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

IMI is celebrating its 10th anniversary!

… and we are proud to be part of its success!

Facts

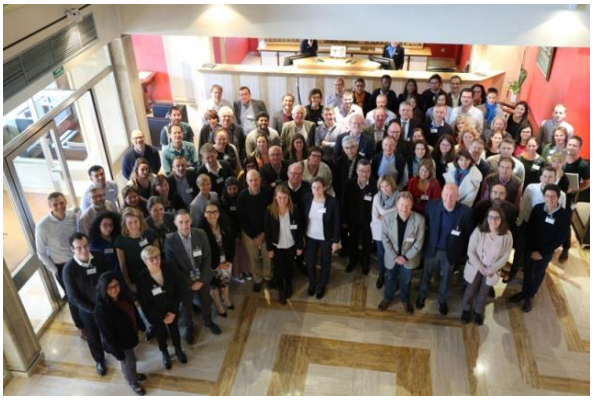
The PERISCOPE consortium unites internationally renowned experts in the largest public-private partnership in Pertussis Vaccine Research in Europe. It was launched in March 2016 receiving support from the Innovative Medicines Initiative (IMI), a joint undertaking of the European Commission and the European 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.



Members of the PERISCOPE consortium during the annual meeting 2018 in Lyon

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.

Main results achieved so far

PERISCOPE has made significant progress towards the goal of developing preclinical and clinical models of Pertussis infection. These models will be used by the consortium to evaluate the immune responses elicited by infection and vaccination. Once established those models will become available for further objectives. The development of a controlled human infection model has been initiated on April 27th, 2017 at NIHR Wellcome Trust Clinical Research Facility in Southampton, UK. The model development consists of two phases: Phase A, is currently underway and involves groups of healthy volunteers being given a low dose of bacteria. After a brief observation phase to study the progress of infection and the immune response to the infection, volunteers will be treated with antibiotics to clear the infection. The detailed protocol of the study has been recently published in the British Medical Journal (an open access publication).

A laboratory model for infection with *Bordetella pertussis* has been transferred to the CEA in France from the laboratory of Dr. Tod Merkel at the Center for Biologics Evaluation and Research (FDA). This model will be used by PERISCOPE to allow an in-depth study of immune responses elicited by infection and vaccination against *B. pertussis*.

In support of the development of the infection models, an assay to quantify life and dead pertussis bacteria has been developed. Such an assay permits monitoring the course of pertussis infection in human and laboratory infection models.

In order to investigate how the immune system responds to a booster vaccination against whooping cough, a clinical study – the BERT study – was initiated. This study started in October 2017, under the sponsorship of the Dutch Institute for Public Health and the

environment (RIVM). The study is conducted at the Spaarne Gasthuis in Hoofddorp, The Netherlands. The influence of age, number of vaccinations and type of vaccines administered during childhood and prior to the booster vaccine given in this study is being investigated. In depth analysis of the immune response to the vaccine will be carried out. The objective is to understand the duration of immune responses induced by vaccination and the mechanisms leading to durable protection against whooping-cough.

In parallel to initiating the pre- and clinical phase of PERISCOPE's objectives, substantial progress was made in the development of (novel) immunological assays or tests to be used as a toolbox to study the response to infection and to vaccination. The majority of these biological tests are already standardized and many are undergoing scientific validation. A small subset of assays has already been deployed to analyse biological samples collected from the nose and blood in the clinical studies described above.

PERISCOPE will also explore the benefits of Pertussis immunisation during pregnancy on protection against disease in new-borns and infants, thus facilitating implementation of maternal vaccination programs in low, medium and high income countries. The clinical protocols for these studies have been developed and are being finalised by the partners for submission to the competent local authorities in 2018.

PERISCOPE is dependent on solid biobanking and data analysis options. PERISCOPE progressed in establishing a multidisciplinary bioinformatics analysis platform and biobank for sample storage from (pre-) clinical studies.

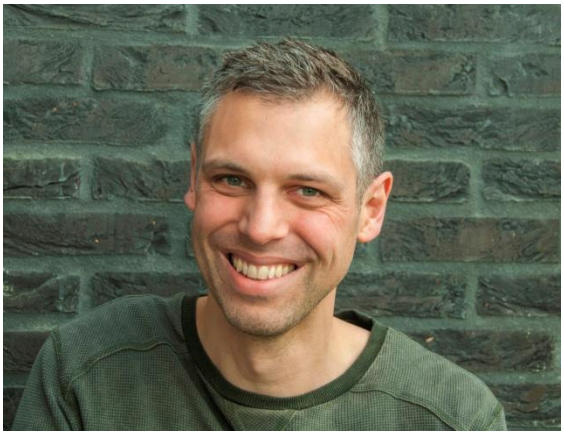
During the second year of PERISCOPE two newsletters were published. Three EuroFlow-PERISCOPE education and training workshops were organized and a workshop to discuss various assays to measure immune responses. A position paper has been drafted and recently submitted.

Portraits

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

Dimitri Diavatopoulos,

Radboud University Medical Center, The Netherlands



Why do we need PERISCOPE?

"Acellular pertussis vaccines may not be as effective as we hoped for in the long term, whilst whole cell vaccines are difficult to standardize and are more reactogenic, which history shows has led to reduced vaccine acceptance by the public. With pertussis being one of the least controlled vaccine-preventable diseases, I see it as an obligation for the scientific, public health and industrial partners to come up with a more effective and durable solution. One of the key issues is the lack of a clear way forward; new vaccines can be developed surely but how will we know that we won't be facing the same issues 10-20 years from now? This is exactly why we need the PERISCOPE project, as PERISCOPE will provide a scientific framework for the rational development of novel pertussis vaccines, as

well as the tools and models to evaluate these future vaccines."

What is your expertise and role in the consortium?

"It has been a real pleasure for me to work on the PERISCOPE project from its inception, starting with the vague contours of a plan and now to see it develop into reality. My background is quite diverse, I started my scientific career working on the molecular microbiology of *Bordetella pertussis*¸ then moving into immunological research on respiratory tract infections. I now head my own research group at RUMC with the aim to understand how immune memory is (re)programmed and maintained during life. I lead Work Package 2, in which we are setting up a controlled human infection model and establish naturally infected patient cohorts to study immunity to pertussis. My group is responsible for investigating the early immune events and pathways that drive the development of protective immunity, both in the vaccination studies and in the challenge studies. Another important focus of our research is on mucosal immunity to pertussis, in particular in the human studies."

What aspect will you enjoy most working with this consortium?

"I believe that the true value of the PERISCOPE consortium lies not in the individual parts but the integration of all studies and knowledge together. When I think about PERISCOPE, I sometimes compare it to the Indonesian layer cake *spekkoek*. With *spekkoek*, the individual layers taste nice but nowhere near as spectacular as when you eat the whole thing! Working with enthusiastic people from different backgrounds, be it from the industry, academia or from different scientific backgrounds, trying to balance the different interests and make sure that everyone speaks each other's language is something that I really enjoy. "

Marcela Silerova,
GSK vaccines, Belgium

Why do we need PERISCOPE?

"PERISCOPE project is a key scientific endeavor aiming to increase our understanding of immunity to pertussis and identify biomarkers of protection. Despite various pertussis vaccination strategies having been in place for decades, the resurgence of the disease has been observed. This unwarranted phenomenon together with changes in pertussis epidemiology are the main drivers for development of a new generation of pertussis vaccines. The aim of PERISCOPE is to accelerate this development."

What is your expertise and role in the consortium?

"I am an immunologist and molecular biologist by training. While working for GSK, I have acquired broad experience in designing and executing clinical trials as well as reporting their results, with a specific focus on infant vaccination. In the PERISCOPE consortium, I am co-leading work package 3 which runs three clinical trials investigating vaccine-induced immunity in different age groups and populations. My role in particular is to bring to the project the industry perspective and experience."

What aspect will you enjoy most working with this consortium?

"The beauty of the PERISCOPE consortium is that it brings together experts in *Bordetella pertussis* immunology, preclinical research, clinical trials and public health, both from academic and private sectors. Only by putting our multi-disciplinary expertise and efforts together we can achieve a common goal – development of improved pertussis vaccine, and ultimately, reducing the burden caused by pertussis infections worldwide. "

Jacques J. M. van Dongen, Leiden University Medical Center, The Netherlands

Why do we need PERISCOPE?

"The PERISCOPE consortium combines vaccine expertise with classical and innovative immunological research strategies and methods to increase our understanding of vaccination-induced immune responses to *B. Pertussis*. These new strategies and methods are used to dissect the serological and cellular immune responses in several model systems, both human and animal. This international project should bring a better understanding of protection, memory and waning of anti-B. Pertussis responses, which form the basis for improved design and validation of new vaccines."

What is your expertise and role in the consortium?

"I am MD, specialized in Medical Immunology with special attention for the development of novel diagnostic strategies, both cellular and molecular. I have coordinated seven European consortia, including the EuroFlow consortium for advanced flow cytometry. My role in the PERISCOPE consortium is to support the coordination of Work Package 5 "*Clinical trial assays and biomarker discovery platforms*". This WP aims at collective development and validation of serological, cellular and functional assays, and apply them to the different clinical studies. Together with the USAL team, my LUMC team guides the EuroFlow-based design, testing, and validation of novel state-of-the-art flow cytometry to dissect the cellular immune response to infection and vaccination, focussing on maturation and activation pathways of many subsets of B-cells, T-cells and innate cells. The detailed flow cytometric B-cell studies support the immunogenetic studies to dissect the building and selection of antibody diversity at the DNA and RNA level. Such molecular knowledge is essential to understand differences in vaccination responses (how broad? how narrow? etc.). These are the aims of Tasks 9 and 10 in WP5."

What aspect will you enjoy most working with this consortium?

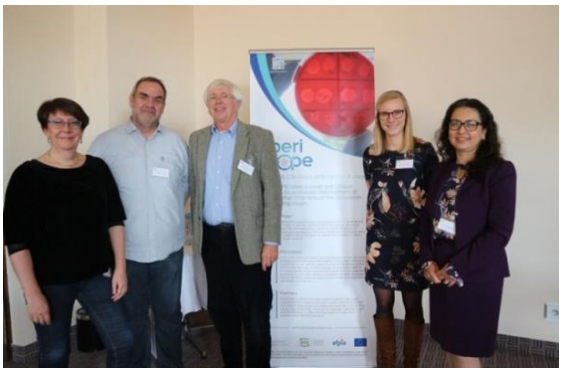
"It is exciting to work with the consortium to unravel the complex cellular responses to both vaccination and infection. The preliminary flow cytometry results have already provided new information: faster kinetics of innate cells and B-cell subsets than reported in the literature and detection of new B-cell maturation patterns, which differ between clinical studies. Such novel insights will be relevant for understanding the observed differences in immune responses and subsequently for improving the effectiveness of vaccination programs. In addition to the development and validation of novel assays, also standardization is essential for multicenter clinical studies. Standardization processes and the related

education and training meetings are time consuming and demanding and are not always valued appropriately. However, it is highly rewarding when fully comparable data are being obtained in different centers and different clinical studies, since this forms the basis for reliable clinical research programs."

PERISCOPE annual meeting 2018 in Lyon

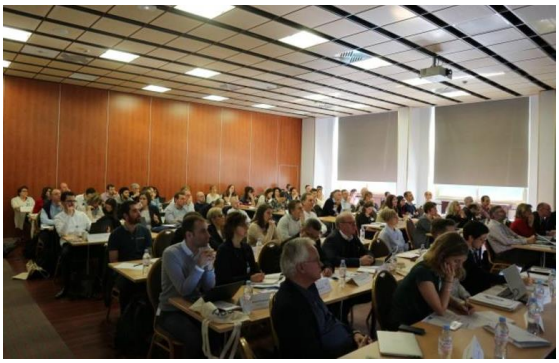
From March 7th to 9th, 2018, the PERISCOPE consortium gathered in Lyon, France, to share project activities and progress.

It started with an exchange with participants from the **FLUCOP** consortium: a collaborative research consortium between academia, vaccine manufacturers and public health authorities to improve standards in the serological evaluation of seasonal influenza vaccines.



Catherine Caillet (Sanofi Pasteur), Frédéric Clement and Gwenn Waerlop (University of Ghent) presented assay development, standardization and validation procedures as well as cell-mediated responses, optimization and standardization of CMI responses within their project.

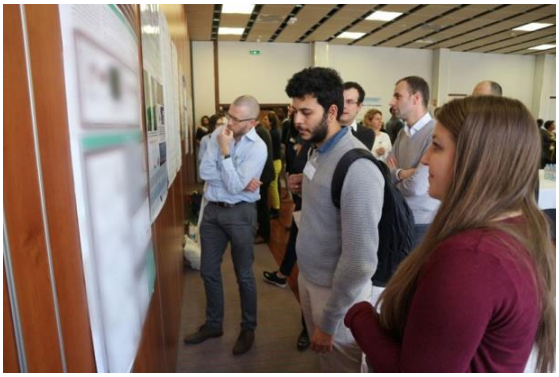
After an introduction by the coordinator Ronald de Groot (RUMC), the major achievements reached in 2017 were presented by the WP leaders during the second day of the meeting. A particular focus this year was the assay development in PERISCOPE.



The third day of the annual meeting was dedicated to 10 different thematic workshops. The WP leaders presented the main outcomes of the sessions to the plenum and opened the floor to Scientific Advisory Board chair Tod Merkel (FDA) and Ethic Advisory Group chair Evert van Leeuwen (RUMC) who both offered their feedback on the progress made so far and processes implemented and adhered to.

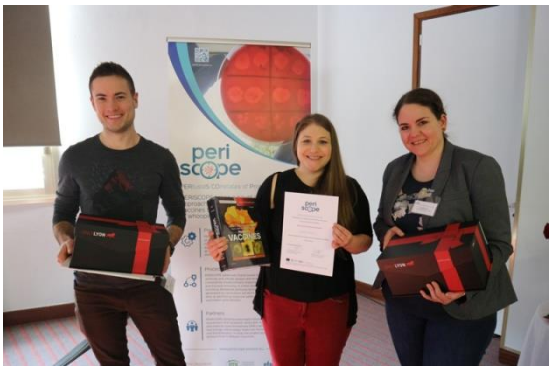
Young Scientist Poster session

Around 20 thematic posters on the PERISCOPE related research conducted by the young scientist within the consortium were presented during the second day of the annual meeting. PERISCOPE members voted for the best poster in their view.



The first prize was won by Breeze Cavel (PHE) who stated: "As always it was interesting to hear the discussions and meet the people who

produced so many key papers in the pertussis field and it was fantastic to take more of an active role this year. It was a great opportunity to present my work and engage with consortium members from a variety of disciplines. I was honoured to have been awarded the best poster prize as there were so many amazing posters and presenters".



The second place was shared by Joshua Gillard (RUMC, on the left) and Lisa Borkner (TCD, on the right).

In 2018, you could meet us at the coming meetings:

- July 2-3rd: Andrew Gorringe (Public Health England) will give a talk at the Clinical Trials in Infectious Disease – From Diagnostic to Clinic (CTIDC2018), London, UK on the Pertussis project: Clinical studies to determine immune correlate of protection for pertussis
- September 2-5th: 2 abstracts from PERISCOPE members were submitted to the European Congress of Immunology (ECI) 2018, Amsterdam, The Netherlands
- October 3-7th: An abstract from PERISCOPE members was submitted to the IDWeek2018, San Francisco, USA

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.