

SUMMARY OF THE FIBEBIOTICS EU PROJECT

Period: 1 January 2012 – 30 June 2013 (project months 1-18)

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 compounds, effect of processing and bioavailability,
- 2) developing standardized in vitro screening methods to be able to predict in vivo effects,
- 3) using dedicated in vivo and ex vivo analyses to study mechanisms of action and to validate biomarkers and
- 4) studying the effect of NPS in humans via a pilot trial and if appropriate via a confirmative trial.

By combining the knowledge that will be gained from molecular, cellular and whole-organism studies, the goal will be to understand the bioactive mechanisms of these NPS 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 sets focus on a selected number of NPS compounds: yeast β -glucan (Wellmune) from Immitec, oat β -glucan from Swedish Oat Fiber, Arabinoxylan (Naxos) from BioActor, Shiitake β -glucan produced by DLO, apple pectin RGI produced by INRA and exopolysaccharide from Lactobacilli produced by TEAGASC. All NPS except the apple pectin RGI were produced in large amounts and in time for the human pilot trial. Biochemical analysis using different characterisation methods have started to fully understand the composition of the compounds. Most of the compounds contained bioactive traces of

bacterial derived lipopolysaccharide (LPS) a strong stimulator of immune responses which can hamper the bioactivity analysis using immune cells. Therefore, the project have set up strategies to further purify NPS for in vitro trials.

In vitro bioactive effects of NPS

Several bioactive mechanisms for NPS can be hypothesised. The first research line for the bioactivity is the direct support of the innate immune system. Currently, the experiments in which epithelial cells are exposed to the NPS samples are performed but microarrays still have to be performed and analysed. Until now, only Wellmune (which is lowest in LPS) was tested on immune cells and resulted in the conclusion that Wellmune increases the ability of dendritic cells to present antigens, stimulate lymphocytes, show immunosuppressive potential and anti-inflammatory effect.

The second line of research is the effect of NPS on the microbiota community in the gut. This is analysed by in vitro models like in a static set up and the dynamic Simulator of Human Intestinal Microbial Ecosystem model for which first experiments have been performed. To support this research, the consortium also worked on Denaturing Gradient Gel Electrophoresis and a new tool to study the microbiota composition, the GA-mapTM technology.

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 indeed result in other amounts and ratios of SCFA.

Ex vivo analysis of NPS

Human bioptic material of the gut will be used to study responses of NPS. As this involves human volunteers the first period focussed on writing the protocol for the ethical commission and developing good protocols for tissue handling. The next reporting period results can be expected.

The human pilot trial

The human pilot trial started in the first project year. A randomised, double blind, placebo-controlled trial was designed with six arms (5 NPS compounds and a control) in each arm 40 persons in the age of 50 years and older. An ethical protocol was written and approved. The primary outcome for health effects is the antibody titre upon vaccination with a standard flu vaccine. Besides that, blood based innate immune biomarkers have been analysed and the microbiota composition will be analysed. Currently, a statistical plan is in preparation and the final planned biomarkers are being analysed.

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, 27 industrial partners have signed the Letter of Support to become an InP member. The first Industrial Platform meeting held was very well attended and evaluated by the attendees as well organised and informative. Currently, the second Industrial Platform meeting is being prepared.

Dissemination via media

The FibeBiotics project have attracted media attention by writing several press releases at the start of the project (in different languages) and also later on the human trial. 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 a 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 and NPS-containing functional food products based on the in vivo and ex vivo analysis as well as based on the result of a human interventions.
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 an 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) for the food industry. The InP will link research, tools, methods etc. developed in the FibeBiotics project with food industry. It would be the clear intention that industrial interest should be maintained 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 fibers/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 might be profitable 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 persons and people at high risk like health care workers. It is however stated that 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 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 the reduction of flu vaccination efficiency and 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, which is the target of the proposal, has a much higher impact via many other immune-related diseases. Besides there is a body of literature describing the effects of fibers on intestinal disorders. Therefore the NPS might have potency to reduce diseases like cancer, Alzheimer, Crohn's disease, arthritis, diabetes etc.

Contact

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