

Dans le cadre de l'École d'été 2017 sur le microbiome: analyse de données massives pour les sciences omiques, il nous fait plaisir d'accueillir le titulaire de la nouvelle Chaire d'excellence: L'axe microbiome-endocannabinoïdome dans la santé métabolique.

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At the turn of the century, the endocannabinoid (eCB) system was considered to be a signalling system composed uniquely of: i) two GPCRs, the type-1 (CB1) and type-2 (CB2) cannabinoid receptors; ii) two endogenous lipid ligands for such receptors, the endocannabinoids (eCBs) N-arachidonoyl-ethanolamine (anandamide) and 2-arachidonoyl-glycerol (2-AG); and iii) eCB anabolic and catabolic enzymes, i.e. N-arachidonoyl-phosphatidylethanolamine-phospholipase D (NAPE-PLD) and fatty acid amide hydrolase (FAAH), respectively, for anandamide; and diacylglycerol lipases (DAGL) α and β and monoacylglycerol lipase (MAGL), respectively, for 2-AG. This system was shown to act as a pleiotropic signalling device of local mediators activated "on demand" and playing a role in all aspects of mammalian physiology and pathology, including the control of metabolism and its disturbances, such as obesity and type 2 diabetes.¹ More recently, anandamide and 2-AG were found to be biosynthesised and degraded by redundant enzymatic pathways and to interact also with non-cannabinoid receptors. Furthermore, several endogenously occurring analogues of both anandamide and 2-AG were discovered (or rediscovered) and shown to act at non-cannabinoid receptors and play a role in metabolism too. These lipids include anandamide and 2-AG congeners, i.e. the N-acyl-ethanolamines (NAEs) and the monoacylglycerols, respectively, as well as other bioactive amides of long chain fatty acids, such as the N-acyl-acyl amino acids, N-acyl-dopamines, N-acyl-taurines, N-acyl-serotonins and the primary N-acyl amides. These lipid mediators often share with eCBs similar anabolic and/or catabolic enzymes. Thus, it can be asserted that a true "endocannabinoidome" (eCBome) exists,² with at least 200 multi-target lipid mediators, and an array of about 20 anabolic and catabolic enzymes and 20 molecular targets, some of which yet to be identified. Evidence suggests that endocannabinoids and NAEs play opposite roles in dysbiosis,³ but whether or not other eCBome members also participate in microbiome-host cross-talk is still unknown. Data indicating that the microbiome and the eCBome can be modified by exactly the same environmental factors, such as the diet, age, dark and light cycles and temperature, will be briefly mentioned, together with the methodologies used to investigate the interactions between these two systems.

1) Silvestri C, Di Marzo V. The endocannabinoid system in energy homeostasis and the etiopathology of metabolic disorders. *Cell Metab.* 2013; 17(4):475-90.

2) Di Marzo V, Piscitelli F. The Endocannabinoid System and its Modulation by Phytocannabinoids. *Neurotherapeutics.* 2015; 12(4):692-8.

3) Cani PD et al., Endocannabinoids--at the crossroads between the gut microbiota and host metabolism. *Nat Rev Endocrinol.* 2016; 12(3):133-43



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From the endocannabinoid system to the endocannabinoidome: a new (h)ome for microbiome-host interactions ?

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Chaire d'excellence
en recherche du Canada

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