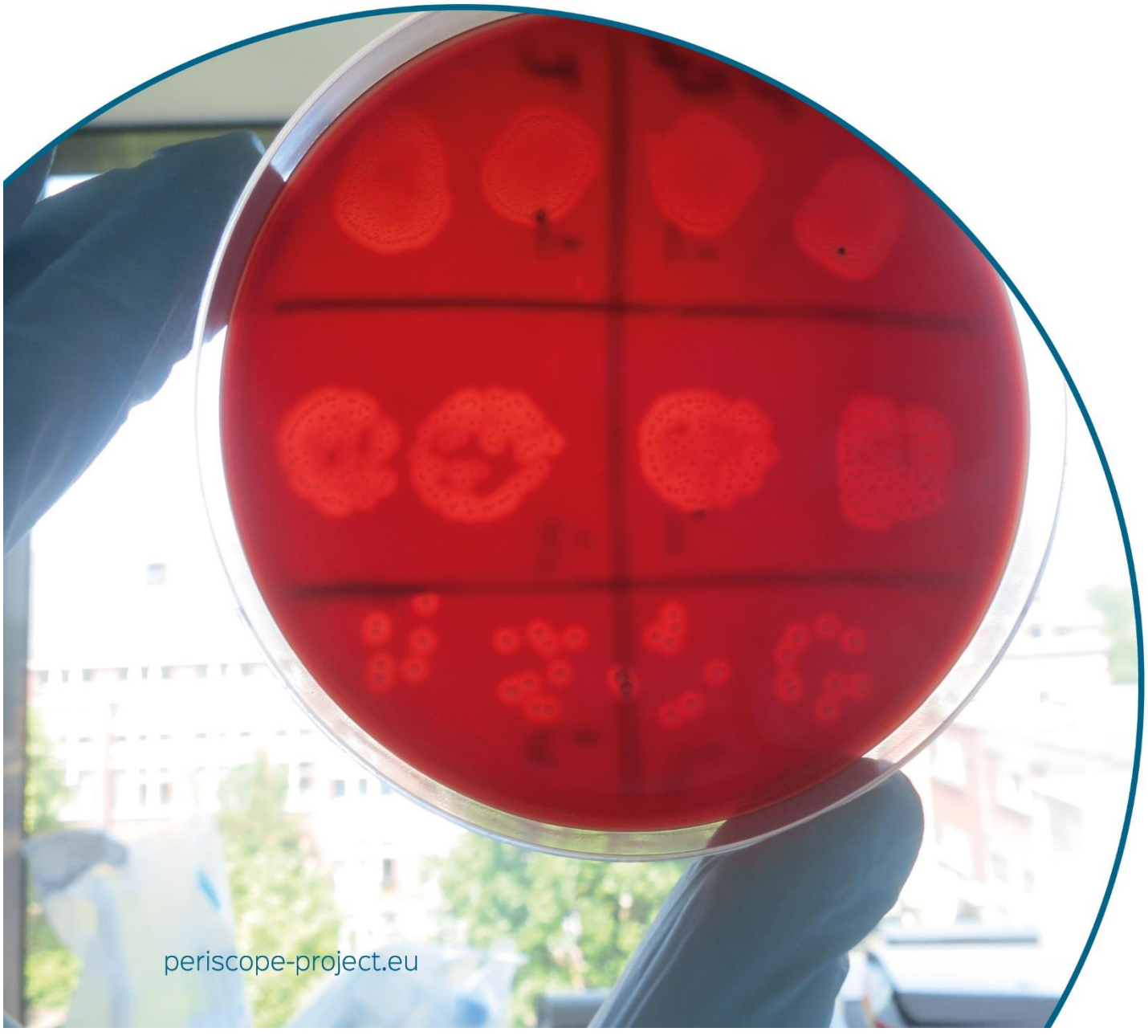
# peri scope

PERtussIS COrrelates of Protection Europe

Newsletter Issue 6 - June 2019



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## Editorial

*Dear colleagues and followers of the PERISCOPE Newsletters,*

We are very pleased to present the fourth 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.

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| **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.

*Members of the PERISCOPE consortium during the annual meeting 2019 in front of the historical University building in Salamanca*

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.

## Start of the Gambia Pertussis Study (GaPs)

This trial is part of a series of clinical studies performed by the PERISCOPE consortium. The objective of the GaPs trial is to generate knowledge on immune responses of vaccinated babies born to mothers who received either a combination vaccine (Boostrix-IPV) against pertussis, diphtheria, tetanus and polio vaccine, or the usually recommended tetanus vaccine during pregnancy. Newborns will receive either acellular (aP) or whole cell pertussis (wP) vaccine at 2, 3 and 4 months of age.

The GaPs study is led by Prof. Beate Kampmann and is conducted at the MRC unit in the Gambia, which is the only site in Africa involved in the consortium.

The GaPs study involves 600 mother/infant pairs. Infant immune responses will be characterized in detail up to the age of 9 months. The samples are initially processed on site at the MRC labs where a number of sophisticated immune-assays are already carried out on fresh blood. Serum and frozen

cells will be sent to the PERISCOPE collaborating labs for specific antibody studies and other cellular assays not available in the Gambia.

## Portraits

*In each newsletter, we portray individual PERISCOPE members. In this fourth issue, we are happy to introduce two of them and their views on the project.*

## Martin Huijnen, Radboud University Medical Center, The Netherlands

*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. "

## Anne-Marie Buisman, National Institute of Public Health (RIVM), Bilthoven, The Netherlands

*Why do we need PERISCOPE?*

"Despite high vaccination coverage, pertussis has re-emerged during the last decades. This resurgence is multifactorial and rather difficult to control. PERISCOPE aims to try to better understand the shortcomings of the current pertussis vaccines and vaccination strategies by bringing together a large group of scientists within Europe with lots of experience in research on *pertussis*, vaccines immunology and bioinformatics. Combined results of in

depth exploration of immune responses to *pertussis* as well as data of immunological core assays involved will enable us to gain a better understanding of the immune mechanisms to *pertussis* as much as possible. Moreover, the unique combination of all these immune parameters in preclinical, clinical and challenge studies aims to get forward to the knowledge needed for inducing a much better protection against *pertussis* by vaccination. Altogether we would like to come to a vaccination strategy to be able to induce long term immunity to *pertussis*."

*What is your expertise and role in the consortium?*

"I am trained as an immunologist in the field of infectious diseases. The core mission of our lab, the Laboratory for Immunology of Infectious Diseases and Vaccines (RIVM) is to provide information and advice about effectiveness of vaccines, vaccination strategies and immune responses against infectious diseases to both the government and the general public. In support of this task, my research is focused on immune surveillance and age-related efficacy of the immune response to vaccine preventable diseases. During the last decade I have been working on long-term memory B and T-cell immunity against these diseases with a focus on pertussis. I have initiated several clinical studies for measuring immune responses in pertussis vaccinated groups of children and adults. Within these studies we collaborated interdisciplinary with other (inter)national research groups off course. As a member of the RIVM PERISCOPE team I am involved in the clinical vaccination studies in WP3. I am happy to share my experience on B-cell responses to *pertussis* into the PERISCOPE consortium as a task leader of task 5.8. Within this task we will be able to measure both antigen-specific plasma B-cell and memory B cell responses in all clinical vaccine studies involved as well as in the human challenge study."

*What aspect will you enjoy most working with this consortium?*

"Within PERISCOPE we are able to share all our expertise on *pertussis* within a large group of enthusiastic experts of both public and private partners. PERISCOPE allows me to enlarge my knowledge to an infectious disease for which the vaccines do not induce long-term immunity. It is rather stimulating doing that together with various experts within Europe and young scientists in the field bringing new ideas on various disciplines. As a large team we will try to tackle an important public health issue. "

## *Alberto Orfao, University of Salamanca, Spain*

*Why do we need PERISCOPE?*

"Vaccination against *B. pertussis* has been established worldwide now for the last 50 years with great success. Thus, along this period vaccination against *pertussis* has proved to be safe and highly effective. However, in the last decade, the epidemiology of the disease has changed in parallel to a progressively lower research effort of the scientific and clinical community focused on

*Pertussis*. Thus, epidemiological findings pointed out the need to revitalise research on *B. pertussis* particularly focused on the identification of (bio)markers of vaccine-induced immune protection and waning in humans, for future development of improved vaccines for longer-term human protection against infection, colonization and transmission of the bacteria, at both the individual and the population levels with special emphasis in those populations at risk (e.g. newborns and younger children)."

*What is your expertise and role in the consortium?*

"Among other achievements, our group in Salamanca has a long and successful track record of developing flow cytometry cell-based assays to identify, enumerate and characterise normal and tumoral immune cells. In 2004, together with Prof JJM van Dongen (LUMC), we initiated a European scientific consortium (EuroFlow) aimed at standardization and innovation in clinical flow cytometry. In recent years within EuroFlow we have developed novel multicolour assays and software tools for (automated and detailed) flow cytometric dissection of immune cells in (human) blood into hundreds (>250) different B-, T-, NK and innate cell populations. Based on these tools new immune monitoring (cell-based) biomarkers have been identified that have provided a better understanding of immune responses and immune alterations in blood associated with multiple diseases and treatment conditions. Thus, the major role of our group in the PERISCOPE consortium is to: i) facilitate implementation of these novel flow cytometric immune monitoring tools in those laboratories from the consortium that participate in the distinct PERISCOPE vaccination trials via SOPs and educational workshops, ii) support flow cytometric sample and data analyses within the trials, and iii) further develop the already implemented flow cytometric immune monitoring assays for identification of multiple distinct functional subsets of *B. pertussis*-specific immune cells, particularly (naïve and) memory B-cells and plasma cells. The ultimate goal of our contribution is that via these novel immune cell-assays new (early) biomarkers of long-term immune protection and waning will be identified by the consortium, that can be used in the future for the development of improved vaccines against *B. pertussis* and potentially also, other microorganisms."

*What aspect will you enjoy most working with this consortium?*

"There are several aspects I enjoy very much working with the PERISCOPE consortium. However, among all such aspects I enjoy most the multidisciplinary nature of the consortium. PERISCOPE consists of basic, translational and clinical researchers with strong expertise in various fields that include from the bacteria itself and its components, to mouse models, the immune response and (protein, cell and functional) immune assays, to (maternal, childhood and adult) vaccination trials and whooping cough disease, as well as biobanking and (big) data management. On top of this, it brings different views from academia and industry in a unique scientific, clinical, epidemiological and (population-based) health care, scientific environment."

## *PERISCOPE annual meeting 2019 in Salamanca, Spain*

From April 3rd to 5th, 2019, the PERISCOPE consortium gathered in Salamanca, Spain, to share project activities and progress.

After an introduction by the coordinator Ronald de Groot, RUMC, and the host Alberto Orfao from USAL, Spain, the major achievements reached in 2018 were presented.

The Prof Rob Read, Univ. Southampton, UK, and his collaborators within the consortium then gave an update on the establishment of a controlled human infection model for colonization with wild-type *B. pertussis* and preliminary results on immunological and microbiological analysis of samples from challenged individuals.
This first session was followed by three workshops in parallel on T-cell assays, data integration and B-cell analysis.
The second session was dedicated to pre-clinical studies and the mechanisms of protective immunity against *B. pertussis* infection with a special focus on nasal colonization, innate immune responses and respiratory tissue-resident memory T-cells.

At the end of this first meeting day, all the participants had the chance to visit Salamanca University and have a get together to exchange ideas in one of the historical rooms of the university.

The second day of the annual meeting was dedicated to the analysis of the specific immune responses generated by acellular pertussis vaccine in selected population cohorts. This analysis was particularly focused on functionality of antibodies, mucosal immune responses and dynamics of B and T cell populations. The afternoon was dedicated to ongoing clinical studies as well as sample management within the PERISCOPE consortium.
A round-table involving PERISCOPE scientists and Tod Merkel, FDA, USA, scientific advisor stimulated discussion on recent knowledge on immunity to vaccination, biomarkers and correlates of protection as well as some regulatory remarks.

## *Young Scientist Poster session*

Congratulations to Annieck Diks (LUMC, The Netherlands who presented two posters and won the first prize of the poster competition.

The second and third prizes went to Anais Thiriard (IPL, France) and Lisa Borkner (TCD, Ireland)

After the meeting, a tour through the old part of the city was organized and discussions continued around some tapas.

## 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 second 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.

## *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.