

ISAPP 2020 Virtual Discussion Group, June 3, 2020:

### **How your gut microbiota can help protect against viral infections**

Around 85 members of the ISAPP community joined the 'Zoom' discussion forum to listen to the introductory presentations and participate in the ensuing debate/discussion.

ISAPP BOD members Karen Scott and Sarah Lebeer were joined by the invited experts Joel Dore (INRAE France), Tine Licht (Technical University of Denmark), Mary O'Connell-Motherway (APC Microbiome, Cork) to introduce the topic and lead the discussions. The discussion started with the gut microbiota, but expanded to include those colonising other body sites, and the impact microbial metabolites produced in the gut, such as butyrate, can have on other body sites.

The human microbiota is diverse, performs many different functions, and crucially the different members of the microbiota interact with each other. These interactions between different members of microbial community were the focus of our discussion – both the positive and negative interactions. Bacterial activities can be widespread, frequent or rare – and it is often the rare activities that have important impacts on the course of a disease. Specific examples discussed were antimicrobial agents produced by some bacteria that prevented *Salmonella* infections in pigs and cured mastitis in cows.

The microbiota has a dual and complex role interacting with viruses. Some members of the microbiota can prevent attachment of the viruses to cell surfaces by offering alternative receptors while in contrast virus particles can utilise other bacterial cells to "mask them" and facilitate entry to host cells. Other members of the microbiota can stimulate the immune system to promote elimination of a viral infection, while, on the flip side this same immune activation may promote viral infection. Thus it is important that any use of specific bacteria (ie probiotics) to help prevent or clear viral infections is first carefully tested to investigate possible unintended consequences. It is possible that probiotics or prebiotics may be considered as an adjunct therapy alongside vaccination. However, any such addition to a vaccine is likely to be secondary as the essential specific testing of the combination would take longer and introduction of an effective vaccine should not be delayed, even if it could then be subsequently improved.

Metagenomics has been widely used to investigate the microbiota in the context of health and disease, with the aim of identifying possible causative and preventative organisms or signatures. Frequently, a disruption in the microbiota composition results in a less diverse, lower 'richness' microbiota, which is often linked to a leaky gut syndrome, higher gut inflammation and more oxidative stress. This increased oxidative stress then exacerbates the microbial dysbiosis, causing more inflammation and increased leaky gut – creating a vicious cycle effect. These four factors are linked to various diseases associated with the central nervous system, the gastrointestinal system and also to metabolic and immunological diseases. These very same diseases represent some of the 'underlying health conditions' that are linked to higher severity and worse outcomes for Covid-19 infections. Thus there is potential for trying to redress the balance in the microbiota to prevent not only those diseases directly linked to the dysbiosis, but also to make people more resilient to other infections such as Covid-19. The diversity of the existing resident microbiota may be increased by the application of probiotics, prebiotics or synbiotics, included within a healthy, diverse, high-fibre diet. These approaches may improve bacterial fermentation in the large intestine, resulting in increased production of important bacterial metabolites, including short chain fatty acids, involved in host signalling and other functions. Such an approach could be particularly important in building up resilience in the elderly population.

The respiratory tract is colonised by its own distinct microbiota, and it also is important to maintain health, playing a crucial defensive role. Probiotics may also have a role here in the battle against Covid-19 (either preventing infection or enhancing recovery), but again these would have to be tested on a case-by-case basis. The best routes for application would also need to be considered. The direct route through nasal application is one option but, given the existence of the gut-lung axis, and transport of gut produced bacterial metabolites around the body, oral administration may also be effective. Probiotics that have already been shown to be effective against other viral upper respiratory tract infections may have promise, and there are already studies underway investigating these.

There was also some discussion around the potential side-effects the worldwide lockdown to contain SARS-CoV-2 may have on other aspects of health. There has been considerable emphasis in different countries on the negative impact on mental health of isolation and the additional stress brought on by direct concern about the virus and the related situation, but also worries about job security. We also spent some time discussing the potential impacts of the improved hygiene measures on the developing microbiota in infants and young children and whether this would result in a rise in allergic and other immune diseases in this “generation C”. This will no doubt be the basis of some new research in the future.

Despite the unprecedented worldwide scientific efforts and collaborative working, it is unlikely that an effective vaccine against SARS-CoV-2 will be widely available soon. Meantime we have to protect ourselves and the ‘at-risk’ population as best we can. Scientific evidence suggests that keeping our gut microbiota as complex and healthy as possible by eating a diverse, high fibre diet (supplemented by fermented foods, probiotics and prebiotics) can help mitigate the spiral into a low richness microbiota and gut inflammation. Similarly, we must also preserve the microbiota on other body sites. This may subsequently reduce development of those diseases represented within the “underlying health conditions” resulting in more severe SARS-CoV-2 infections. In essence, we need to keep our own microbial army in prime condition and armed to fight off unwelcome invaders.

**Summary prepared by Karen Scott and Sarah Lebeer**