Center for Infection & Immunity of Lille

CIIL

NEWSLETTER

#5 | December 2021

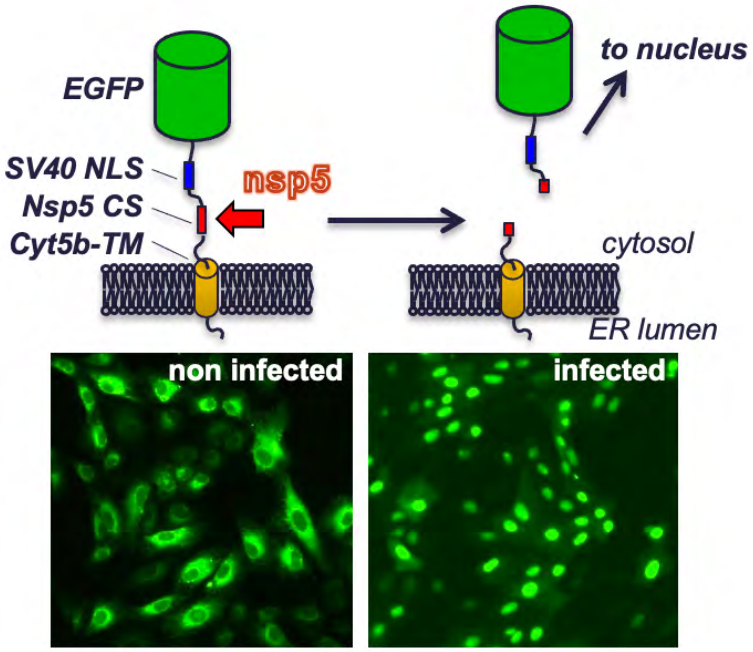
Between the first lockdown and the end of the summer break 2021, major events of the CIIL were cancelled, postponed or organized by videoconference due to the COVID-19 pandemic. We were therefore very excited to meet again during the annual retreat of the CIIL that was organized the 28th of September. On this occasion, in addition to scientific exchanges, Layal Massara presented her project for the creation of the CIIL Junior Research Association. I would like to take the opportunity of this message to thank the members of the team in charge of the CIIL animation for the organization of this event as well as for their involvement in the organization of the weekly seminars of the CIIL. In October, several members of our Center also volunteered to participate at the Science Week. In November, we had also the opportunity to celebrate the 100th anniversary of the first administration of the BCG vaccine in the context of an international symposium organized by Camille Locht. The last issue of the CIIL Newsletter summarizes these major events and focuses on some scientific developments, including the presentation of the team PYP dedicated to the study of plague and the involvement of the team MCV in the creation of a new national platform dedicated to the screening of antivirals.

Jean Dubuisson

The CIIL is involved in the ViroCrib program

The current health crisis has revealed our lack of preparedness to rapidly react to new infectious threats of pandemic potential. To be better prepared for future emerging or re-emerging pathogenic viruses that could lead to global health crises, the Institute of Biological Science (INSB) of the CNRS has created ViroCrib a shared infrastructure for the screening of antiviral molecules. Supported by the French Ministry of Higher Education and Research, ViroCrib brings together a consortium of virologists, research teams and screening technology platforms. The Molecular and Cellular Virology (MCV) team of the CIIL is the coordinator and one of the founding teams of this consortium together with VirPath team from CIRI in Lyon, the Cemipai in Montpellier and the Institute of Regenerative Medicine and Biotherapy of Montpellier. ViroCrib will focus on respiratory viruses which are recurrent global threats and will expand its expertise and models by integrating other research teams and technological platforms. This infrastructure could be rapidly mobilized at any time to fight new viruses, even in case of emergency. This will be possible with the help of the tools developed by this consortium which could rapidly be exploited even during crisis periods.

https://www.insb.cnrs.fr/fr/cnrsinfo/virocrib-une-infrastructure-partagee-de-criblage-de-molecules-antivirales



® *Image from Yves ROUILLÉ, Molecular & Cellular Virology Team*

Plague & Yersinia pestis

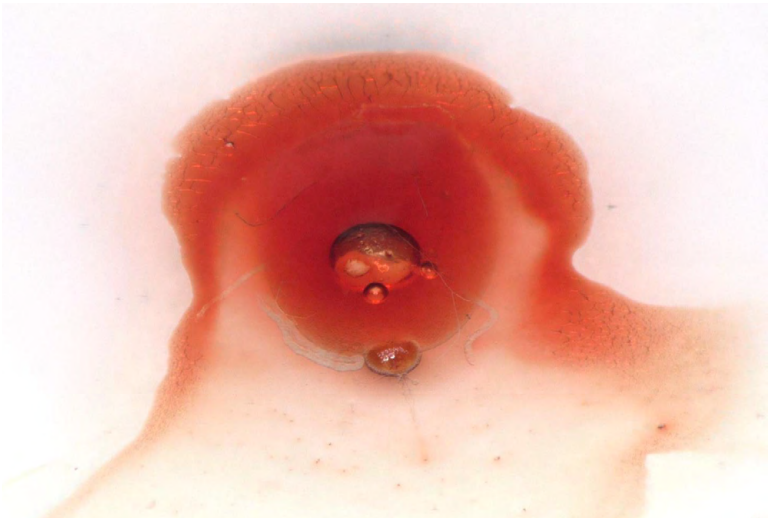
No other disease has so deeply shaped our civilizations as Plague. Even today, during the Covid-19 pandemic, is it not the book The Plague by Albert Camus that has become the symbolic novel of this very special period? If in Europe, this disease is considered eradicated, it has never disappeared on other continents. It is still endemic in many parts of the world: from Madagascar to the United States through China and, it is more than 3,000 cases that have been reported in the world between 2013 and 2018. The disease has also reemerged in North Africa after several decades of absence (Algeria in 2003, 2008 and Libya in 2009) and in Central Asia (Kyrgyzstan in 2013). The World Health Organization has classified plague as a re-emerging disease and emphasizes the impact of climate change, migration flows, trade and the risk of terrorism on the re-emergence of plague.

In 1894, Alexandre Yersin isolated the plague bacillus, which was named Yersinia pestis in honor of his discoverer. *Y. pestis* circulates naturally within rodent populations and their fleas. In humans, the disease has three major forms: bubonic, septicemic and pulmonary. All of them result directly and/or indirectly from a deposit of bacteria in the skin following an infected flea bite. The pulmonary form can also be contracted through inhalation of contaminated aerosols. In the absence of early antibiotic treatment, the septicemic and pulmonary forms are fatal in nearly 100% of cases, while the bubonic form results in death in 40 to 60% of cases. Since 1995, strains of *Y. pestis* multi-resistant to the antibiotics used to treat the disease have been isolated in Mongolia and Madagascar. These findings highlight the possibility of a plague impossible to cure with existing drugs. It is therefore urgent to better understand the infectious cycle, in order to be able to counter plague with new strategies.

As the only laboratory in Europe and one of the few in the world that can study the entire plague infection cycle, our research covers the different facets of the disease: from its emergence to the molecular aspects of the infection in rodents and fleas, including the study of new antibacterials. Since 2020, we are also one of the four teams of the International Pasteur Unit «Plague Evolution and Dispersion» with the Pasteur Institute in Paris (Dr Javier Pizarro-Cerda) and the Pasteur Institute of Madagascar (Dr Minorarisoa Rajerison and Dr Mireille Harimalala).

Recently, in two articles published respectively in PLoS Pathogens and The ISME journal, we have refined the model of transmission of the plague bacillus by fleas and identified possible targets for disease control.

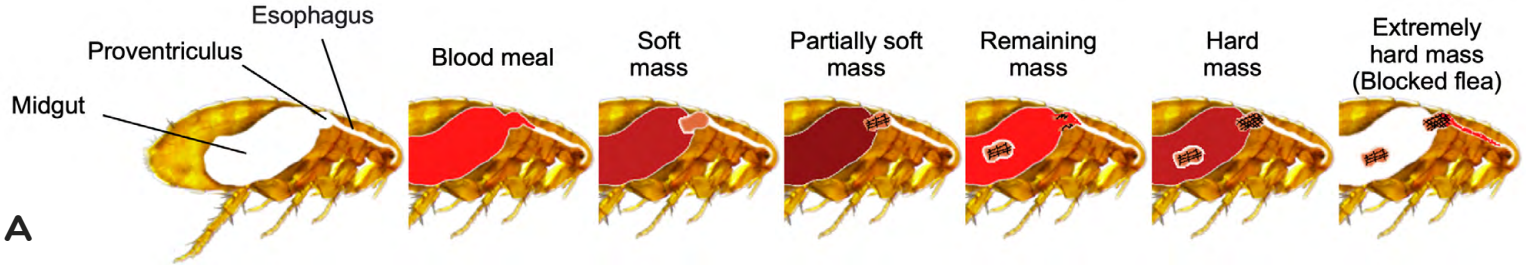
Following a blood meal on an infected mammal, the flea ingests *Y. pestis*. During ingestion, the bacteria pass through the esophagus and proventriculus - a valve that opens periodically to allow blood to pass through and prevent *regurgi*tation at the point of suction - before reaching the midgut. Y. pestis establishes itself and remains confined in the insect's digestive tract. Within the first few hours after infection, many bacteria become trapped in the proventriculus in a soft, toxic mass in which *Y. pestis* replicates and



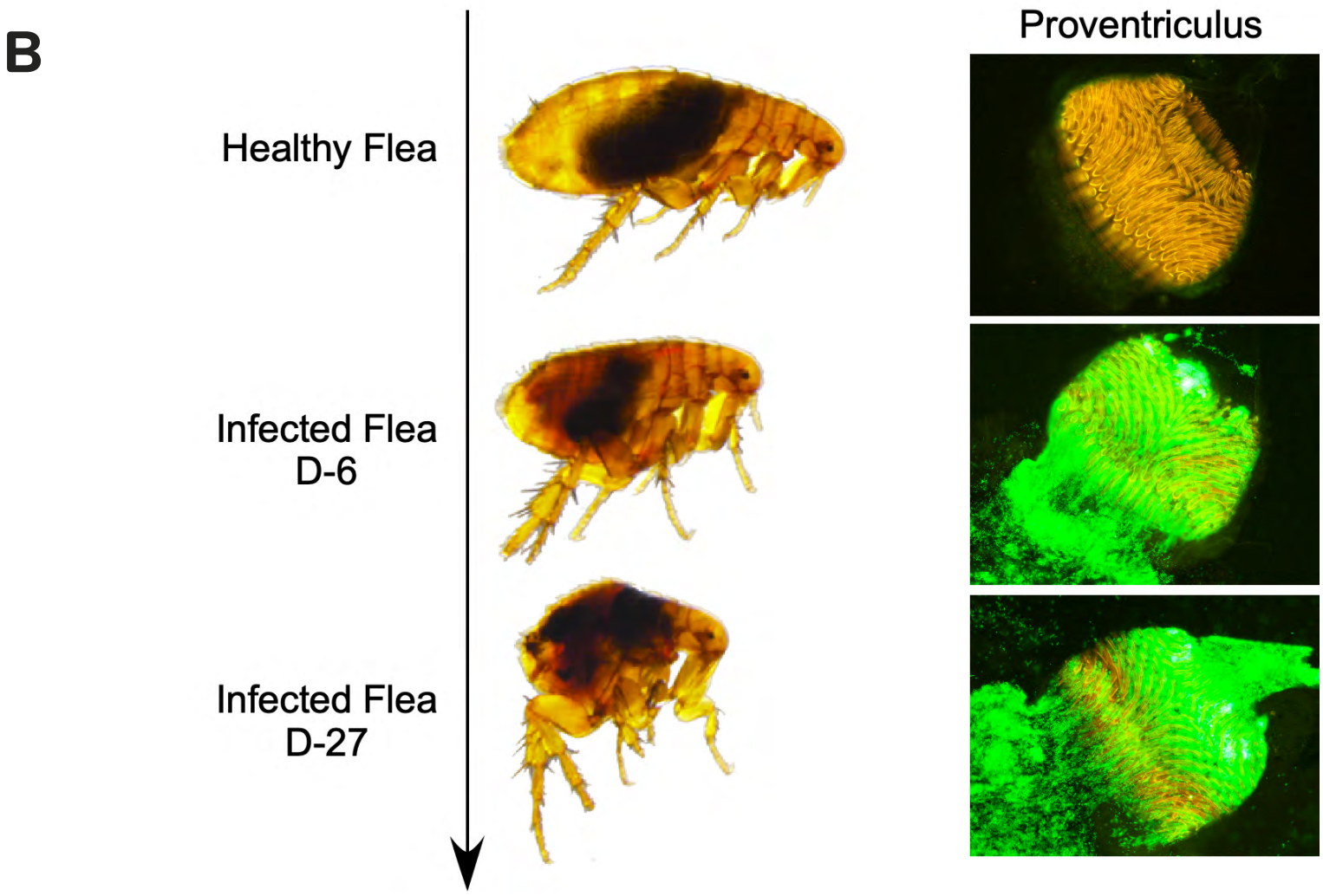
consolidates via the production of a sugar polymer (of N-acetyl-glucosamine). This consolidation completely obstructs the digestive tract of the insect so that the latter can ingest blood only up to the bacterial plug and not in its midgut. The insect then becomes hungry and bites its host relentlessly. It is during these multiple unsuccessful attempts to take blood that bacteria are detached from the bacterial plug and regurgitated with the blood freshly sucked at the point of bite.

The blockage of the insect's digestive tract is a crucial element in the transmission of plague. The initial working model assumed that the blockage was due to bacteria from the midgut. Our work demonstrated that the blockage would result *from* the primary infection of the proventriculus. In other words, *Y. pestis* colonizes the proventriculus and the midgut at the same time. The bacteria present in the proventriculus would trigger an immune reaction and would be trapped in a bactericidal mass. During the different meals, this mass is partially dislodged and reconstituted thanks to the bacteria still present. During these cycles of destruction-reconstruction of this mass, the bacteria would consolidate it via the synthesis of a carbohydrate polymer, forming a biofilm and thus a solid plug resistant to the incoming blood flow.

More information is needed in this model of flea colonization by



Y. pestis. The bacterium, in order to successfully establish a transmissible infection, must find the nutrients necessary for its proliferation in the arthropod's digestive tract while simultaneously resisting the immune system's attacks or the toxic compounds generated by the digestion of blood. Of the more than 4,500 genes in the plague bacillus genome, only ten have been associated with the above mechanisms. Our two studies added fourteen genes to this list. For example, rpiA and rpe are involved in bactericidal mass consolidation. Or the three genes in the lipoate biosynthetic pathway (lipA, lipB) and lipoate salvage pathway (lplA) increase the rate of transmission of *Y. pestis* by fleas.
Developing new strategies for plague control requires intense and painstaking basic research to understand the molecular mechanisms that allow the spread of the plague bacillus by fleas. The discovery and characterization of these genes is therefore a decisive first step towards this ultimate goal.

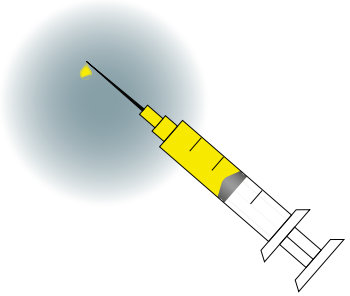


Colonization of the rat flea Xenopsylla cheopis by Y. pestis. In A, physical model of the process leading to flea blockage by Y. pestis. In B, evolution of the disease in the flea and colonization of the proventriculus (orange) by the bacterium (green). A. Dewitte et al., PLoS Pathogens, 2020.

Team:
Plague & Yersinia pestis
Florent SEBBANE

100 years of the anti-tuberculosis vaccine BCG

100th anniversary
of the first administration
of the BCG



July 1st, 1921 was the day of the first administration of the anti-tuberculosis vaccine BCG (for Bacille Calmette-Guérin) to a human being. A newborn baby born in a family plagued with tuberculosis was given the vaccine orally and did not develop the disease. Subsequent large-scale clinical trials have shown more than 90% vaccine efficacy against tuberculosis-caused mortality in newborns. The vaccine was then distributed to all corners of the earth. It is today the most widely used vaccine in the world and the oldest vaccine still in use.

As the vaccine was developed at the Institut Pasteur de Lille by its first Director General Albert Calmette, together with his co-worker Camille Guérin, the Center for Infection and Immunity of Lille, together with the Institut Pasteur de Lille have decided to celebrate this important event by organizing an international symposium, held from November 17 to 19, 2021. This symposium gathered close to 200 participants from all five continents, 2/3 of which participated on-line.

Although 100 years old, the BCG has still numerous secrets to be uncovered. Initially designed as a vaccine against tuberculosis, it has become quickly evident that the vaccine may have interesting non-specific effects. Soon after its implementation, all-cause childhood mortality was found to be strongly reduced in vaccinated compared to unvaccinated children, and this could not be accounted for only by the protective effect against tuberculosis. It has been shown that the BCG protective effect extends to sepsis and respiratory infections unrelated to mycobacteria, potentially including COVID-19, and improves immune responses to other vaccines. In the 1980s it became also clear that BCG treatment of non muscle-invasive bladder cancer strongly reduced the probability of relapse. More recently, a protective effect of BCG has also been reported against auto-immune disease, such as multiple sclerosis and type 1 diabetes, as well as against inflammatory disease, including allergies and even Alzheimer's disease. These non-specific effects are most likely related to training of innate immunity triggered by BCG.

Yet, BCG is not perfect, and efforts are under way to improve BCG, either by genetically modifying the organism, or by creating new versions of BCG, based on targeted genetic attenuation of the human tubercle bacillus. Genetic modifications of the current BCG strains may also potentially improve their non-specific effects. Alternative routes of BCG vaccination are also being explored, as are various BCG re-vaccination strategies.

These and additional subjects have been discussed during the symposium by the international experts in their respective fields, and the symposium was concluded by a most enlightening lecture delivered by Prof. Stanley Plotkin, putting the BCG vaccine in the perspective of the future of vaccinology. While much progress has been made over the decades, we do not have a full understanding yet of the immune mechanisms induced by BCG and it is likely that the full potential of BCG has not yet been completely explored. Therefore, this centenary vaccine continues to draw the attention of scientists and physicians, and it is expected that new and exciting developments on the biology of BCG will continue to emerge in the next decades.

BCG Symposium organizer
Camille LOCHT

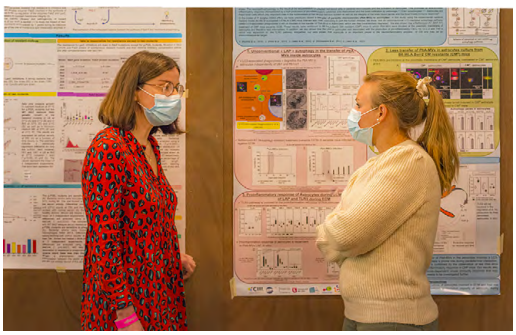
The annual retreat of the CIIL, a much appreciated moment of shared conviviality

On the 28th of September 2021, we were finally able to hold our CIIL off-site day. After a welcome with goodies bearing the CIIL logo, the unit director gave an introduction by presenting the major events of 2021, as well as the newcomers. This was followed by a review of intra-CIIL 2020 projects and a brief overview of the 2021 projects. Doctors C. Andrejak (EA4294-AGIR Université de Picardie / CHU Amiens Picardie) and S. Dhenin (CHU Amiens Picardie) presented the FHU RESPIRE and the possibilities of interactions between the different partners. The morning continued with the presentation of the future association of doctoral and post-doctoral students of the CIIL led by Layal Massara (Team P. Gosset). Finally, Frank Lafont made us aware of the gender equality and climate change with the various eco-campus actions carried out with the Institut Pasteur of Lille. The members of the CIIL were able to show their best smile for the group photo which took place in a good mood thanks to our photographer Sophana Ung. After a meal rich in revelations and conviviality, the students and post-doctoral fellows presented their latest work in the form of posters and were evaluated by a jury composed of their peers. This session was an opportunity for lively discussions and scientific exchanges that were lacking during the pandemic. In the afternoon, we had presentations on the progress of the CIIL COVID Task Force. The animation team had invited Dr. Laurent Dubuquoy from the INFINITE team for the presentation at the end of the day in order to reinforce the link between our two units. To close the day, the three best posters and the winners of the quizzes received prizes. A new event is in preparation and we hope that it will meet your expectations. Thank you again for a great day!

Christine PIERROT, Patricia DE NADAI, Muriel PICHAVANT
CIIL's scientific animators

The speakers

Poster session



The laureates

Vincent GIROD

Marad BALDRY

The president of the jury

Jérôme VICOGNE

CIIL Junior Researcher Association

The CIIL is a large unit gathering 14 Teams working in the field of infection and immunity. The scientific animation of the unit is well coordinated by Muriel Pichavant, Patricia De Nadai and Christine Pierrot. However, interactions between young researchers and PhD students remain to be improved. For this reason, we propose to create an association dedicated to young researcher. After brainstorming with the animation team and with the support of the direction of the CIIL, we are happy to introduce the aim of this future association.

This association will be dedicated to both internal matters and external activities. The internal activities will be focused on improving connection between young researchers. That's why we aim to create links and promote the spirit of the center by proposing some events such as after-works, cultural events, and the portrait of the month. For the external activities we will focus on the creation of an alumni network, popularization events, and finally doctoral school impact.

The first activity will be after-work. Indeed, exchanging opinions will positively impact our communication and create a collaborative spirit. Another way to improve integration is cultural events. Each year, many international students and post-docs join the CIIL. So cultural events aim to promote diversity and facilitate integration of the newcomers.

To share technics and experimental skills across CIIL teams, we propose Meal-tech. It will be an opportunity to enjoy lunch while discovering new technical approaches. This will promote internal collaborations and enhance cohesion and synergy. Finally, we will launch the portrait of the month. This consists in an interview by a young researcher of a senior scientist out of their comfort zone. The objective of this activity is to break the hierarchy and initiate young researchers to ask questions in seminars. Ozmen Cobanoglu has volunteered to launch this activity. In parallel to internal activities, we will perform external activities. First, we will re-establish contact with ex-CIIL students and post-docs, create CIIL ambassadors in order to improve our national and international image, build new collaborations and implement a mentor relationship to help junior alumni to get in touch with senior ones willing to share their experience and expertise. We will also improve CIIL visibility by involving young researchers in vulgarization events. All this work will not be possible without your implication. If you are interested, don't hesitate to send us an e-mail at :

Layal MASSARA

layal.massara@pasteur-lille.fr or by calling 03.20.87.72.08

Sustainable development at CIIL

The influence of the rise in greenhouse gases as a result of human activity is proven and the climate emergency based on the work of scientists is becoming obvious. The reports of intergovernmental agencies, such as the IPCC, based on a rigorous scientific analysis are now imposed on all. The UN, at its summit on September 25, 2015, proposed a 2030 agenda for universal sustainable development adopted by 193 countries and which is based on 17 goals and 169 targets to stop the various forms of poverty and fight against inequality in a context of global change aimed at a more equal society in the face of the climate crisis.

The CNRS has taken up this initiative for its part and has set up «sustainable development referents» in the same way that the University of Lille has its «zero-carbon referents». For the CIIL, Frank Lafont has accepted this mission and has set up a Sustainable Development Committee made up of Cécile-Marie Alouat, Alain Baulard, Céline Boidin-Wichlacz, and Mathieu Gissot. It works in close collaboration with the Eco-Campus of the Pasteur Institute of Lille. It meets every two months. This Committee is open to all, join it!

Since its creation in 2021, several actions have already been carried out within this framework: sorting day and waste collection, mobility for example. In December 2021 and spreading over January 2022, «Climate Fresco» workshops (https://fresqueduclimat.org) will be proposed and a conference is also planned at the beginning of the year. The climate fresco is an action that allows in a playful, creative and collective intelligence way to become familiar with the issues of the climate crisis. In order to better integrate the basics of sustainability (economic, social and environmental) into their current activity in the laboratory, research personnel are advised to take into account the environmental impact of the laboratories. Among the tools developed, there is the greenhouse gas balance, ges1point5, developed by labo1point5 involving more than 2,000 research staff grouped in a Research Group (https://labos1point5.org/ges-1point5). This tool makes it possible to establish the Unit's carbon footprint and to evaluate its evolution, constantly integrating new features. An objective for 2022 and to realize it for the years 2019 and 2020, you will be contacted in this sense by Sébastien Janel and Frank Lafont.

For any proposal in favor of sustainable development in the professional context, do not hesitate to approach the CIIL SD Committee to evaluate how to implement it!

Team:

Cellular Microbiology And Physics Of Infection

Frank LAFONT

The news in brief ...

In the context of internal mobilities of the CNRS, -winter campaign-, two positions are proposed within the CIIL:
- An engineer position is open at the CIIL to work on research programs aimed at discovering new antiviral molecules.
- An Assistant Engineer in financial and accounting management dedicated to the operation of the IBL Building which will be managed by the Center as of January 1, 2022

François MASSOL has been nominated as a member of the « Collège des Sociétés Savantes Académiques de France » and he is an elected member of the Board of the University of Lille.

On October 21, we had a general assembly of the human resources of Inserm employees. On this occasion, Estelle PERU, the new head of human resources department of the Regional Delegation of Inserm came to present her department and its missions and to exchange with Inserm employees of our unit.

On October 21, IBL hosted the DELEG'TOUR, an opportunity to present some of the Centre's scientific activities to the agents of the CNRS Delegation.

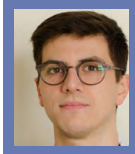
Presentation of the Schistosoma cycle by Jérôme VICOGNE.

Fête de la Science 2021

We welcome our new PhD students :

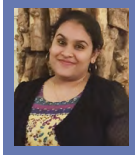
Lola GURGOGLIONE,
Dir. Sabrina MARION
Équipe J. KHALIFE

Oriane RIVIERE,
Dir. Alain BAULARD
Équipe N. MIELCAREK



Kevin SERMET,
Dir. Emmanuel FAURE
Équipe P. GOSSET

Justine PETERS,
Dir. E. M. ALIOUAT
Équipe J. KHALIFE



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Équipe F. LAFONT

Victor MARGELIDON,
Dir. Cécile CHENIVESSE
Équipe A. TSICOPOULOS

Julien LOMBARD,
Dir. François MASSOL
Équipe P. BRODIN

Enjoy
the Christmas break
and see you in January
for a new year full of events.

Many thanks to our contributors :

- Sébastien BONTEMPS-GALLO
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- Patricia De NADAI
- Muriel PICHAVANT
- Frank LAFONT
- Christine PIERROT
- Camille LOCHT
- Florent SEBBANE

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