

Microbial Endocrinology: Interaction of the Microbial Hormones with the Host

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ARTICLE INFO

Received: 📅 December 19, 2019

Published: 📅 January 06, 2020

ABSTRACT

Abbreviations: QS: Quorum Sensing; AI: Autoinducer; ACTH: Adrenocorticotrophic Hormone; SCFAs: Short-Chain Fatty Acids; AD: Autoimmune Disease

Citation: EM Ahmed, Marwa Al-Moghazy. Microbial Endocrinology: Interaction of the Microbial Hormones with the Host. Biomed J Sci & Tech Res 24(2)-2020. BJSTR. MS.ID.004015.

Short Communication

Recent studies of the human microbial ecology, studying the communities of bacteria within the human bodies. The genetic information of the bacteria within the human bodies can be 150-fold greater than the human genome. A complicated interaction between the host and the microbial gut. Indeed, the gut microbiota plays important roles in host metabolism, immunity and even behavior. Mechanisms by which the microbiota are known to mediate these functions include breaking down dietary components, educating the immune system and degrading toxins [1-3]. In recent years modulation of hormonal secretion revealed the nature of the host bacteria interaction. Actually, direct after birth, bacterial colonizing the intestine perform by a critical role in the maturation of the immune system [2] and the endocrine system (Clarke 2013).

Hormone Production by Bacteria

Bacteria can produce hormones that can affect host metabolism, immunity and behavior. This interplay is bidirectional, because the microbiota has shown to be both affected by and to affect host hormones, this can be called microbial endocrinology. Lyte and Ernst were the first to define the field of microbial endocrinology research, after observing that stress-induced neuroendocrine hormones can influence bacterial growth [4]. More researches

concerned with microbial endocrinology discovered hormone receptors in microorganisms and hypothesized that they represent a form of intercellular communication [5]. As an example, pathogenic neurotoxins such as neurotoxin 6- hydroxydopamine were shown to alter norepinephrine levels in mice presenting the bidirectional nature of the host-microbe interaction [6]. An interesting study showed that many enzymes involved in host hormone metabolism (including epinephrine, norepinephrine, dopamine, serotonin, melatonin, etc.) might have evolved from horizontal gene transfer from bacteria [7].

Crosstalk between bacteria and the endocrine system came from the discovery of interkingdom signaling, including the hormonal communication between microorganisms and their hosts [8]. This field evolved from the initial observation that bacteria perform quorum sensing (QS), communication based on producing and sensing autoinducer (AI) molecules. These AI molecules are hormone-like elements that regulate functions including coordinated bacterial growth, motility and virulence [9]. Some AI molecules have crosstalk with host hormones for activating signaling pathways [10]. The hormone of the human host can affect the bacterial gene expression [11], for example, catecholamines enhance bacterial attachment to host tissues, and affect growth and virulence of

bacteria [12,13]. In contrast, the human sex hormones estradiol and estradiol decrease bacterial virulence by inhibiting QS [14].

Neurohormones and Stress Hormones: Neurohormones are secreted from neuroendocrine cells in response to a neuronal input. Although they are secreted into the blood for a systemic effect, they can also act as neurotransmitters. Modulation of behavior by the microbiota (such as anxiety in mice) is believed to occur through neurohormone precursors (e.g. serotonin, dopamine) (Lyte 2013). Gut bacteria can produce and respond to neurohormones such as serotonin, dopamine and norepinephrine (Roshchina 2010). Catecholamines can alter growth, motility, biofilm formation and/or virulence of bacteria (Lyte 2003) [10-13]. The microbiota may help keep us calm and balanced by altering stress hormone levels. The mice have elevated plasma levels of the stress hormones corticosterone and adrenocorticotropic hormone (ACTH) in response to mild stress [15,16], increasing behaviors associated with anxiety and stress. ACTH affect the hypothalamic–pituitary–adrenal axis by further producing corticosteroids. Accordingly, two specific species, *L. helveticus* and *B. longum*, reduce levels of the stress hormone cortisol and anxiety-like behavior in both rats and healthy humans [17]. Furthermore, mice chronically treated with the probiotic *L. Rhamnosus* had lower levels of corticosterone and less depressive behavior in a forced swim test than controls [18].

Pheromones and Sex Hormones: Pheromones are hormones that play important roles in sexual recognition, attraction and mating behavior as well as aggression behavior and dominance. Pheromones are also termed ectohormones, chemicals secreted outside of the body of one individual and affect the behavior of others. Since four decades the effect of sex hormones on the bacteria has been reported. For instance, *Prevotella intermedia* takes up estradiol and progesterone, which enhance its growth [19]. The composition of the intestinal microbiota can be affected by the change in the genes in expression of the estrogen receptor, ER- β [20]. This interaction goes both ways, as several types of bacteria have also been implicated in steroid secretion or modification [21]. *Clostridium scindens* converts glucocorticoids to androgens, some male steroid hormones [21]. Adlercreutz et al. [22] reported that, use of antibiotic decreases the level of estrogen so intestinal bacteria play a role in estrogen metabolism. The levels of urinary estrogen and fecal microbiome richness, as well as presence of Clostridia, including non-Clostridiales, and three genera within the Ruminococcaceae suggested a kind of correlation.

Feeding and Metabolism: A classic role of the gut microbiota is in digesting a variety of carbohydrates and fermenting them into short-chain fatty acids (SCFAs). For example, subtherapeutic doses of antibiotics, which do not eliminate the gut microbial community but rather cause significant changes in its composition, lead to increased levels of SCFAs and to weight gain in mice [23]. This effect can extend to the levels of the glucose and the triglyceride.

Immune System and Immune Responses

Many evidences linked both hormones and the microbiome to immune responses under healthy conditions and autoimmune disease (AD). The intestinal microbiome has an impact on immune system development and differentiation. It is well known that the microbiome affect the initiation and progression of infectious diseases [24]. The gut microbiota can send signals to stimulate the normal development of the immune system and the maturation of immune cells (Louis 2014). The gut bacteria stimulates the secretory IgA response that is involved in inactivating rotaviruses, competes *Clostridium difficile* colonization, and neutralizes cholera toxin [25]. There are many interconnections that the microbiome and hormones may affect the immune system through shared pathway. The immune and neuroendocrine systems share a common group of hormones and receptors. Glucocorticoids such as corticosterone and cortisol regulate inflammation levels and have effects both on the innate and adaptive immune responses [26].

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ISSN: 2574-1241

DOI: 10.26717/BJSTR.2020.24.004015

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