SUMMARY OF THE FIBEBIOTICS EU PROJECT

Period: 1 July 2013 – 31 December 2014 (project months 19-36)

Summary description of project context and objectives

The goal of the project is to support the development of functional food ingredients and products that are beneficial for the human gut and immune system and therefore of crucial importance for quality of life. The project will study the effects of specific non-digestible polysaccharides (NPS) which have shown potential health effects towards the gut and immune system. The health effects of NPS will be focused around enhancing immune defence against pathogens, the reduction of infectious diseases such as common cold and influenza of elderly and will make use of European Food Safety Authority (EFSA) supported biomarkers that enable immune function claims and underpin the mechanism involved. The studied mechanisms are the innate and adaptive immune system and the possible involvement of the microbiota and microbiota-mediated products such as short chain fatty acids. To achieve this goal, new and existing NPS are studied for their health effects in a systematic way by developing a toolbox of dedicated assays and models that can be used by industry and authorities to study and approve food ingredients with a similar health focus.

The project is:

1) performing biochemical analyses to study NPS composition and to study effect of processing (food preparation) and fermentation (in the gut) on the NPS,
2) developing standardized in vitro screening methods (for immune effects and gut health via the microbiota and metabolites formed in the gut) to be able to predict in vivo effects,
3) using dedicated in vivo and ex vivo (like effect towards gut bioptic material) analyses to study mechanisms of action and to validate biomarkers and
4) studying the effect of NPS in humans via a pilot trial (based on vaccination efficiency), dedicated trial towards barrier function and a confirmative trial (towards URTI).

By combining the knowledge that will be gained from molecular, cellular and whole-organism studies, the goal will be to understand the mechanisms of how these NPS exert their bioactivity and to use this knowledge to design functional food products. SMEs make a very large contribution to the project, both as beneficiaries in the products and as a technology service provider related to health research. Besides that the food industry can directly benefit from this project via the established Industrial Platform. The FibeBiotics project hopes to provide the scientific basis for international nutritional organisations to recommend an immune-related functional health claim for some of the NPS studied.

Description of work performed and main results

The NPS compounds of interest

The consortium focuses on the NPSs: yeast b-glucan, oat b-glucan, arabinoxylan, shiitake b-glucan, apple pectin RGI and exopolysaccharide (EPS) from Lactobacilli. All NPS except the apple pectin RGI were included in the human pilot trial. Biochemical analyses using different analytical methods have resulted in a full characterisation of the NPSs and indication of strategies for characterisation of similar polysaccharides. As a result of the biochemical analysis of the supplements used in

the pilot trial it was concluded that the EPS sample was very low in concentration. Effects on fermentation in the gut of the NPSs have been studied revealing different dynamics of breakdown of NPSs. Most of the compounds contained traces of lipopolysaccharide (LPS). A method have been developed by which LPS can be removed with maintenance of the NPS structure. These purified samples can now be used in in vitro research directed towards direct immune effects of NPSs.

In vitro bioactive effects of NPS

Several mechanisms for bioactivity of NPS have been hypothesised. The first research line is the direct support of the innate immune system, like strengthening of the barrier function of the intestinal epithelium. Experiments in which small intestinal epithelial cells are exposed to NPS samples have been performed revealing activation of NFkB pathway of some of the NPSs and influence of cytokines related to cross talk with immune cells.

The second line of research is the effect of NPS on the microbiota community in the gut. This is analysed with the SHIME model. Results indicate an NPS dependent shift in microbiota composition. To support this research the GA-mapTM technology, a fast and cheap method to analyse a dedicated set of bacterial genera and species in samples, was developed. In order to develop SOPs for in vitro fermentation and interventions to study effect on the microbiome a microbiota community of bacterial strains was set up together with a tRFLP profiling method.

The third line of research is that NPSs can be fermented into short chain fatty acids (SCFA) which are important for energy and immune function of the gut cells. Fermentation studies indicated that fermentation of different NPSs result in different concentrations and ratios of SCFA.

Ex vivo analysis of NPS

To reveal potential direct effect of NPS towards gut epithelial tissue, human bioptic colon material have been exposed to some of the NPSs in Ussing chambers. First analysis indicate significant effects towards translocation of marker molecules over the tissue which indicate a potential direct effect on regulation of the barrier function of intestinal cells.

The human pilot trial

A randomised, double blind, placebo-controlled human pilot trial was designed with six arms (5 NPS compounds and a control) in each arm 40 persons in the age of 55 -70 years and older. Antibody titre upon vaccination with a standard flu vaccine was the primary outcome for health effects. Positive trends have been found for some of the NPSs studied. Besides that, blood based innate immune biomarkers have been analysed together with the microbiota composition. As not all biomarkers have been analysed, no final conclusion have been drawn. However, the pilot trial have led to the choice of NPS and design of the pivotal trial which is currently running in winter season 2014-2015.

The project website and database

At the start of the project, a public website (www.fibebiotics.eu), an intranet website and an Industrial Platform domain have been opened to inform the general public and to file and exchange documents. Next to that, a specific restricted site has been created which has been designed as a warehouse/database for all the data generated from the FibeBiotics project.

Dissemination via Industrial Platform

One of the highlights in dissemination is the initiation of an Industrial Platform (InP) and a special website which contains information about the project partners and their core business and project results. Currently, 33 industrial partners have signed

the Letter of Support and became an InP member. Until now three Industrial Platform meeting have been organized which were well attended and evaluated as very informative by the attendees.

Dissemination via media

The FibeBiotics project have attracted media attention by writing several press releases at the start of the project (in different languages). Also, a number of publications in professional magazines and online journals were issued. The FibeBiotics project was also presented during several (inter)national meetings and during bilateral meetings with the food industry.

Expected final results and potential impacts

The expected final outcomes of the FibeBiotics project can be summarized as:

1. Defined Standard Operation Procedures and efficient strategies to detect and characterize purified and processed NPS. These methods should determine the biochemical character of an NPS when designing functional food products and by that secure quality of the product. This information should also lead to the required information for an EFSA claim submission.
2. Highly standardized methods to classify NPS based on their bioactive effects. The methods will be based on immune cells and microbiota and microbiota-mediated metabolites using in vitro and ex vivo assays.
3. Improved knowledge on the mechanism of action of NPS based on in vivo and ex vivo analyses as well as based on the result of human intervention trials.
4. Determination of base line characteristics and methods to perform human clinical studies in the area of food products that target the gut and immune system.
5. Development of a database and supportive data analysis tools that can be used to predict bioactive effect of NPSs without the use of animal trial and resulting in a high success rate when testing NPS products in human trials.
6. Support the industry with translational activities for implementing this knowledge to support claim substantiations for NPSs.
7. Initiate a network of excellence in the field of health effects of NPS and build on a link with the food industry to apply the knowledge in developing new functional foods.

The FibeBiotics project will have impact on the food industry and the European consumers. It is self-evident that the project is to support the food industry with innovations in the area of gut & immune supportive products, with a science based evidence for its bioactivity. That is why we initiated an Industrial Platform (InP). The InP will link research, tools, methods etc. developed in the FibeBiotics project with food industrial practise and interest. It would be the clear intention that industrial interest should be sustained after the end of the project in order to make full benefit of the gathered experience with a final goal of entry into the national, regional and global marketplace. Food products aiming to support the gut & immune system have a very high market value. Currently the main health component in this kind of products are based on probiotic bacterial strains. The impact of fibres/prebiotics/NPS can grow in importance and even can be combined with probiotics (like in synbiotics). Products with an accepted health claim (which have not been approved for probiotics yet) are expected to gain attention of the consumers and therefore will create opportunities for the food industry.

Viruses are the most common infectious agents humans may contract. Cold and influenza viruses result in significant costs to the economy considering lost workdays but also cause morbidity and mortality. Research that integrated all costs (including

absence of employees with sick children at home) showed that common colds and flu are responsible for a cost of $ 40 billion annually. Because of the potential severity and epidemic/pandemic threat, the Advisory Committee on Immunization Practices (ACIP) recommends annual immunisations for elderly and people at high risk like health care workers. However, the effectiveness of these vaccines declines with increasing age. Because of the enormous impact on the quality of life, life expectation and health care costs, a reduction of common cold incidences and reduced duration of the illness will have significant outcomes. The NPS products in the FibeBiotics project will be studied with a focus on enhanced vaccination efficiency and reduction of cold and flu symptoms as an endpoint. Whether endpoint disease parameters will fully be communicated to consumers and in health claim submission will depend on advances in EFSA regulation. It is important to mention that the immune system, the target of this project, has a much high impact on many diseases. Besides, there is a body of literature describing the effects of fibres on intestinal disorders. Therefore, the NPS might potentially aid in reducing diseases such as cancer, Alzheimer, Crohn's disease, arthritis, diabetes etc.

Contact

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