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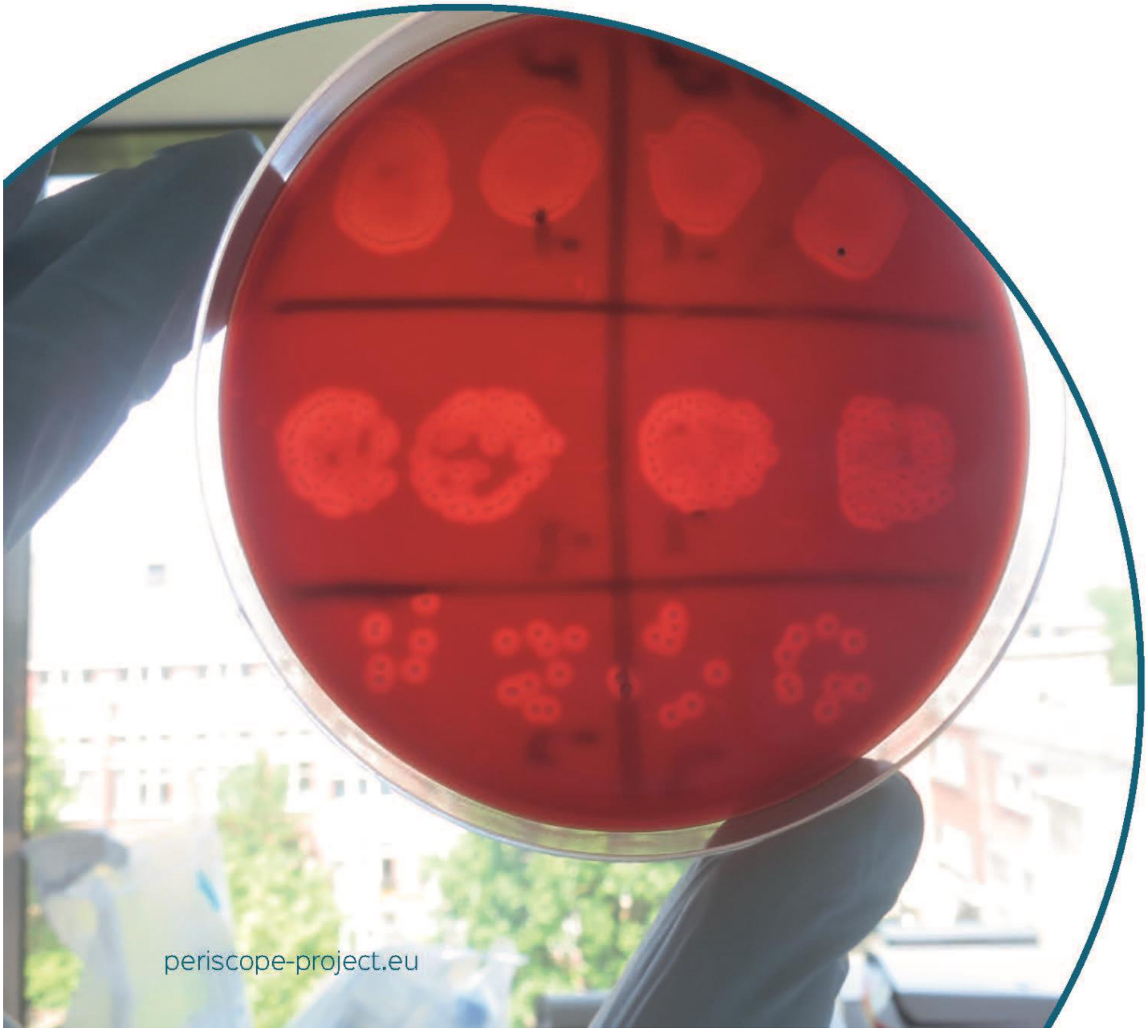
PERtussIS COrrelates of Protection Europe

Newsletter Issue 7 - December 2019



periscope-project.eu

Editorial

Dear colleagues and followers of the PERISCOPE Newsletters,

We are very pleased to present the seventh issue of our e-newsletter of the PERISCOPE consortium. This semi-annual document offers the opportunity to keep you updated on the latest progress of this project.

Any feedback and suggestions to make this PERISCOPE newsletter a unique tool to present our activities are very welcome. Please do not hesitate to also share this newsletter with colleagues and friends who might be interested in this project.

You can subscribe and unsubscribe via the PERISCOPE webpage (www.periscope-project.eu).

We hope that you will enjoy reading our latest news.

Best regards,
Martina Ochs and Nathalie Mielcarek (editors)
The PERISCOPE Communication Team

Facts

The PERISCOPE consortium unites internationally renowned experts in the largest public-private partnership in Pertussis Vaccine Research in Europe. It was launched in March 2016 receiving support from the Innovative Medicines Initiative (IMI), a joint undertaking of the European Commission and the European Federation of Pharmaceutical Industries and Associations (EFPIA). Additionally, PERISCOPE is the first IMI project to receive funding from the Bill & Melinda Gates Foundation (BMGF). The participating experts are combining many years of experience in *Bordetella pertussis* (Bp) research, clinical trials, bioinformatics, immunology and public health.

Acronym:	PERISCOPE
Full title:	PERtussIS COrrelates of Protection Europe
Call Topic:	IMI2-2015-03-05 - Vaccines
Contract N°:	115910
Duration:	60 months (01/03/2016 -28/02/2021)
Funding:	28.000.000 €
Partners:	22
Website:	www.periscope-project.eu

PERISCOPE has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 115910.
This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA and BMGF.

Objectives of the PERISCOPE project

The PERISCOPE consortium was created to facilitate an environment conducive for the development of a new generation of pertussis vaccines by facilitating collaboration between Pertussis stakeholders, particularly from vaccines manufacturing and the academic and public research communities in Europe.

The key objective of the project is to gain a better understanding of the immune mechanisms needed to ensure long lasting immunity to Pertussis in humans. This will be achieved through investigation of the immune response generated by infection and colonization of *Bordetella pertussis* and by comparing the immune response to whole-cell and acellular Pertussis vaccines in humans and preclinical models. To achieve this goal, the consortium aims to develop an extensive tool box of bioassays to apply in vaccination studies in Europe and the Gambia. It is expected that the data generated will ultimately allow the vaccine-R&D community to define an ideal immunological profile or signature that vaccines need to generate to ensure durable protection against Pertussis infection and disease in humans.

What opportunities is PERISCOPE offering to young scientists ?

Education of young scientists in vaccinology, especially targeting pertussis, and in the use of state-of-the-art technological tools to discover biomarkers of protection is an important priority for the PERISCOPE consortium Many trainings (workshops on specific assays, EuroFlow trainings,…) have already and continue to be organized by PERISCOPE members

We asked Magda Berkowska, a young scientist involved in the project from its start, which opportunities the PERISCOPE consortium offered her to develop her expertizes and her network.

"Since 2016, I work in the PERISCOPE consortium in the research team of prof. J.J.M. van Dongen at the Leiden University Medical Center in The Netherlands. As a team, we focus mainly on flow cytometric evaluation of immune cell responses to vaccination and bacterial encounter, and on the molecular characterization of B-cell receptors specific to *B. pertussis.*

The aspect of the PERISCOPE consortium that I enjoy the most is its international character and the opportunity to collaborate with scientists from various backgrounds: from academic researchers to clinical trial leaders and representatives of industry. Having only an academic experience, I see it as a great opportunity to broaden my understanding of scientific development and its implementations. I appreciate the open attitude of senior scientists and their willingness to share experience and provide feedback.

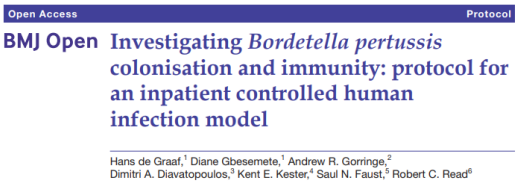
In contrast to several smaller projects in which I have been involved in the past, the duration of the PERISCOPE project gives a great opportunity to explore the topic, develop methodology and draw valid conclusions. It also allows for integration of data generated by different partners which often sheds new light on the obtained results. Despite the high workload at certain times, clear deadlines and necessity of reporting enforce good structure and task organization, which are valuable skills in any profession.

Besides all organizational aspects of the PERISCOPE, I appreciate the opportunity to work on a topic which is socially relevant. I see it as a great application of my previously obtained knowledge of B-cell maturation, reactivity and formation of immunological memory.

PERISCOPE is the first project in which I not only focus on my own research, but also have an opportunity to supervise a PhD student and technicians. Although challenging at first, I see myself grow in time and people management. This is a great school of all soft skills that are so crucial both in and outside of academia. I am sure that this will be beneficial for my future career.

Results of the first-in-human controlled infection with *Bordetella pertussis* published in *Clinical Infectious Diseases*

An important step of the PERISCOPE project has been reached with the development of a protocol for controlled infection with *B. pertussis* in human volunteers which was described in the paper de Graaf *et al.* in 2017.


Open Access Protocol

BMJ Open **Investigating *Bordetella pertussis* colonisation and immunity: protocol for an inpatient controlled human infection model**

Hans de Graaf,[1] Diane Gbesemete,[1] Andrew R. Gorringe,[2] Dimitri A. Diavatopoulos,[3] Kent E. Kester,[4] Saul N. Faust,[5] Robert C. Read[6]

The team now recently published the results of their study entitled "Controlled Human Infection with Bordetella pertussis Induces Asymptomatic, Immunizing Colonization" by Hans de Graaf *et al.* in Clinical Infectious Diseases.

"The work showed for the first time that asymptomatic infection and colonisation of the upper respiratory tract can be induced by nasal inoculation of healthy adults with *Bordetella pertussis*. The volunteers who were colonised produced an immune response in most cases and we learned that nasal washing is the most efficient method to make a microbiological diagnosis." said Rob Read from University of Southampton, UK, and senior scientist in charge of this project (see his portrait in PERISCOPE Newsletter 2).


Clinical Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America hivma hiv medicine association

Controlled Human Infection With *Bordetella pertussis* Induces Asymptomatic, Immunizing Colonization

Hans de Graaf,[1] Muktar Ibrahim,[2] Alison R. Hill,[2] Diane Gbesemete,[1] Andrew T. Vaughan,[2] Andrew Gorringe,[2] Andrew Preston,[4] Annemarie M. Buisman,[5] Saul N. Faust,[1] Kent E. Kester,[4] Guy A. M. Berbers,[5] Dimitri A. Diavatopoulos,[7] and Robert C. Read[1]

"In the study we selected people with low titres of anti-toxin antibodies – in other words people with no evidence of recent infection. All of the participants had received whole cell vaccination in childhood."

"The next step is to repeat this on a larger cohort – this time without selecting people with low antibodies. We hope to find out which immune markers are associated with resistance to colonisation in this model. We will also do the study as an outpatient in order to make it a more practical model."

Portraits

In each newsletter, we portray individual PERISCOPE members. In this seventh issue, opportunity is given to three senior PERISCOPE scientists to introduce themselves and present their views on the project.

Jussi Mertsola, University of Turku (UTU), Finland

Why do we need PERISCOPE?

"We need PERISCOPE to have a concerted effort, providing independent expertise and many levels of observation, to better understand immunity against *B. pertussis* and how we can improve it."

What is your expertise and role in the consortium?

"My expertise is the analysis of 'omics types of data and obtaining of biological insight from such high dimensional data. Within the PERISCOPE consortium, in addition to the analysis of 'omics data, I am involved in maintaining the database with all the molecular data and I am responsible for the biobank."

What aspect will you enjoy most working with this consortium?

"The aspect I enjoy most in this consortium is to cross the gap between molecular data and clinically relevant outcomes. The interactions with the scientists that challenge my own ideas and teach me the many layers of complexity of the immune system in general and vaccinology in particular. "

Françoise Mascart, Université Libre de Bruxelles (ULB), Belgique

Why do we need PERISCOPE?

"PERISCOPE is a unique opportunity to share experience with European scientists and medical doctors who want to find a solution to the actual resurgence of *Bordetella pertussis* infections. This consortium is necessary to put together experts from different fields, not only microbiologists and immunologists but also epidemiologists, pediatricians, statisticians…. All these experts apply their knowledge to *B. pertussis* infections allowing the whole group to develop a real translational approach of the research. Active participation of medical doctor who have access to large cohorts of subjects who may be included in different vaccination studies is also a clear added value of the consortium and this should enable us to identify biomarkers of protection against *B. pertussis* colonization and/or infection and disease."

What is your expertise and role in the consortium?

"I am involved in the consortium as a "T cell expert". My research laboratory, LoVMI has a more than 20 years long experience in the characterization in humans of antigen-specific T cell responses especially in the field of

bacterial infectious diseases (*Mycobacterium tuberculosis* and *Bordetella pertussis*). In the field of whooping cough and related vaccines, we were among the first research groups to characterize in humans and especially in children and in very young infants, Bp-induced cytokine T cell responses, using ELISPOT, ELISA and flow cytometry as readouts of these cytokine productions. More recently, in the field of *M. tuberculosis* infections, we have developed antigen-specific whole blood assays that need only a small blood volume and who better reflect the in vivo situation compared to results obtained on frozen peripheral blood mononuclear cells.

Thanks to this experience, we were asked to coordinate in the consortium a task aiming at the development of a robust Bp-specific T cell assay achievable on a very small blood volume to be used on infant's samples, and avoiding major artefacts possibly induced by previously reported tests (artefact due to long in vitro stimulation of blood with antigens for reason of sensitivity of the technique, artefact due to the isolation of peripheral blood mononuclear cells which is associated to some degree of cell activation, artefact due to the frequent cryopreservation of cells before the antigen presentation step, etc.). We were also involved in the development of optimal combinations of antibodies to be used for sensitive and reproducible monitoring by flow cytometry of T cells and NK cells subpopulations (Euroflow immune tubes)."

What aspect will you enjoy most working with this consortium?

"From my point of view, the most enjoying aspect of the PERISCOPE consortium is the opportunity to be in contact with scientists coming from other horizons than mine. I am an immunologist and discussions with clinicians, epidemiologists, and microbiologists, are really interesting and challenging. Moreover, the consortium offers the opportunity to share experience on specific points with other immunologists and this is feasible within a very good atmosphere of the group. "

Andrew Gorringe, Public Health England (PHE), UK

Why do we need PERISCOPE?

"Whooping cough (pertussis) is more prevalent than many people imagine and as well as causing a very serious disease in infants it is often the cause of persistent cough in adults. We need Periscope because current pertussis vaccines are imperfect. They are effective in protecting infants from serious disease but don't offer the long-term protection that would enable a reduction in the disease in all age groups. To get a new and improved vaccine we need new ways to show the vaccine will be effective. Periscope is about finding these new ways to assess pertussis vaccines which can guide vaccine development and provide evidence whether the vaccine will work."

What is your expertise and role in the consortium?

"My first job in science after university was with a research group developing an acellular pertussis vaccine. This vaccine was assessed head to head with other vaccines in a large clinical trial. It didn't make it to market but some of our approach was adopted by one of the most widely-used vaccines. Since then I

have maintained a strong interest in the biology of *Bordetella pertussis* and how the bacterium interacts with the immune system. In recent years my group has focused on functional antibody immunoassays for a range of pathogens, including *B. pertussis.* We are using these assays to evaluate sera from Periscope clinical studies. I have also played a role in developing the concept for the human challenge model of *B. pertussis* colonisation which is a key activity of the consortium, which may allow us to link particular immune responses with protection from colonisation."

What aspect will you enjoy most working with this consortium?

"The consortium brings together a group of people with a long-term passion to understand pertussis and develop improved vaccines with individuals with new approaches and technology to enable a fresh look at an old problem. I enjoy the fact that Periscope opens up many new opportunities to understand immune responses that protect against pertussis infection and disease. It is great to work with such an interesting and helpful group of scientists on the important disease."

PERISCOPE Stakeholder meeting 2020 in Ghent, Belgium

We are very happy to invite you to the **2020** PERISCOPE Stakeholder Meeting in Ghent, Belgium. The meeting will take place on **March 31st 2020**, from 10am to 4pm CET at the Marriott Hotel at Ghent.

The topic of the 2020 stakeholder meeting will be: ***"New models for development of next generation pertussis vaccines: potential impact on regulatory pathway".***

Registration is free but mandatory.
If you are planning to participate, we kindly ask you to fill in the registration form below by January 17th, 2020 at the latest:
http://eu.123formbuilder.com/form-24423/registraton-form-stakeholder-meeting-march-31-2020

This stakeholder meeting will be followed from April 1st to 3rd, 2020, by the PERISCOPE annual meeting of the consortium (restricted to consortium members) to share project activities and progress.

About PERISCOPE- *Progress beyond the state of the art*

Beyond the public health objectives of PERISCOPE, the project will revitalize and connect the Pertussis research community in Europe and beyond. It is expected that this network of stakeholders will continue to contribute to the development of novel vaccines and immunization methodologies beyond the life of the project. A variety of discussion forums and meetings have been held throughout this third year of the program in order to plan the operational aspects of the PERISCOPE program. Through these discussions, areas for future work were identified, new interfaces created among partners and long-standing collaborative links strengthened. This has already had a positive impact on the Pertussis community in Europe and beyond.

Bringing together industrial and academic partners with different approaches and working practices means that both learn from each other, not only about what they do, but also how they do it.

We wish you all a happy end of the year!

Partners and experts in PERISCOPE

The PERISCOPE consortium brings together internationally renowned scientists with many years of experience in *Bordetella pertussis* (Bp) research, clinical trials, bioinformatics, immunology and public health.