Plaza and Hulak, J Pharmacokinet Exp Ther 2016, 1:1
http://dx.doi.org/10.4172/jpet.1000102

Journal of Pharmacokinetics & Experimental Therapeutics

Mini Review Open Access

Human Gut Microbiota, a Component to Have in Mind during Drug Discovery, Taking the Interdisciplinary Road

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During the past 23rd International Symposium on Glycoconjugates, Dr. Tim Spector presented in a plenary lecture his current and previous research about twins in the UK, with impressive results that are helping to understand how much is the genotype accounting for certain traits or conditions. An example of such is myopia in Taiwan. As he cleared although the environmental component just accounts for 10% of variability, and the genetic component accounting for the highest part of it [1], the rate of myopia in children is much higher than expected. In this case the environmental conditions are forcing the phenotype. Besides those interesting results, he presented the new direction in his research, the study of the gut microbiota within the British Gut project. This one and the American Gut project, can both give an idea of the importance of gut microbiota for biomedicine nowadays. Although in early experimental phases in many cases, the interest of the scientific community is growing and the steps to its consolidation are steady.

We cannot forget that the gastrointestinal tract is directly involved in the absorption of orally administered drugs, and the potential effect that they may have over the human gut microbiota should be carefully evaluated [2], because some components could alter the population resulting in dysbiosis [3]. This is important, because the human gut microbiota has been shown to have a very important role for health and the normal immune system activity [3,4], besides it has potential applications as biomarker, either the gut one, or the bacterial oral community [5,6].

Understanding how does microbiota work is relevant for the development of new drugs, not only to know if our treatment is affecting the balance of microflora, but also because we could use some type of antimicrobials or probiotics in order to modulate the levels and balance in the bacterial population [7]. In this sense, new drug formulations could include these extra components in order to control certain populations, or increase the ratio of certain ones.

A new type of clinical practice is the transplantation of microbiota from healthy donors, which is currently used only in cases of patients infected with *Clostridium difficile* that do not response to standard treatments of antibiotics [6]. This new developments as an alternative treatment are encouraging, although if not administered by a certified professional (and this field is really new) it could become a dangerous practice, especially because the new trend of DIY in fecal microbiota transplantation [8]. Not testing for the suitability of microbiota in terms of safety regarding pathological agents could bring new infections. It is then why establishing the core collection of bacteria of a healthy individual is so important. This collection can help to improve the status of a patient sooner, and accelerate its recovery after a treatment with antibiotics, or in the case of a viral infection to help to decrease the viral load.

It has been addressed that the taxonomic composition of the microbiota is largely variable between individuals [9] as affected by the eating habits, geographical location, age, or even the circadian rythms [10]. Because the species composition is subjected to so much variation, the establishment of a core collection of bacteria in healthy individuals can be eased if we think on a transcriptomics profile of that bacterial population. That is, while the species composition may not be completely homogeneous, we could aim for a core set of transcripts in this metabiome [11]. It has been indicated that the transcriptome is more conserved [9] between bacteria, and it seems logical that different bacterial species respond in a similar manner to a certain type of biotic or abiotic stimuli. For example the genes involved in bacterial glycolytic metabolism which is more conserved and present in many species, which would be expressed when this pathway needs to be carried out. Reducting to the absurd, despite differences in race, nationality, religion, or geographical location, when humans are hot they sweat in order to dissipate temperature. In a molecular way, something similar can be proposed. Furthermore, the metabolomic component could be a great aid in defining this set of bacteria in the healthy. All these technologies and approaches are essentially complementary, and can be a great opportunity for new developments [12,13].

Regarding viral infections, there have been recent publications relating them with the microbiome, where interestingly host immunity has been described to be modulated by the own host microbiome. The characterization of a microbiome of viral infected patients is *per se* interesting as a basic research question, besides the potential biomedical implications that it has. In this direction, it has been suggested that microbiota could modulate indirectly viral infections produced by HBV (Hepatitis B virus) through the immune system [14]. Furthermore, recent results in mice have indicated that gut microbiota plays an important role in the clearance of the virus through stimulation of liver immunity in adults. Lastly, it has been demonstrated that gut microbiota can regulate immunity in non-connected mucosal in response to influenza A, a respiratory infection [15].

Characterization of human gut microbiota is a necessary effort, and many projects have been developed in this way. For the development of new drugs to know the composition of a healthy microbiota, and the implications that dysbiosis may have is of paramount importance, as some treatments may cause negative effects over the immune system indirectly through the bacterial population. It could also be an advantage for developing more efficient drugs, which could include certain type of antimicrobials for decreasing certain species, or probiotics in order to promote the most convenient types. This field of research promise to be an exciting source of inspiration and discoveries in future.

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Received January 25, 2016; **Accepted** January 28, 2016; **Published** January 31, 2016

Citation: Plaza JJG, Hulak N (2016) Human Gut Microbiota, a Component to Have in Mind during Drug Discovery, Taking the Interdisciplinary Road. J Pharmacokinet Exp Ther 1: 102. doi:10.4172/jpet.1000102

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