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MAKING SENSE OF GUT SENSING

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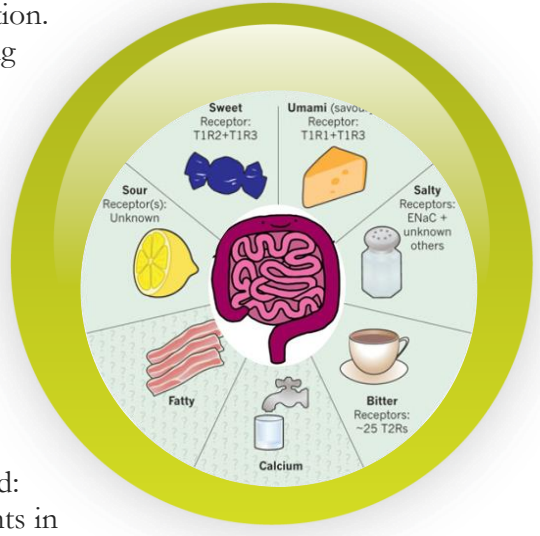
In January, the British Journal of Nutrition released a special issue entitled "*Nutrient sensing and signaling in the gastrointestinal tract.*" Pancosma played a key role in the content of this publication; we co-organized the scientific meeting on which the special issue is based, and we were invited to co-author the Preface. Each article in the special issue discusses unique and newly-discovered molecular mechanisms underlying gut sensing. Taken together, the articles shed an important and clarifying light on the mechanisms of gut sensing and the key players involved and support Pancosma's concept, Gut Effect (Sensing) [1], which is the foundation on which our innovation is now based. What relevance does gut sensing have to animal feeding, and how can we use this information in the field when interacting with customers?

Looking back, Pancosma has successfully used flavors and taste modifiers to target the senses in the nose and tongue to manipulate small and taste perception, and consequent feed intake. Looking forward, an improved understanding of how gut sensing works will allow us to use feed additives with a new and highly precise approach since we will be able to target very specific physiological responses depending on the additive used. Indeed, as we already know [2], the gut is now considered as a sensory organ – with the ability to "taste" ingested molecules and respond accordingly. This sensory feature has clear implications for both animal and human nutrition and health. Research in gut physiology has continued to reveal new mechanisms by which gut sensing occurs, and these findings have opened the door to new potential targets for feed additives. In short, Pancosma has identified a new sensory organ as a potential target for feed additives, and we are at the forefront of this exciting new field of technology that will undoubtedly revolutionize animal feeding as we know it today.

We already know that the enteroendocrine cells are constantly monitoring the contents of the gut and communicating this information to other organs via neural and hormonal signals. Precisely, nutrients and non-nutrients are sensed by G-protein couple receptors (GPCR) expressed on enteroendocrine cells. Therefore, these cells are ideal targets of feed additives aimed at influencing digestion, absorption of nutrients, feed intake, and insulin sensitivity; all physiological functions that play a pivotal role in production animal health and nutrition. Understanding the mechanisms underlying gut sensing will help to guide us in developing and further refining our feed technologies. This was the basic idea behind the symposium called "Nutrient sensing and signaling in the gastrointestinal tract". We brought together key researchers in the field of gut sensing to discuss recent progress in the field and opportunities for using nutrient sensors as targets for improving animal health. The papers from each researcher highlight the key issues discussed: mechanisms by which GPCR sense nutrients in the gut, other types of receptors or other cell



types that can respond to nutrient sensing. In particular, Prof. Shirazi-Beechey's paper described the role of the T1R receptors in gut sensing. These receptors are already well described and are key players in the Gut Effects observed with SUCRAM® [3]. Briefly, it has been established that T1R2 and T1R3 combine and bind to SUCRAM® with very high affinity and elicit an increase GLP-2 secretion, improved gut integrity and enhanced the uptake of glucose from the gut. In contrast, the combination of T1R1 and T1R3 are known to sense "umami" flavors and this causes changes in the secretion of another gut hormone (CCK) which decreases appetite.

When taken together, what do these research findings tell us and how can we use this information in the field? In the continuum of target to physiological outcome, there are several key components that are identified in the work described in the British Journal of Nutrition special issue. We have now identified some of the key players in the molecular detection system expressed on gut epithelial cells and the messengers that are released by them. These messengers then communicate to other organs of the body, and the message is amplified before eliciting a measureable physiological response in the animal. Importantly, the detector (receptor) and the messenger (hormone) are often co-expressed, and this allows for extremely fast and efficient communication.

"65 years ago, Pancosma created scents for the nose and, 20 years ago, created artificial sweeteners for the tongue. Now, Pancosma is creating new technologies for the gut. All three – nose, tongue, and gut – are epithelial surfaces with sensory properties. So, it is all about the senses at Pancosma! The gut may be an iconoclastic sensory organ, but that is what it is. This is the new paradigm the new mindset of Pancosma that makes use of another sensory organ." Dr. David Bravo (Head of R&D)

These novel insights revealed the high potential of these key players as targets for feed additives aimed at improving nutrient utilization; altering appetite to increase or decrease feed intake, and decreasing inflammation of the gut during disease and during dietary transitions, such as weaning. Therefore, when thinking of Gut Effects, we need to remember the key players and the key components involved:

- The detector: the receptor that senses, for example T1R2/T1R3 that senses SUCRAM®
- The cells expressing and responding to the detector: for example, enteroendocrine cells
- Co-localization of the detector with a messenger: for example, T1R2/T1R3 and GLP-2
- The messenger that is released upon activation of the detector: for example, GLP-2
- The physiological response: for example, increased growth of gut cells in response to SUCRAM®

As we strive to better understand each player, and the factors that influence each component of gut sensing, we will improve our ability to refine our feed additives, become extremely precise in targeting specific detectors and their associated physiological outcomes, and improve animal health and nutrition in ways we never imagined.

[1] The history of Gut Effects. Pancosma Research News 26. 2012.
[2] Gut Effects, a brief history of Pancosma innovation. Pancosma Research News 46. 2013.
[3] SUCRAM®, beyond sweetness, the true story. Pancosma Research News 19. 2011