.

<u>Nutritional Transition</u>

One of the most profound impacts on the microbiota is diet. There has been a huge change in diet over the last industrialisation and westernization, in particular the amount of fibre we eat.

- Pre-industrial populations had high fibre diets (rich in grains, fruit).

- They ate 50-100g of fibre/day.

- This has been replaced by a diet that is high in fat, sugar and salt which affects the microbiota.
- The average fibre intake in the Australian diet is 16g/day which is half of what is recommended for good health.

-Recommended fibre intake is 25-38g/day.

<u>Dietary fibre</u>

- Also known as microbial accessible carbohydrates (MAC) that reach the lower gut

• Fibre refers to complex carbohydrates which are digested and go through the small intestine to the large intestine and bowel where they're consumed/partly degraded by the microbiota.

3 types of dietary fibre

- **Non-starch polysaccharides** (20-90% fermentable) which includes cellulose and hemicellulose (the matrix component of plant cell walls). Hemicellulose includes pectins, β-glucans, xyloglucans and arabinogalactans. They are fermented/degraded by the bacteria.

• **Resistant starch** (100% fermentable) is in high grain food or is resistant because of the cooking process it has been through and is protected from the amylases in the small intestine, therefore it reaches the large intestine.

- R1-R4

• **Soluble oligo/polysaccharides** (100% fermentable); inulin, FODMAPS (fermentable oligo-, di-, mono-saccharides and polyols)

Alterations in the gut microbiota have been associated with a plethora of human diseases

- Changing life styles, diet, hygiene, antibiotics/medications, etc drive fundamental changes in our gut microbiota, which underlie the rise in many diseases.

Key questions:

- To what extent are changes in the microbiota causal in promoting diseases?
- What is the function of microbiota and microbiota-derived metabolites?

Although there is huge species diversity of the bacteria, there are similar classes of genes being expressed across all the different microbiota which reflects the basic need of the microbiota to digest a variety of food types.

Gut microbiome, by species

- Four major phyla dominate gut microbiota (~90%): Firmicutes, Bacteroidetes, Actinobacteria and Proteobacteria

Diet drives the species composition of the microbiota. European children vs African children

- Pre-industrial diet: More Bacteroidetes compared to Firmicutes.
- The westernized diet: Much more Firmicutes compared to Bacteroidetes.
- Non-western individuals have high microbiota gene count, diversity and propensity for fibre digesting species.
- Diet has dominant role in shaping gut microbiota over ethnicity, sanitation, hygiene, geography and climate. Some species of gut microbiota are now extinct in Westernized communities
- European children had a westernised diet whereas African children had a pre-industrialization high-fibre diet. Their major classes of bacterial species were completely opposite.

Gut microbiome, by ecology

Many bacteria enter through our food or through taking probiotics.

Probiotics: These tend to be transient commensals (an association between two organisms in which one benefits and the other derives neither benefit nor harm) of the gut microbiota but they can confer health benefits and support/promote the growth of beneficial bacteria.

Examples: Bifidobacterium spp, lactobacillus spp

Autobionts: the true residents of the gut microbiome They are permanent members of the gut microbiome, symbiotic (mutually beneficial relationship) and immunomodulatory. They are part of the normal microbiota and have a direct influence on host metabolism and immune function.

Examples: Bacteroides fragilis, Clostridium XIV

Pathobionts: permanent members of the gut microbiome, they are parasitic/infectious. They do not cause disease in presence of normal microbiota but cause disease when microbiota/immunity is perturbed (dysbiosis)

Examples: Clostridium difficle, Helicobacter hepaticus

- 3 glycan chaperones