"Training and research in *Listeria monocytogenes* adaptation through proteomic and transcriptome deep sequencing analysis"

Newsletter n°1

October 2015-March 2016

LIST MAPS

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Editorial

Enrolling in a PhD is a major step in the training of young scientists to become successful experienced researchers. Universities and other research institutes are in charge of this training. As you will read below, supported by the European Commission, List_MAPS is a network of European Universities, research institutes and private companies who brought together their skills and expertise in order to develop a state-of-the-art, research orientated, training programme for early stage researchers.

Centred on the ecology of *Listeria monocytogenes*, a life threatening food pathogen, List_MAPS develops an ambitious collaborative research programme requiring the joint efforts of 11 young scientists. It addresses major food safety issues.

At the time I am writing these lines, Amber, Angela, Bohyung, Catarina, Ibrahim, Ignasi, Miguel, Natalia, Patricia, Tiago and Vanessa have been working on their own part of the project for the last 6 months. The first operating year of List_MAPS is already rich in network-wide events: training on outreach activities last October, ISOPOL conference in June, Summer School in July and workshop in October.

The periodic issues of this newsletter will give the opportunity to follow the life and advances of List_MAPS throughout the duration of the network.

Dr Pascal Piveteau

Coordinator

PRESENTATION

WHAT IS LIST_MAPS?

4 **YEARS**

5 **COUNTRIES**

9 **PARTNERS**

11 **EARLY-STAGE-RESEARCHERS**

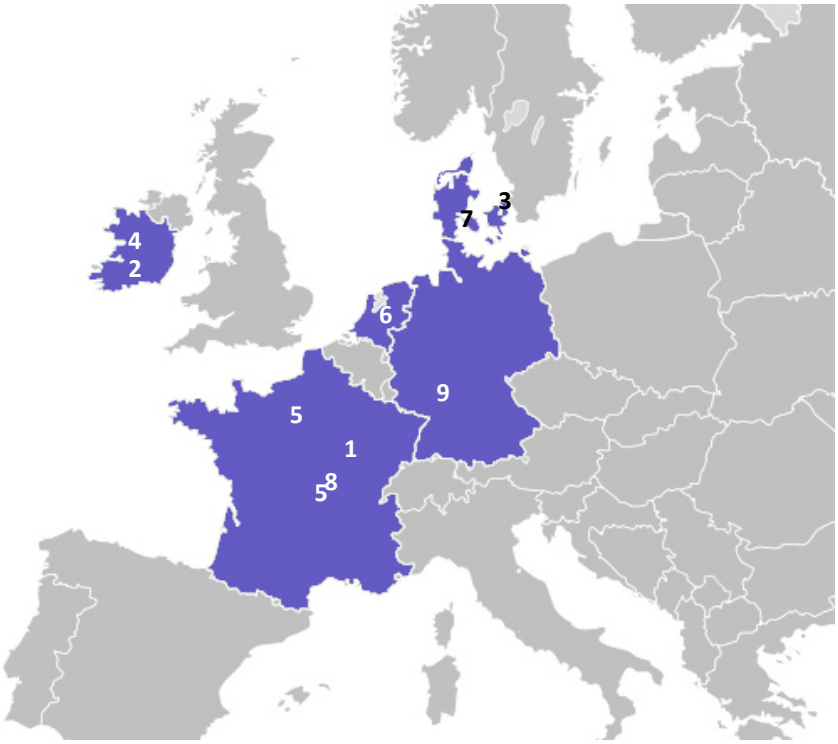
List-MAPS is a European research project funded under the Marie-Skłodowska Curie actions ITN (Innovative Training Network) from the Research and Innovation programme of the European Union Horizon 2020. The project started the 1st of March 2015 and will last 4 years.

List_MAPS focuses on the bacterium *Listeria monocytogenes* with the overall objective to understand how the conditions of the environment affect the capacity of *L. monocytogenes* to generate infection.

The project is coordinated by the Université de Bourgogne in Dijon (France) and associates 9 beneficiaries' partners and 2 associated partners situated in 5 European countries. In addition, the network is composed by 11 ESRs (Early-Stage Researchers) recruited for 24 to 36 months.

Each ESR has a specific and individual project on the subject that is connected to the others. In that way they work, through cooperation, together and contribute to the overall research programme. Through the network's events and meetings, the international events and the secondments, List_MAPS provides a world-class training to help the ESRs to be the next generation of creative, entrepreneurial and innovative researchers.

PARTNERS AND EARLY-STAGE RESEARCHERS



1

University of Burgundy (UB)
Dijon, France-UMR Agroécologie
Dr. Pascal Piveteau, Coordinator
ESR1 : Angela Rocio Ortiz Camargo / ESR8 : Catarina Moreira Marinho

2

University College Cork (UCC)
Cork, Ireland-School of Microbiology
Dr. Cormac Gahan,
ESR2 : Vanessa Las Heras

3

University of Copenhagen (UCPH)
Copenhagen, Denmark-Biology of human food relevant pathogens
Dr. Hanne Ingmer,
ESR3 : Miguel Villoria Recio

4

National University of Ireland-Galway (NUIG)
Galway, Ireland-Bacterial Stress Response Group
Dr.Conor O'Byrne,
ESR4 : Amber Dorey / ESR8 : Catarina Moreira Marinho

5

French National Institute for Agricultural Research (INRA)
Saint-Genès-Champanelle, France- Microbiologie
Dr. Michel Hébraud,
ESR5: Tiago Santos
Jouy-en-Josas, France- MaIAGE
Dr. Vincent Fromion,
ESR9: Ibrahim Sultan

6

Wageningen University (WUR)
Wageningen, The Netherlands-Laboratory of food microbiology
Dr. Tjakko Abee,
ESR6: Natalia Crespo Tapia

7

University of Southern Denmark (SDU)
Odense, Denmark-Department of Biochemistry and molecular biology
Dr. Birgitte Kallipolitis,
ESR7: Patrícia Dos Santos

8

BioFilm Control (BFC)
Saint-Beauzire, France
Dr. Thierry Bernardi,
ESR11: Bohyung Lee

9

GenXPro (GXP)
Frankfurt, Germany
Dr. Björn Rotter,
ESR10: Ignasi Ferrer Lluis / ESR11: Bohyung Lee

In addition to the partners' beneficiaries, two partners are associated to the project:

THE RECRUITMENT PROCESS

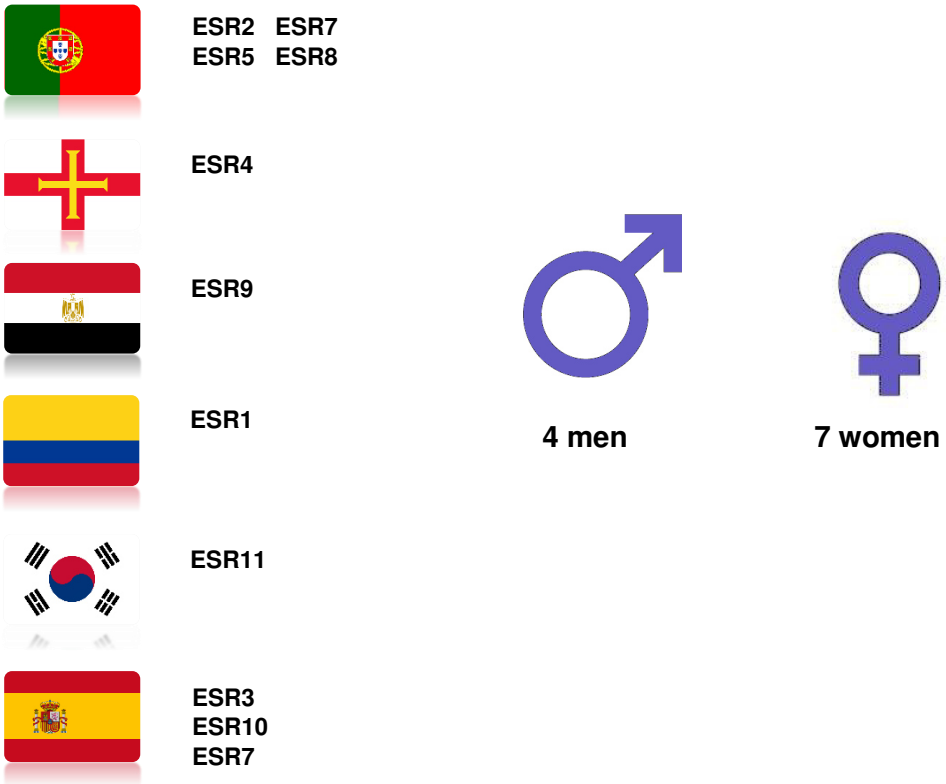
In summer 2015 List_MAPS started the recruitment process to fill the 11 positions available.

Almost 600 applications from 77 European and international countries were received.

The European criteria were:

- Researchers may be of any nationality.
- Candidates shall at the time of recruitment by the host organization, be in the first four years (full-time equivalent research experience) of their research careers.
- Candidates must not have a doctoral degree.
- Mobility rules: candidates shall not have resided or carried out their main activity (work, studies) in the country of their host organization for more than 12 months in the 3 years immediately prior their recruitment.

Recruited ESR are from 2 EU countries (Spain and Portugal) and from 4 international countries (Colombia, Egypt, Guernsey and South Korea).



OBJECTIVES AND IMPLEMENTATION

The overall objective of List_MAPS is to tackle food safety through the combination of high throughput Epigenetics, Deep sequencing of transcripts, Proteomics, Bioinformatics, Mathematics and Microbiology to decipher the transcriptional regulatory circuitry that drives adaptation and virulence of *L. monocytogenes* from farm to fork. List_MAPS focuses on these major objectives:

- Understand how environmental conditions in soil, plants, biofilms and food matrices influence the capacity of *L. monocytogenes* to cause infection.
- Develop an integrated model of the regulatory circuitry of the pathogenic bacterium in order to refine our knowledge of the environmentally-dependent gene modules that underpin its ubiquitous nature and its capacity to generate infection.
- Assess intraspecific diversity of virulence potential and biofilm in relation to environmental cues.
- Develop a cost efficient, rapid semiconductor sequencing application designed to assess the virulence potential of large numbers of isolates, sparing the cost, burden and ethical issues related to animal models.

These objectives allow to understand how the conditions of the environment affect the capacity of *L. monocytogenes* to generate infection.

List_MAPS is implemented in 7 Work packages, which 4 are dedicated to the research objectives and 3 to the training, management and communication:

WP1 : Data collection and integration in the specific environments

WP2 : Linking environmental cues and expression of virulence

WP3 : Tools for evaluation of intra-specific phenotypic diversity

WP4 : Systems biology approach

WP5 : Training

WP6 : Management

WP7 : Communication, dissemination and public engagement

INDIVIDUAL PROJECTS

Investigation of the adaptative strategies of *L. monocytogenes* in soil/plants mesocoms
ESR1: Angela Rocio Ortiz Carmago
Institution: University of Burgundy

Stress pre-adaptation and virulence potential of *L. monocytogenes* in the food matrix
ESR2: Vanessa Las Heras
Institution: University College Cork

Regulation of the virulon of *L. monocytogenes* by carbohydrates
ESR3: Miguel Villoria Recio
Institution: University of Copenhagen

Role of σB regulon of *L. monocytogenes* in environmental stress resistance
ESR4: Amber Dorey
Institution: National University of Ireland, Galway

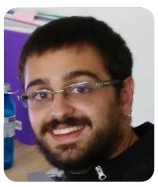
Role of protein secretion in adaptation of *L. monocytogenes*
ESR5: Tiago Santos
Institution: French National Institute for Agricultural Research

Biodiversity and transmission of *L. monocytogenes* in the food chain
ESR6: Natalia Crespo Tapia
Institution: Wageningen University

Role of non-coding sRNAs in the transmission of *L. monocytogenes* between environments
ESR7: Patricia Dos Santos
Institution: University of Southern Denmark

Investigation of interconnections between AgrA and σB regulons
ESR8: Catarina Moreira Marinho
Institution: University of Burgundy/National University of Ireland Galway

Transcription regulatory network construction
ESR9: Ibrahim Sultan
Institution: French National Institute for Agricultural Research



Development of bioinformatics tools for the analysis of MACE data
ESR10: Ignasi Ferrer Lluis
Institution: GenXPro

Development of innovative tools for rapid phenotypic characterization of intraspecific diversity
ESR11: Bohyung Lee
Institution: BioFilm Control/GenXPro

Thermo Fisher SCIENTIFIC

The world leader in serving science

Presentation of the company

Thermo Fisher Scientific Inc. is the world leader in serving science, with revenues of $17 billion and approximately 50,000 employees in 50 countries. Our mission is to enable our customers to make the world healthier, cleaner and safer. We help our customers accelerate life sciences research, solve complex analytical challenges, improve patient diagnostics and increase laboratory productivity. Through our premier brands – Thermo Scientific, Applied Biosystems, Invitrogen, Fisher Scientific and Unity Lab Services – we offer an unmatched combination of innovative technologies, purchasing convenience and comprehensive support. With the Ion Torrent semiconductor sequencing technology we allow for fast and inexpensive sequencing of genomics and transcriptomics material from any type of organism. The Market Development group is responsible for identifying new applications, empowering users and working with consortia.

Why the company participates to List_MAPS?

More than instruments, we at Thermo Fisher Scientific provide our customers with solutions to be successful in their research and daily work.
Our massively parallel semiconductor sequencing technology Ion Torrent demonstrated its power in the microbial area, and in particular its pathogenic aspect, when we participated in front row to the sequencing of the 2011 German *Escherichia coli* O104:H4 outbreak strain: speed and data quality really mattered and we were able to develop a detection assay within one week only, a real game changer!
In the meantime our Invitrogen Ambion expertise is unanimously recognized worldwide when it comes to isolation, detection, analysis and discovery of RNA from various sample types and organisms.
Finally, we are always keen on participating to consortia: it allows us to share our knowledge but also to learn from the participants and thus improve even more the quality of service we offer to our customers.
So with RNA, sequencing and a consortium, enrolment in List_MAPS was an obvious decision. On top of the scientific aspect, already very interesting when food production is under stress, the training of researchers is something most of us would have beneficiated during our studies and we are glad to participate to this adventure.

Alain Rico, Global market development manager[1]

Website: https://www.thermofisher.com/fr/fr/home.html

[1] See the page of the company and the presentation of Alain Rico on the website of List_MAPS : http://blog.u-bourgogne.fr/list-maps/consortium/partners-organizations/thermofischer-scientific/

KICK-OFF MEETING

Tuesday afternoon, presentation of ESR4 Amber

Tuesday afternoon, presentation of ESR6 Natalia

From the 13th to the 14th of October 2015, the Kick-off meeting of List_MAPS was organized at the coordinator's institution in Dijon, France. It was the first meeting of the project and an opportunity for all the participants (partners and ESRs) to meet each other and better understand the project.

During the morning of the first day an overall presentation of the project was given by the coordinator and the project manager to explain the guidelines of List_MAPS. On the afternoon the ESRs presented their project at this first stage with a presentation of their background.

It was an essential moment to discuss the next steps, share ideas and be ready to officially start the project!

Tuesday evening, restaurant at "La Dame d'Aquitaine" in Dijon

OUTREACH WORKSHOP


Thursday afternoon, main hall of the school Charles de Gaulle

After the Kick-off meeting, the first workshop for ESRs was held. On Wednesday 14th afternoon they received their first training in outreach communication provided by the department "Experimentarium" of the Université de Bourgogne. The aim of this training was to prepare them to talk about their project to pupils for the next day. Thus they went on Thursday to the international school « lycée Charles de Gaulle » in Dijon to meet around 60 pupils and put their training in practice. Each ESR met several groups of five pupils during a limited time length of 10 minutes for a "speed-searching" to explain their research project. It was the first time for most of the ESRs to explain a scientific project to a non-specialized public. They acquired during this workshop specific skills in communication:

- To know how to present themselves and their background,
- To choose a right support which would be efficient to illustrate their project,
- To use simplified sentences to speak about their project and be understood,
- To exchange and discuss with pupils about research, how to be a researcher and how the research is financed.

Pictures chosen by the ESRs to explain their projects

The workshop was successful and a great experience for all ESRs as they explain it:

ESR2 "(...) the students were very interested in our background, what did we studied and where. I really like the attention they were giving to what we were saying (...)."

ESR5 "(...) I learnt how to talk about my work in a simpler way and to better interact with a group of people outside my field of work (...)."

ESR8 "I found it very challenging to explain it by a non-scientific point of view, using understandable terms to the general public."

ESR4 "(...) I found it a very good tool for focusing my project. (...) It made me think very clearly about what my project was about and the methods I would be using to conduct it."

ESR3 "Inspiring other people at earlier stages of their studies or encourage them to feel curious about the science behind infection is very rewarding."

ESR9 "My overall evaluation of the workshop is definitely positive. (...) I liked the activity and I am looking forward for the next workshop".

ESR7 "I never imagined that it would be possible to explain my project to them and make them understand it."

ESR1 "I loved the idea of bringing science to non-scientists, translate our ideas and our project in simple words to make others interested and enchant the wonders of science".

ESR11 "(...) I became more confident in what I am doing. (...)I think some kind of mentee-mentor program for high school students that link PhD students can be beneficial for both parts."

ESR6 "(...) everything went alright, and the kids seemed really interested in the topic. They asked many questions, some of which were actually quite hard to answer!"

ESR10 "(...) it was really rewarding the idea of feeling I might be a motivation for some of the young students to carry on their studies in a close field to what I have studied and I am currently working on."

ESR2 Vanessa Las Heras

How do you adapt to Cork in Ireland?

Adapt to Cork was surprisingly easy. It's a beautiful dynamic town, with a lot of events during the year. Everybody is very welcoming and eager to share their culture. Cork is known to be the capital of food in Ireland and I have the pleasure to leave very close to the street with the best restaurants in town. Furthermore Cork is also the city of jazz, so I found unbelievable the amount of great musicians in the city, playing everywhere. Cork is quite a small city, meaning that I can walk everywhere, which is very convenient. One of the best things in Cork is the river Lee, a beautiful river that I have the pleasure to walk by every day before and after work. My group in the lab is very social to, which made it easier to make new friends and be integrated. Overall, I am really enjoying my time in Cork.

What activities do you enjoy outside the laboratory?

In Cork, very close to the university, there is a health and leisure center called Mardyke, where you have multiple sports and fitness classes available for free. I love to go there before work every day so I can start the day full of energy. Every Friday I like to relax from the stressful week and join my friends for some food and live music after work. In Cork you can easily find a good pub with excellent food and even better music. As my colleague Catarina mentioned, every Portuguese loves their food and I am not an exception. My Saturday morning is dedicated to food shopping in the English Market. The English Market is located in the city center and has a very diverse offer of very fresh products. There you can find the best local products side by side with a broad selection of international products.

What do you find the most challenging in your work so far?

In my project I am investigating, in an *in vivo* model, how the virulence of *Listeria* is affected by its adaptation to the different environments and the presence of other microorganisms inside the gastrointestinal tract. In order to do this I am administrating different diets to the host and see how these diets are affecting the microbiota and the expression of the virulence factors of *Listeria monocytogenes*. The most challenging part of my project so far has been planning the animal trials. Nothing can fail when you work with animals and for this reason it requires a lot of planning and organization skills. Furthermore animal trials originate a lot of data, not only associated with *Listeria* but also with the host and with the microbiota. It is very challenging to interpret, correlate and organize this data.

You will have your first secondment in a few months in GenXPro in Germany, how do you feel about that? Can you explain, how this secondment will help your work?

To be honest I feel a bit nervous because it will be a new working environment for me, however I think I will easily adapt. During this secondment I will have the opportunity to develop my skills in techniques that are new to me, next generation sequencing and transcriptomics. These two techniques are crucial for my project since part of it is to analyze variations in microbiota (through 16S sequencing) and expression stress adaptation and virulence genes in *Listeria* (through transcriptomics). Without this secondment I would not have the opportunity to learn this techniques and apply them to my one samples, since the common practice is to send these samples to private companies that will do the analysis for you.

ESR8 Catarina Moreira Marinho

You have been in Dijon, France, for a few months now, do you feel more comfortable?

I arrived in Dijon 5 months from now and ever since I've been feeling more and more comfortable in here. Dijon is a small city (152.071 habitants) when compared with other French cities, but it is so lovely as well organized. The fact that amazed me the most was that all museums have free entry every day! At first I have to confess that not knowing enough of the French language was a little bit troubling, but sooner I started having French classes at the University of Burgundy and every weekend I can I'm traveling to other French cities by carpooling, which allows me not only to improve the vocabulary but also to meet new people while I'm travelling, something that I really enjoy.

Do you find some time for your hobbies?

If there is something that I really enjoy doing is cooking, specially baking cakes and make deserts. I usually bake during week-ends and for me it has two positive sides, first of all it allows me to relax and afterwards I can share a piece of cake and a glass of Port wine with my friends! All Fridays after work at INRA we have an event called "beer time" where all PhDs, post-docs and other employees are invited to hangout while having a beer. I found these meetings very amusing so I can get to know my peers and have some fun time with them. I also enjoy readying good novels or watching American tv series. In fact, I think that I'm addicted to it, although I find it helpful to relax from my daily routine.

Could you describe your first steps in List_MAPS?

I started my experiments on the lab by constructing a collection of mutant strains that will be the object of study on my project, and accessed their phenotype under some stress conditions. The research team at INRA-Dijon made me feel very comfortable on the lab, allowing me to conduct my experiments independently, even though they are always available in case I have any doubt. Therefore, I had to put on practice some of my knowledge regarding bacterial transformation acquired during my Bachelor and Master degrees in Molecular Genetics, something that I found very challenging and afterwards rewarding to contemplate the results. Since I'm in a joint supervised position, I have regular skype meetings with both my supervisors in order to discuss my results and delineate the next steps according to their guidance. The fact that List_MAPS is such an ambitious project it promotes the cooperation among different areas of research in *Listeria monocytogenes*; thus, it was possible for me to initiate an *in silico* analysis hypothesizing the role of sRNAs mediating the interconnection of the two regulons I'm studying, as a collaboration with Dr. Birgitte Kallipolitis and my colleague ESR Patricia dos Santos. This is a promising study that I'll conduct during my first secondment on University of Southern Denmark at the end of this year.

In the next year, you will continue your Ph.D in Galway, Ireland. Can you explain why you are in a joint supervision?

My Ph.D project is a joint supervision between University of Burgundy / UMR1347 INRA, Dijon (France) and the Bacteria Stress Response Group of the National University of Ireland, Galway (Ireland) with two supervisors, one per institution. While the first team has a large experience on studying agr regulon on *L. monocytogenes*, accessing its involvement on bacterial adaptation to environmental conditions; the second has an extended knowledge regarding σ^B regulon in response to stress conditions. The main aim of my PhD project is to explore the connection of those two regulons on *L. monocytogenes*, knowing that its interconnection have already been suggested in other bacteria. Therefore, a joint supervision makes all sense in this case, allowing a connection link between those two teams in terms of sharing their expertise in order to archive a major answer to a mutual question.

DELIVERABLES AND MILESTONES

All the expected deliverables were submitted on Participant Portal and the milestones were done. The EC services made a change with the ethics requirements. Initially we had one deliverable about ethics (D6.5) and beside were ethics requirements. Now the ethics requirements are not a separate table but have been converted into ethics deliverables. In the grant agreement of the project we have thus 8 work packages (WP1: Data collection and integration in the specific environments; WP2: Linking environmental cues and expression of virulence; WP3: Tools for evaluation of intra-specific phenotypic diversity; WP4: Systems biology approach; WP5: Training; WP6: Management; WP7: Communication and public engagement; WP8: Ethics).

List of the submitted deliverables:
D6.4: Supervisory board
D6.5: Ethics
D8.1.2.3.4.5.6.7.8.9: Ethics requirements
D5.2: Network-wide events year 1
D1.1: Database structured
D6.1: Progress Report

List of the achieved milestones:
M1: Recruitment completed
M2: Network-wide events year 1 organized
M3: Transcriptome database structured

OPEN ACADEMIC ENVIRONMENT (OAE)

The collaborative platform OAE is in progress. The coordinator had three meetings (05.11.2015; 29.02.2016; 08.04.2016) with the department of the Université de Bourgogne in charge of the creation of the platform. The platform will be available and open for the beginning of the second academic year.

COMMUNICATION

The website of the project is available online: http://blog.u-bourgogne.fr/list-maps You will find there detailed information about List_MAPS: objectives, partners, ESRs, events.

List_MAPS opened social networks accounts (Facebook, Twitter, Google +, LinkedIn). You can find there the latest news of the project and news on the subject. These tools are made to interact, share and discuss between the members of the network and with the general public.

https://www.linkedin.com/company/list_maps-itn

https://plus.google.com/109296663228314816120/posts

https://twitter.com/List_MAPS

https://fr-fr.facebook.com/ListMAPS

In addition to these tools, List_MAPS will use a leaflet, a press book and this newsletter which will be biannual. All these tools will be available on the website.

WHAT'S NEXT ?

EVENTS AND MEETINGS

4th of May: Supervisory Board meeting

14-17 June: ISOPOL XIX

4-6 July: Summer School 1

10-14 October: Scientific workshop and annual meeting

SECONDMENTS

ESR9: Ibrahim in GenXPro

ESR2: Vanessa in GenXPro

ESR1: Angela in INRA unit Microbiologie

ESR3: Miguel in UCC

ESR10: Ignasi in INRA unit MaIAGE

ESR7: Patricia in NUIG

ESR8: Catarina in SDU

DELIVERABLES AND MILESTONES

D2.1: Effect food characteristics upon virulence (leader: UCC)

D4.1: First model regulatory network (leader: INRA)

M4: Network-wide events year 2 organized (leader: UB)

M5: release of the 1st draft of regulatory circuitry model (leader: INRA)

List_MAPS Consortium

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Website: http://blog.u-bourgogne.fr/list-maps

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