



Cross-Talk Newsletter # 1

Cross Talk: Let's get started!

"It's no use, Gentlemen, science is and remains international."

Emil Fischer (1852-1919), Nobel Prize in Chemistry

Our project has officially been existing for almost a year now, but only recently has it achieved its first most important objective: all the students are now recruited! The project brings together 16 PhD students and a young researcher, representing 12 different nationalities, from Europe, Asia and South America, carrying out their work in 8 European countries!

Marie Curie actions favor this spirit of exchange between people from different horizons, a spirit that has always characterized Research. In this respect, we view the network formed by the Cross Talk students as a great opportunity to promote transnational exchange of knowledge through mobility and regular group meetings. Of course, in order to be fully valuable, the network cannot be solely self-centered. This is why we strongly recommend and encourage openness to scientific events outside the project and development of your communication and organization skills. We aim and hope to make this network a dynamic element for your future career.

This first network newsletter is partly dedicated to the Kick-Off meeting that took place in April 2009. This first network event was the occasion for a detailed presentation of the project, for students to get to know each other and for all the participants to share a nice moment!

Let there be many more moments like this... starting with Aberdeen next October!

Cross Talk Coordination Team

Cross-Talk Kick Off in Jouy-en-Josas.

On Monday, April 27th, all 17 selected candidates but one were gathered in the Cafeteria of the INRA research centre in Jouy en Josas. Unfortunately, it was not possible for Vanessa, who was selected 3 days before, to organize a trip from Spain. Emmanuelle Maguin, Yoni Winogradsky and Hervé Blottière welcomed all the fellows around a cup of coffee and cookies. All the rights and duties of the Cross-Talk fellows were presented by Emmanuelle. The students were asked to select two delegates to represent them at the General assembly. Edouard and Arunima were elected. In the evening, all the partners came to Jouy en Josas and we all met for a diner. The cocktail and meal were a good opportunity to get to know each other and for the Cross-Talk fellows to discuss with their supervisors. Then, under a heavy rain, the French partners brought back everyone to their hotel, for a night rest, the program of the two following days being very intense.

On the 28th, the meeting room in the INRA castle was just large enough for all the fellows and partners.



Emmanuelle summarized the goal of the project and the different tasks to fulfill. Three lectures on the main aspects of the Cross-Talk project were given by Hervé, Joël Doré and Per Brandtzaeg. After an excellent lunch, every research project supervisor gave a brief overview of their respective RP, explaining the rationale, the goal and the various expected deliverables. This intensive afternoon was ended by the General Assembly. Florence Haimet exposed all the financial aspects and rules of Cross-Talk. The first “fall school” and network meeting will be held in Aberdeen in late September-October. Then, a discussion arose about the opportunity to organize the second workshop together with the first MetaHIT Conference on Human Metagenomics that will be held in Shenzhen, China in March. The majority agreed that it was a valuable opportunity for the fellows to attend such an exciting research meeting with the participation of the leading international scientists in the field. The dinner that followed was a nice time to socialize and to prolong the scientific discussions which arose during the day. Monday 29th of April was the official kick-off. It was open to every participant. Muriel Mambrini, the President of the INRA Research Centre in Jouy en Josas, welcomed all the participants and introduced the importance of “Cross-Talk” in the research landscape of South Paris area. Emmanuelle Maguin offered an overview of the Cross-Talk project. Aat Ledebor presented the industrial platform LABIP, associated partner of the project, and the role of industrial company in the project. Then, Tim King who is in charge for the project of the follow-up of the network training program explained how Cross-Talk will aim to create a network of Doctoral Schools. This will be based on mutual recognition and concerted actions to improve career prospects for fellows. After a coffee break, Samuel Bottani, Professor at Necker Medical School showed us the example of the Centre for Interdisciplinary Research at the Paris Descartes University.

The second part of the meeting was dedicated to the different scientific aspects and was organized following the 3 work axes of the project. To begin with, Hauke Smidt explained us how Cross-Talk will provide important knowledge on “the Molecular mechanism of the cross-talk between commensals and Host”. After Hauke’s lecture, it was time for lunch. During the buffet lunch, the fellows presented their poster. On it, the young recruited researchers offered an overview of their backgrounds, outlined their expectations and showed a synopsis of their own Research project. Back to the amphitheatre, Denise Kelly described Work Axis 2 explaining the role of Host-Microbiota interplay in gut physiology. Work axis 3 is dedicated to in vivo validation in animal models and alternative human derived models, and Finn-Eirik Johansen displayed the potential models that may be used in the frame of Cross-Talk, their interest and limits. The Kick-Off ended by a lecture from Pierre Chambon of the University of Strasbourg on the control of TSLP gene transcription and its role in atopic affections. This talk given by a leading scientific researcher was inspiring and thought-provoking. After a few closing remarks from Joël Doré, it was time for each partner to travel back and for a few fellows to climb the stairs of the Eiffel tower.



The recruited Research fellows.

Sixteen PhD students and one Post-doc were recruited in the frame of the Cross-Talk network; however three of them are not financed by the EC.

Corinna Ceapa (RP1) has obtained a Masters of Biochemistry and Molecular Biology from the University of Bucharest in 2008. In the frame of an Erasmus Program, she spent 5 months in Lille (France) to work on structural glycobiology of the sea pineapple (*Halocynthia roretzi*). Corinna believes that “Cross-Talk” will have a great impact on the human health and wanted to be a part of our Network.

Born in Serbia, Dragana Dobrijević (RP2) obtained her Diploma in Molecular Biology and Physiology at the University of Belgrade in December 2008. She worked on the cloning and production of recombinant peanut allergens. Dragana indicates that she is attracted by the fact that Cross-Talk is a link with industry, applied and collaborative research, laboratory exchanges and dynamic training.



Vanessa Ferraria from Portugal (RP3) carried out her Masters in the Department of Technological Innovation and Valorization of Seafood products, in Lisbon. Her studies focused on the chemical and nutritional characterization of seafood products especially on fatty acids, cholesterol and heavy metals. Through Cross-Talk, Vanessa's objective is to acquire knowledge on immunology, microbiology and cell biology and also practical experience on molecular biology techniques.

On RP4, Malgorzata Nepelska from Poland, call her Gosia, was recruited after obtaining a Masters from the Warsaw Agricultural University. During her training, she spent almost two years in laboratories in Seibersdorf, Austria and a year in Athens with a Marie Curie Scholarship. She applied to Cross-Talk for its potential to develop her scientific career at the international level as well as participating in competitive project extending knowledge of a not well-known human - microbiota crosstalk.

Graduate from the University of Torino, Italy with a Masters degree in Research in Industrial Biotechnology, Oriana Rossi (RP5) previously worked in two laboratories in France (INSERM, Rouen and INRA, Jouy-en-Josas) in the frame of European projects. She aims at better understanding the cross-talk between host and microbiota and the mechanisms that prevent indiscriminate inflammatory responses in the intestinal tract.

Coming from the Universidade Federal de Minas Gerais in Brazil with a Masters in Molecular Genetics of Microorganisms, Marcella Azevedo (RP6) worked on bacterial diversity and antibiotic resistance. Marcella points out that Cross Talk offers her the opportunity to interact with scientists in the area of recombinant Lactic acid bacteria and to acquire new knowledge and another culture. Rejoanoul Islam (RP7), call him Reja, from Bangladesh obtained a Masters degree in Biomedicine from the University of Gothenburg in Sweden. During his training, he worked on *H. pylori* and Gastric Cancer Immunology to obtain a new serology screening assay. He believes that to create a new dimension or to achieve a totally new objectives, diversity is needed and collaborating platform facilitates this type of opportunity.

With a recently obtained PhD in March 2009 at the University of Paris, Elise Heuvelin (RP8) is the only post-doc.

of the project. Her work focused on the effect of probiotic and commensal bacteria on epithelial function in inflammatory condition. Elise is motivated to go from basic to applied research and that Cross-Talk will extend her network in the area of mucosal immunology.

Previously Research assistant at Jawaharlal Nehru Centre for Advanced Scientific Research in Bangalore, India, Arunima Chatterjee (RP9) obtained her Masters degree in Molecular and Human Genetics in 2005 from the Banaras Hindu University in Varanasi. She developed molecular genetic studies of hereditary hearing loss in humans. Opened to learn the beauty of various cultures, languages, working styles and thoughts, Arunima believe that Cross-Talk will convert her dreams to reality.

With a Masters degree in biotechnology in animal production and health protection from Warsaw University of Life Science, Agata Korecka (RP10) studied LPS-induced signalling regulating IL-6 transcription in macrophages. Agata believes that being part of a big European project will provide her the opportunity to collaborate with big European scientific communities.



In 2005, Edouard Monnais (RP11) obtained his Masters in Structural and Functional Biochemistry of Proteins at the University Claude Bernard in Lyon, France. After his Masters, while working at the Zurich Veterinary Hospital, he revealed the presence and functionality of TLR3 in bone marrow-derived adipocytes. Joining the Cross-Talk project, he will strive to decipher the TLRs trafficking following microbial associated molecular patterns recognition, and then specialize himself in gut immunology.

Born in Athens, Katerina Tsilingiri (RP12) graduated in Biochemistry and Biotechnology at the University of Thessaly, in Greece, in the year 2007. Doing so, she obtained an Erasmus fellowship to perform her lab project in Madrid. She believes that Cross-Talk is a great opportunity for young researchers to work on a very interesting field.

Sukithar Rajan (RP13), studied and worked in Kerala, India. Then, he moved to Skövde, Sweden, where he obtained two Master degrees in Biomedicine and Bioinformatics. He applied bioinformatics to perform a time scale analysis of

cancer progression. Sukithar indicated that for him, bioinformatics seems to be the “hot cake” for this century, which blends the advances and applications of Biology and Informatics.

After studying at the East China University of Sciences and Technology in Shanghai, China, Zhengyu Du (RP14), call her Dudu, received a MSc degree in Medical Pharmaceutical Sciences at the Groningen Rijksuniversiteit in the Netherlands. Dudu is eager to learn, aiming to be an expert in the relationship between inflammation in intestine and gut microbiota.

With a Masters of Science and Engineer in Biotechnology from the Cieszkowski Agricultural University of Poznań, Poland, Krzysztof Regulski (RP15) came to France to work on the molecular biology of the legume-Rhizobium interactions. Krzysztof thinks that Cross-Talk, as an international network, will give many opportunities for young scientists to meet and collaborate with the best academic and industrial leaders.

Emelyne Lecuyer (RP16) obtained her Masters Degree in Integrative Biology and Physiology with a specialization in Nutrition at the Pierre et Marie Curie University, in Paris. She completed a proteomic analysis of human intestinal microbiota associated with obesity. Highly motivated, she wanted to participate to our multidisciplinary European training network expecting regular scientific exchanges.

Food engineer with a Masters degree in Nutrition and Health obtained at Agro-Paristech, Bertrand Rodriguez specialized in studying probiotic strains and their benefits on health. Bertrand considers that joining Cross Talk is a great opportunity to improve his professional skills in science and communication and to start up his career path.



Summary of the three lectures by Cross-Talk’s fellows.

Physiology of the Digestive Tract, held by *Hervé Blottière*

The “Physiology of the Digestive Tract” lecture, given by Hervé Blottière, introduces the anatomy of digestive tract and its main organ function. The first section of the presentation shows a schema of different digestive organs and microscopy images of those organs’ tissues, whereas the second part explains enzymatic reactions appearing in digestive tract and organs regulation processes.

The Human Gastrointestinal (GI) tract is an expanded and complex system that allows to maintain diverse internal environments. Organs that make up the digestive tract are the mouth, esophagus, stomach, small intestine, large intestine—also called the colon—rectum, and anus. Inside these hollow organs is a lining called the mucosa. The digestive tract also contains a layer of smooth muscle that helps break down food and move it along the tract. Accessory organs to the alimentary canal include the liver, gallbladder, and pancreas.

Alimentation is directed towards digestion and absorption into cells as soluble molecules. Enzymes that break down polymeric macromolecules are classified by their substrates: proteases and peptidases split proteins into amino acids, lipases split fat into three fatty acid and glycerols, carbohydrases split carbohydrates such as starch into sugars, and nucleases split nucleic acids into nucleotides. Thanks to microvilli (also known as a “brush border”), the epithelial barrier is essential in intestinal absorption and the total surface area of the intestine has almost 200 square meters. The food transit in digestive tract is strictly timed with enzymes secretion and organ activity.

General view on digestive tract in this lecture gives us clear description of the gut microbiota environment. The exact knowledge about digestive tract composition and food digestion will help to better understand how bacteria survive and which role plays in cross-talk between them and host.

Krzysztof

The Gut Microbiota, held by *Dr. Joel Doré*

Dr. Joel Doré discussed the importance of studying the human microbiota since it can influence our biology in profound and diverse ways. Several diseases, including Crohn's disease, ulcerative colitis and obesity, have been associated with imbalances in the gastrointestinal microbiota, demonstrating the importance of commensal microorganisms in maintaining gastrointestinal health. For that reason, it is fundamental to know the microorganisms that live in the gut and their relationships with host physiology. Since 70% of the intestinal commensals cannot be cultured, genomic strategies have been developed to overcome this limitation. According to Dr. Joel Doré, one of these strategies is the metagenomic approach, which

appears most promising to explore human intestinal microbiota and identify new targets and strategies, from bacterial strains to metabolites, for nutritional and/or therapeutic applications in intestinal disorders. Analysis of 16S ribosomal DNA libraries revealed that the human microbiota is composed mostly of species from Bacteroidetes and Firmicutes phylum. It was observed that the microbiota is specific of each individual, stable over time and resilient upon antibiotherapy. Other techniques bypassing the cultivation of microbiota, such as proteomics, are also becoming a useful tool to monitor the functional products of the microbiota. Since it is a feasible approach to analyze complex bacterial ecosystems, it is being important to define "normal" microbiota and, thus, to explore the dominant intestinal microbiota in patients compared to healthy individuals. This opens novel fields of exploration, such as the mechanisms by which the intestinal microbiota acts in chronic, immune, metabolic or degenerative pathologies. Another strategy that can be used to explore bacteria-host crosstalk is the cloning of the metagenomic DNA and the functional analysis of the metagenomic clones. Taken together, all these tools will help to clarify the mechanisms of food-microbiota-host interactions with relevance to health-nutrition.

Marcella

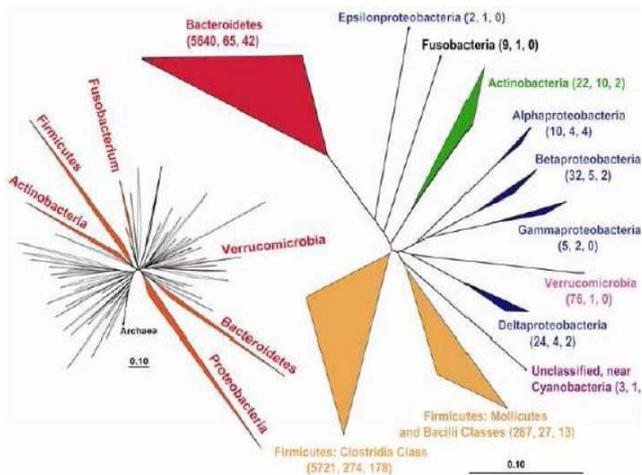
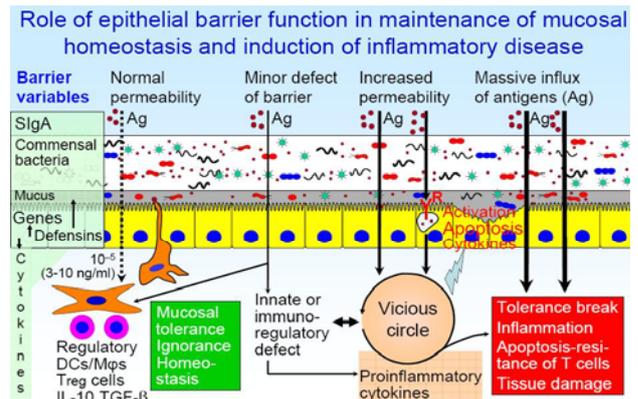


Figure : A limited fraction of known bacterial phyla within the dominant human intestinal microbiota.

References:

Manichanh C., Rigottier-Gois L., Bonnaud E., Gloux K., Pelletier E., Frangeul L., Nalin R., Jarrin C., Chardon P., Marteau P., Roca J., Dore J. Reduced diversity of faecal microbiota in Crohn's disease revealed by a metagenomic approach. *Gut*. 205-211. (2006).
 Metagenomic approach was used to investigate the intestinal microbial diversity. Two libraries of genomic DNA isolated from faecal samples of patients with Crohn's disease were analysed for the 16S rRNA gene. The study suggests that faecal microbiota analysed contains a markedly reduced diversity of Firmicutes.

Eline S., Klaassens., Willem M., de Vos., Elaine E., Vaughan. Metaproteomics Approach to study the functionality of the microbiota in the human infant gastrointestinal tract. *Applied and Environmental microbiology*. Vol. 73, No. 4. p. 1388-1392. (2007).
 A metaproteomics approach was used to the largely uncultured infant fecal microbiota. The fecal microbial metaproteome profiles changed over time, and one protein spot contained a peptide sequence that showed high similarity to those of bifidobacterial transaldolases



The mucosal Immune System, held by Per Brandtzaeg

The mucous membranes are linings involved in absorption and secretion, covering various body cavities comprising skin, airways or intestinal. They are in fact an enormous battle field continuously exposed to both pathogen as well as beneficial commensal microorganisms. The most exposed to challenge are intestinals - the largest mucosal surfaces in the body (approx.100 m²). In order to prevent pathological condition homeostatic balance between tolerance and immunity is indispensable. In charge of maintaining this homeostasis are intestinal epithelial cells, although once considered a simple physical barrier, are a crucial cells for maintaining intestinal immune homeostasis. Intestinal epithelium is equipped in unique regulatory mechanisms allowing staying tolerant to commensal microbiota and food proteins. On the epithelial barrier we can find a range of recognizing receptors that orchestrate the host innate response those nuclear receptors and Toll-like receptors are suggested to act as second messengers in the communication between microorganisms and epithelial cells, additionally immune cells are distributed in gut-associated lymphoid tissues (GALT). To the gastrointestinal mucosal immune system specialized structures belong Peyer's patches in which immune responses are thought to be initiated. The B and T cells eventually exit the Peyer's patch and guard against microbial penetration by patrolling the subepithelial regions throughout the intestine. The key players in maintaining mucosal homeostasis are subsets of lymphoid cells particularly IgA and T memory cells. These cells are characterized by immunological hyporesponsiveness to commensal bacteria and any dysregulation of the homeostasis can lead to inflammation or food allergy.

Gosia

References:

R. B. Sartor. Microbial influences in inflammatory bowel diseases. *Gastroenterology*.(2008)
 Crohn's disease, ulcerative colitis are the result of continuous microbial antigenic stimulation of pathogenic immune responses as a consequence of host genetic defects in mucosal barrier function, innate bacterial killing, or immunoregulation. Altered microbial composition and function in inflammatory bowel diseases result in increased immune stimulation, epithelial dysfunction, or enhanced mucosal permeability.

Artis D et al. Epithelial-cell recognition of commensal bacteria and maintenance of immune homeostasis in the gut. *Nat Rev Immunol*. (2008)
 Mucosal surfaces such as the intestinal tract are continuously exposed to both potential pathogens and beneficial commensal microorganisms. This creates a requirement for a homeostatic balance between tolerance and immunity that represents a unique regulatory challenge to the mucosal immune system. Recent findings suggest that intestinal epithelial cells, although once considered a simple physical barrier, are a crucial cell lineage for maintaining intestinal immune homeostasis. This Review discusses recent findings that identify a cardinal role for epithelial cells in sampling the intestinal microenvironment, discriminating pathogenic and commensal microorganisms and influencing the function of antigen-presenting cells and lymphocytes.