Alimentary Pharmabiotics: Common Ground for Academia with the Food and Pharmaceutical Industries

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"…remember that words are signals, counters. They are not immortal."
—Brian Friel (*Translations*)

The changing landscape for research and development in the pharmaceutical and food industries, coupled with changing societal attitudes and requirements, creates new challenges and opportunities for industry-academe collaborations. The case of alimentary pharmabiotics is a representative niche area with opportunities for both industrial sectors. Although manipulation of the gut microbiota in the treatment and prevention of several disorders has become a plausible strategy, a more intriguing prospect is the potential to "mine" diet-host-microbe interactions for functional food ingredients and for novel discovery.

Changing Landscapes

As the pharmaceutical industry faces increasing challenges in drug discovery, new models for research and development (R&D) are called for (Crommelin *et al.,* 2010; Shah *et al.*, 2010). The landscape today is dominated by declining output of new molecular entities, more outsourcing of R&D, partnerships and alliances, increasing emphasis on biologics over small molecules and a commercial imperative for agility and flexibility. At the same time, advances in understanding major disease processes promise to open the way for definition of subsets of patients at a molecular level, with genotyping replacing historic approaches to phenotyping diseases. This will tend to fragment the industry's mass markets into genotype segments and will undermine the old blockbuster model ("one-size-fits-all drug") with a new era of personalized medicine.

The degree to which this brave new world will prevail is likely to vary for different diseases, and will be influenced by societal attitudes toward the treatment and prevention of disease, in particular, depending on whether a pharmacological or non-pharmacological approach is favored (Crommelin *et al.* 2010). The pharma sector is likely to remain dominant in innovation and may engage with academia in pursuit of solutions for chronic inflammatory, infectious and neoplastic diseases. For other disorders, particularly where alternatives to drug treatment are desired, small companies, academia and publicly funded institutions are likely to take a leading position with declining involvement of big pharma. Examples of the latter may include the exploration of functional-food ingredients or the pursuit of remedies for heterogeneous "functional" disorders and for those euphemistically referred to as "lifestyle" disorders (Crommelin *et al.* 2010).

Against these changing scenarios, opportunities for the food industry, especially in the functional-food business, must be considered in light of greater regulatory constraints, more stringent requirements for claims on food products, and a modern society that is risk averse. Thus, the distinction between a functional-food ingredient and a drug becomes blurred. Furthermore, pressure to control prices and focus on niche markets will affect both the food and pharma industries.

Opportunities for industry-academe interactions in both the food and pharma sectors will flourish, provided an entrepreneurial approach to science is encouraged, and where academic institutions provide for greater flexibility and agility in adapting to change. The case of alimentary pharmabiotics, as an example of a common ground for the food and pharmaceutical industries to explore in collaboration with academia, is summarized below.

Alimentary Pharmabiotics

Despite major technologic and conceptual advances in biology, new drug development in gastroenterology appears to be in decline (Parsons and Garner, 1995; Caskey, 2007). While large fortunes have been expended by the pharmaceutical industry in synthetic-drug development, it is noteworthy that about half of the drugs approved by the Food and Drug Administration (FDA) in the United States in the past twenty-five years have been derived from natural living material in the wider environment (Newman and Cragg, 2007; Bernstein and Ludwig, 2008). Therefore, it seems logical and timely that the inner microenvironment of the alimentary tract might be another rich repository from which functional-food ingredients and new drugs can be mined (Shanahan *et al.*, 2009; Shanahan, 2010).

An alimentary "pharmabiotic" is the name that we have given to products derived from mining host-microbe interactions in the gut that have a proven health benefit. This encompassing neologism overcomes the limitations of restrictive definitions of probiotics, prebiotics, synbiotics and postbiotics. Thus, it embraces whole organisms, live or dead, components and metabolites thereof, and genetically modified organisms and the concept has the potential for translation to the marketplace by either the food or pharmaceutical industry. Representative examples of the potential for mining microbe-microbe interactions, host-microbe and diet-host-microbe interactions in the gut are summarized in Table 1.

Table 1. Opportunities for "mining" the gut microbiota for pharmabiotics.

Interaction	Pharmabiotic	Reference
Microbe-microbe	Exploration of bacteriocins against specific pathogens (*e.g. Clostridium difficile*)	Rea *et al.* (2007)
Host-microbe	Anti-inflammatory drugs from bacterial components or metabolites that modify mucosal inflammation (*e.g.* lipoteichoic acid, CpG DNA)	Grangette *et al.* (2005); Obermeier *et al.* (2003) Rachmilewitz *et al.* (2004)
Diet-host-microbe	Immunomodulatory drugs from bacterial cell-wall polysaccharides	Mazmanian *et al.* (2005, 2008)
	Analgesic activities (some but not all probiotics are beneficial in irritable bowel syndrome and visceral hyperalgesia)	Rousseaux *et al.* (2007)
	Manipulation of the microbiota may alter bioavailability of dietary calories	Bakhed *et al.* (2004)
	Interaction between the microbiota and dietary components may alter the composition of host adipose tissue.	Wall *et al.* (2009)

Whether pharmabiotics mined from the natural environment of the gut will be exploited by the food or the pharma sector will depend in part on whether a small molecular entity or a bacterial fragment is involved, the nature of the desired effect, and the clinical indication. The clearest delineation will be the treatment of established disease or biomarkers of early disease in the case of the pharmaceutical sector, whereas the food industry is more likely to focus on disease prevention as measured by reduction in a biomarker of risk. Opportunities for academic collaborations exist in both scenarios. To that end, academic research centres, such as the Alimentary Pharmabiotic Centre (http://www.ucc.ie/research/apc/), have espoused the virtues of hybrid science and hybrid scientists capable of working across the boundaries of traditional disciplines and at the food-pharma interface. These include scientists, clinicians, and clinician-scientists with the collective ability to bring scientific ideas from the laboratory through the clinic to the bedside and marketplace. Research in academic centers can be aligned to simultaneously suit the requirements of both the food and pharma industrial sectors while fostering an environment conducive to entrepreneurship and freshness of ideas. For those who doubt it can be done—it *can* be done because it *is* being done!

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