

Press Release UNDER EMBARGO until 01.00hours GMT 25 August 2017

Thinking Small - APC Microbiome Institute Scientists Show Surprising New Impact of Gut Bacteria on Gene Expression in the Brain

Small things can sometimes make a big difference and this may be doubly true considering the crosstalk between the microbes in our gut (microbiome) and the brain. The extent, and the manner, of this dialogue is made clear in research published in the journal *Microbiome*, revealing a new level of communication between the gut microbiome and the brain.

The research, from scientists at the Science Foundation Ireland-funded APC Microbiome Institute at University College Cork shows, demonstrates in animal models that the trillions of bacteria within the gastrointestinal tract can influence microRNAs (miRNAs) in areas of the brain, such as the amygdala and prefrontal cortex that are involved in anxiety and fear-related behaviours. These miRNAs, which can regulate gene expression, may then act 'upstream' of our gut microbes to fine tune physiological processes that are fundamental to the functioning of the central nervous system.

Dr Gerard Clarke and Professor John F. Cryan, along with their PhD student Alan Hoban, used mice and rats that have either no gut microbes at all or depleted gut microbes and demonstrated that the miRNA expression profile is dysregulated in the amygdala and prefrontal cortex brain regions. The amygdala is responsible for the emotional response to fear stimuli, while the prefrontal cortex is key to higher cognitive functions and in the expression of anxiety and social behaviours.

The team was able to show that some of the miRNA alterations seen could be rescued by adding back the gut microbiome later in life. However we also noted a number of miRNAs that remained altered following exposure to microbes, which supports the concept of critical neurodevelopmental windows during which the gut microbiota is essential in influencing brain development.

miRNAs are small nucleotide sequences and have recently emerged as a new class of gene-expression regulators because miRNA-expression levels are altered in patients suffering from depression and anxiety and in animal models of these disorders. The possibility of using miRNAs for the treatment of psychiatric disorders is thus under consideration. Research in this area has faced several challenges and the development of safe compounds that are able to cross the blood-brain barrier and target brain regions relevant to anxiety was considered paramount for the emergence of novel, efficacious miRNA-based therapies in the clinical arena.

To our knowledge, this is the first time that the gut microbiome has been so clearly implicated in miRNA expression in both the amygdala and the prefrontal cortex. This study gives a better understanding of the factors that control miRNA expression and suggests that some of the hurdles impeding the exploitation of their therapeutic potential could be cleared by instead targeting the gut microbiome. This tallies with an increasing body of the work over the past decade that highlights the influence of our gut bacteria on brain function and behaviour.

'Altered expression of these miRNAs is implicated in the support of neuronal survival, growth and development, as well as neurogenesis, all important targets for the treatment of stress-related psychiatric disorders' said Dr Clarke.

'The Psychobiotic Revolution is coming' says Prof Cryan *'and we can now add miRNAs to an expanding range of therapeutic targets in the brain that can potentially be controlled by manipulating the bacteria in our gastrointestinal tract'*. Both Clarke and Cryan caution however that more work is needed before the full benefits of this exciting work can be moved into a clinical setting and that we need a more advanced understanding of the underlying mechanisms before such essential translational progress can be made.

Dr Clarke acknowledges the support of the Brain and Behaviour Research Foundation in funding this important and ground-breaking research and continued that *"The possibility of achieving the desired impact on miRNA expression in specific brain regions by therapeutic targeting of the gut microbiota is an appealing prospect that may expedite the promise apparent in these two previously disparate approaches'*.

Publication of the research coincides with the APC Microbiome Institute's hosting of NeuroGASTRO 2017 (<http://www.neurogastro2017.org/>), the flagship meeting of the Neurogastroenterology and Motility Society (ESNM; <http://www.esnm.eu/>). This will see an influx of more than 400 delegates from all across Europe and indeed worldwide and will provide an important forum for Dr Clarke and Prof Cryan to discuss this new research in the company of leading investigators in the field of Neurogastroenterology.

Their research is being published in the high impact Journal *Microbiome* and was supported by Science Foundation Ireland through a Centre grant to the APC Microbiome Institute and by the Brain and Behaviour Research Foundation. The research was co-authored by APC researchers at UCC, Alan Hoban, Roman M. Stilling, Gerard Moloney, Rachel Moloney, Fergus Shanahan and Timothy G. Dinan.

Full reference:

Alan E. Hoban, Roman M Stilling, Gerard Moloney, Rachel D Moloney, Fergus Shanahan, Timothy G. Dinan, Gerard Clarke & John F. Cryan (2017) "Microbial Regulation of microRNA Expression in the Amygdala and Prefrontal Cortex" *Microbiome* DOI: 10.1186/s40168-017-0321-3

***** During the embargo period, the article is available here: <http://bit.ly/2fNH0eq> *****

After the embargo lifts, the article will be available at the journal website:
<https://microbiomejournal.biomedcentral.com/articles/10.1186/s40168-017-0321-3>

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About APC Microbiome Institute:

The APC Microbiome Institute (APC; <http://apc.ucc.ie>) was formed in 2003 with funding from Science Foundation Ireland and in conjunction with key industry partners. It represents a seamless collaboration between University College Cork, Teagasc (the Irish Agriculture and Food Development Authority) and Cork Institute of Technology. It is widely recognised that the gut microbiota plays an important role in human health and has become one of the most dynamic, complex and exciting areas of research in both food and pharmaceutical arenas. Over the last decade the APC has established itself as one of the leading global centres in gut microbiota research. The APC has made several landmark discoveries and has published over 1,000 research articles in peer-reviewed journals, generating many journal covers and associated editorials. The APC comprises over 300 individuals, from the scientific PI's (the APC Faculty) funded by the partner Institutions, the management team, and a dedicated group of research scientists, research assistants and postgraduates students.

About Brain & Behaviour Research Foundation:

The [Brain & Behavior Research Foundation](#) (BBRF) began as a family movement in 1981 and has since become the world's leading private funder of mental health research. Since awarding the first NARSAD Grant in 1987, the Brain & Behavior Research Foundation has awarded more than \$365 million to fund more than 5,000 grants to more than 4,000 scientists around the world. The BBRF is committed to alleviating the suffering caused by mental illness by awarding grants that will lead to advances and breakthroughs in scientific research.

About Microbiome:

The central purpose of *Microbiome* is to unite investigators conducting microbiome research in environmental, agricultural, and biomedical arenas. Topics broadly addressing the study of microbial communities, such as, microbial surveys, bioinformatics, meta-omics approaches and community/host interaction modelling are published. Through this collection of literature, *Microbiome* hopes to integrate researchers with common scientific objectives across a broad cross-section of sub-disciplines within microbial ecology. *Microbiome* has a high impact factor (8.5), is published by BioMed Central and is one of the top journals in microbiome science.