KEYNOTE LECTURE 3

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GUT MICROBIOTA: FELLOW TRAVELLERS THAT REGULATE BRAIN & BEHAVIOUR ACROSS THE LIFESPAN

The microbiota-gut-brain axis is emerging as a research area of increasing interest for those investigating the biological and physiological basis of neurodevelopmental, age-related and neurodegenerative disorders. The routes of communication between the gut and brain include the vagus nerve, the immune system, tryptophan metabolism, via the enteric nervous system or via microbial metabolites such as short chain fatty acids. These mechanisms also impinge on neuroendocrine function at multiple levels. Studies in animal models have been key in delineating that neurodevelopment and the programming of an appropriate stress response is dependent on the microbiota. Developmentally, a variety of factors can impact the microbiota in early life including mode of birth delivery, antibiotic exposure, mode of nutritional provision, infection, stress as well as host genetics. Stress can significantly impact the microbiota-gut-brain axis at all stages across the lifespan. Moreover, animal models have been key in linking the regulation of fundamental brain processes ranging from adult hippocampal neurogenesis to myelination to microglia activation by the microbiome. Finally, studies examining the translation of these effects from animals to humans are currently ongoing. Further studies will focus on understanding the mechanisms underlying such brain effects and developing nutritional and microbial-based intervention strategies and how these interact with various systems in the body including the cannabinoid system.

KEYNOTE LECTURE 4

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NEW THERAPEUTIC APPROACHES IN THE RENIN-ANGIOTENSIN SYSTEM

The classical or canonical renin-angiotensin system (RAS) plays a key role in regulating cardiovascular function. Angiotensin (also known as angiotensin-(1-8)) is the major effector of the RAS, which is formed by the action of proteases (renin and angiotensin I converting enzyme (ACE)) on substrate precursor peptides. Angiotensin II exerts its actions by activating several receptor subtypes of the GPCR family, especially the AT1R. The proteases mentioned above and the AT1R are pharmacological targets, and several drugs have been developed to treat cardiovascular diseases. However, an alternative SRA has
been discovered, and this non-canonical system includes the peptides angiotensin-(1-7) and angiotensin-(1-9) and the proteases ACE and ACE2 and the receptors MAS. AT2R and MrgD. This new SRA has opposed action to the classic SRA and offers new drug targets for developing the cardiovascular drug. In this presentation, I will present our work on this new alternative SRA and critically analyze the recent discoveries.

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