

DEVELOPMENT OF MATHEMATICAL ALGORITHMS FOR MODULATION OF GUT MICROBIOTA THROUGH DIET

More than one hundred trillion microorganisms live in the human intestine and make up the intestinal microbiota. This microbial community affects the development of many diseases related to the lifestyle of industrialized countries, such as obesity or diseases related to the immune system. The gut microbiota responds to diet, and processes many of the nutrients that are ingested with food. Today's personalized nutrition tools primarily use genetic data from the patient.

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This approach is incomplete and poorly optimized because it does not take into account the metabolic contribution of the intestinal microbiota. The incorporation of the intestinal microbiota in personalized nutrition programs has enormous potential because the compounds produced by a well-balanced microbiota can protect us from the development of chronic diseases.



Stance4health partners have developed the **AGREDA** bioinformatic tool, a system that will help design personalized nutrition programs that do take into account the composition of the gut microbiota in each individual. **AGREDA** enables a better understanding of how the processing of nutrients by the intestinal microbiota takes place and that of the compounds that are produced in this process, which can have a positive or a negative impact on health (Figure 1).

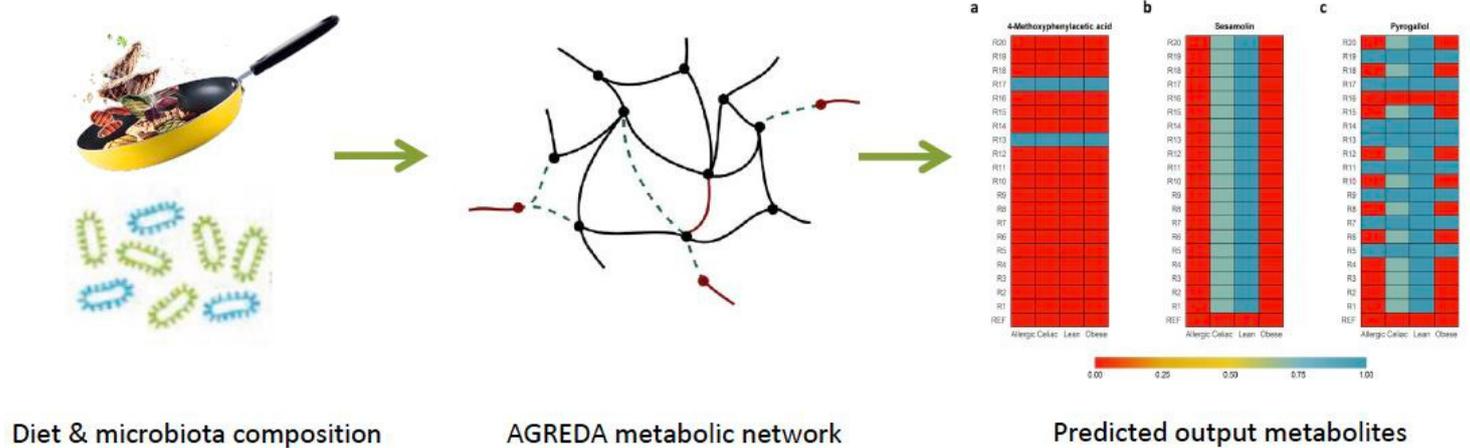
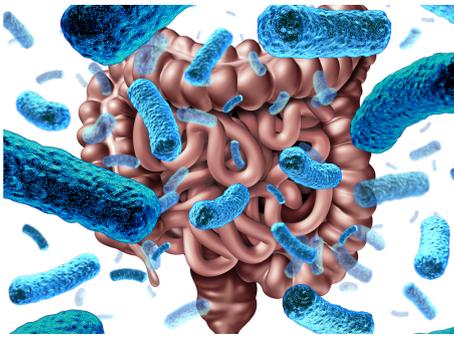


Figure 1. AGREDA enables the prediction of microbiota-produced metabolites based on a person's specific diet and microbiota composition.

The gut microbiota produces different metabolites from dietary nutrients in each of us.

AGREDA has been developed using information from various genomic and biochemical data repositories, generating a computational metabolic network that globally represents the metabolism of the human gut microbiota. In particular, we focused on including as many biochemical reactions as possible that are involved in the metabolism of nutrients, an aspect that had been little emphasized in previous work investigating the microbiota metabolism. Thanks to this, **AGREDA** includes the metabolism of 250 nutrients, such as phenolic compounds, present in plant foods such as fruits, vegetables and legumes and in beverages such as tea and coffee. The metabolic pathways involved in the metabolism of amino acids and caffeine, among others, have also been extended.

AGREDA opens new avenues for the development of personalized nutrition programs that direct the composition and activity of the microbiota in the optimal direction for a given individual.



To accomplish this, **AGREDA** will be combined with the **i-Diet** nutritional software, which will design and propose diets with a pre-established nutrient content, optimally defined by **AGREDA** based on the composition of an individual's intestinal microbiota.

This will allow modulating the metabolites produced by the intestinal microbiota in a way that contributes to maintaining or improving health. In upcoming work within the **Stance4health** project, the inclusion of **AGREDA** in the **i-Diet** nutritional software will be optimized and its usefulness will be tested in various interventions with adults and children in Germany, Greece and Spain. In particular, its usefulness in the design of diets that contribute to improving the health status of children suffering from obesity, celiac disease and food allergies will be validated.

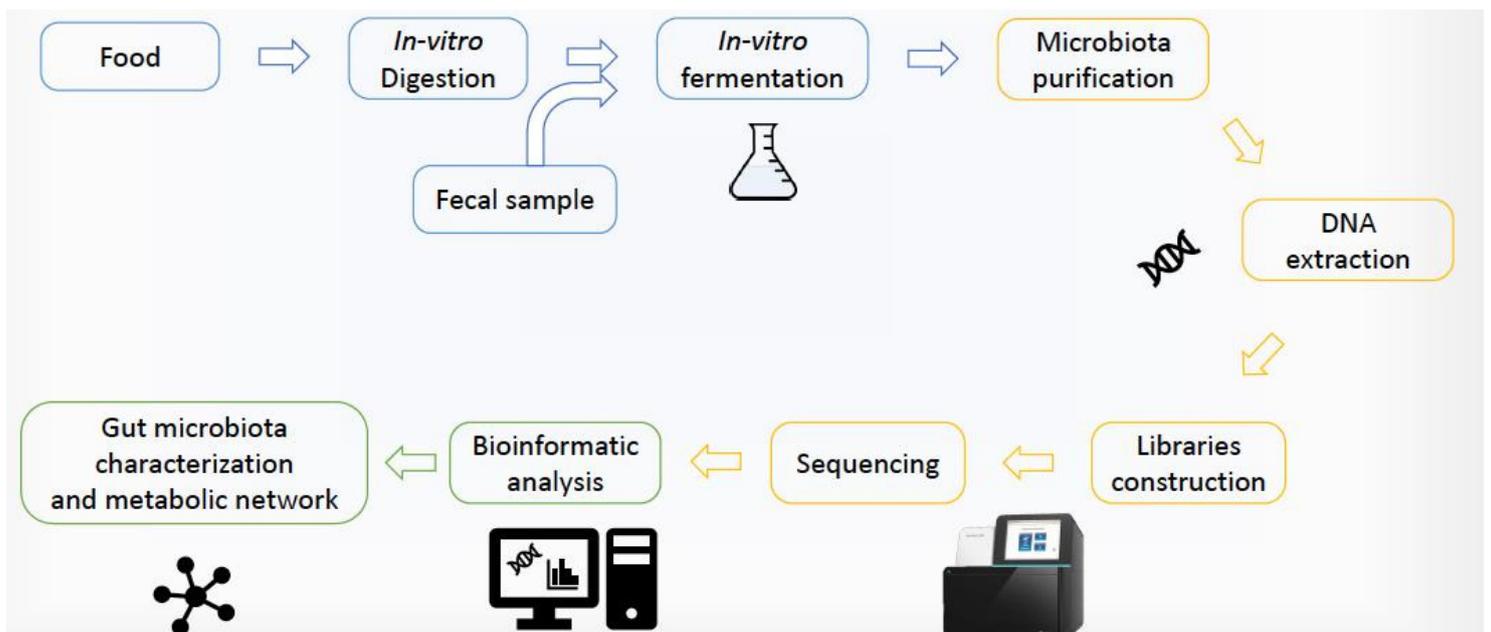


Figure 2. Workflow employed to study the effect of the main foods and culinary practices of the Western and Mediterranean diets on the gut microbiota.

In addition, **Stance4health** partners are analyzing experimentally the effects of different combinations of foodstuffs (i.e. meat, fish, vegetables, fruits, cereals, pulses, etc.) and cooking methods (i.e. boiling, frying, grilling, baking, etc.) on the composition of the gut microbiota, using an in vitro digestion and fermentation system that imitates the conditions of the human gastrointestinal system (Figure 2).



Different foods & cooking methods produce significant differences in the abundance of some bacterial species present in the gut microbiota!

These analyses are showing that different foods and cooking methods produce significant differences in the abundance of some bacterial species present in the gut microbiota. Therefore, these foods could be used to modulate the composition of the intestinal microbiota towards a desirable composition. For instance, garlic increases the abundance of *Bacteroides uniformis*, a species that has been demonstrated to be beneficial to health by reducing metabolic alterations associated with high-fat diets, whereas carrot, eggplant, lettuce, and other vegetables favor the increase of *Ruminococcus bromii*, a species known to participate in the production of beneficial Short Chain Fatty Acids.



These in vitro experiments have shown that the addition of tannins to some food products promotes healthy changes in the human gut microbiota. Moreover, nutrient analysis of the different foods investigated in these in vitro experiments indicates that some specific nutrients contained in various of these foods can drive the gut microbiota composition of children who suffer from obesity, celiac disease and food allergies towards the composition of healthy children. The results will further inform the choices of i-Diet to include specific foods and nutrients in the recipes proposed to the software users based on their microbiota composition and individual health needs.

Visit www.stance4health.com for more information about our project.

