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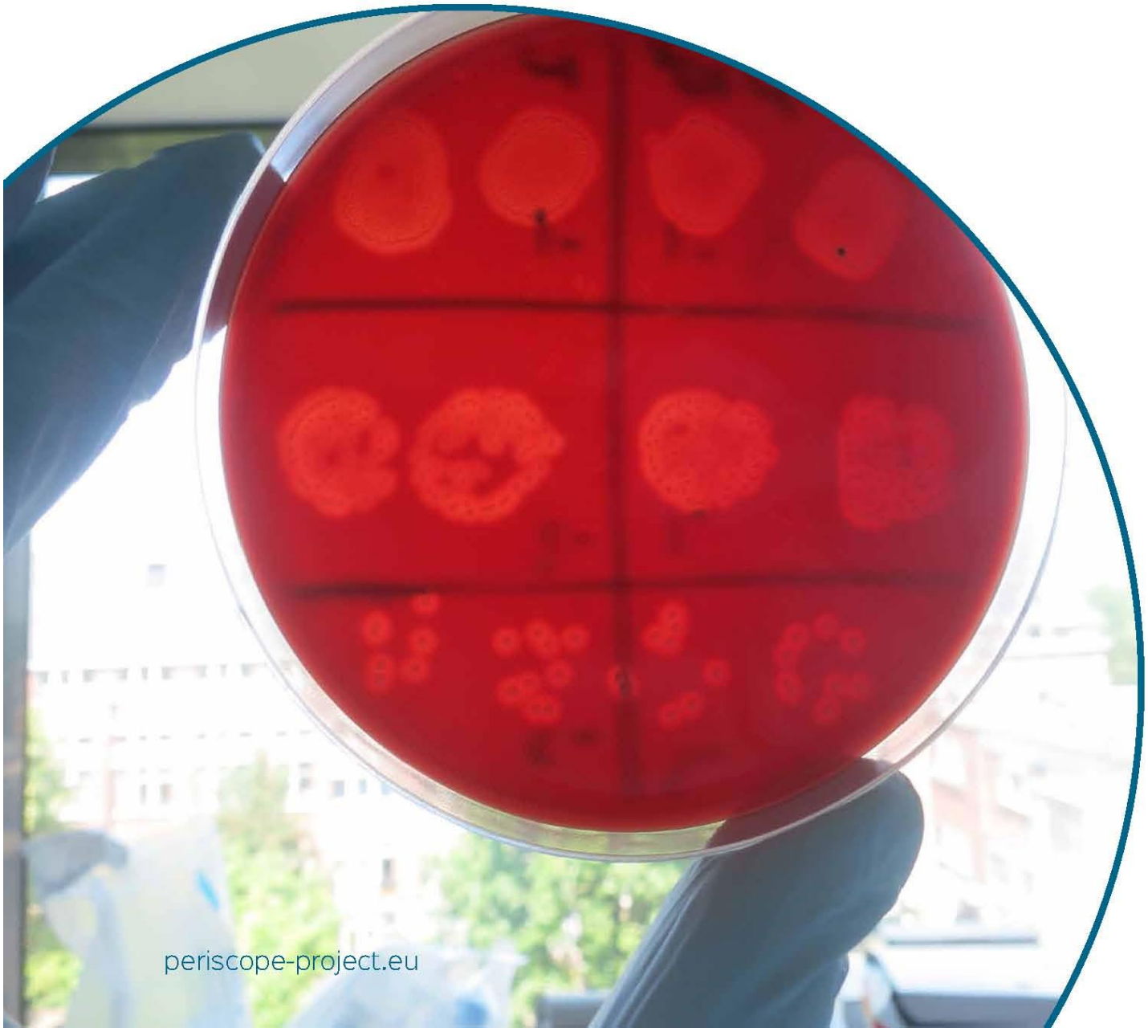
PERtussIS COrrelates of Protection Europe

Newsletter Issue 5 - December 2018



periscope-project.eu

Editorial

Dear colleagues and followers of the PERISCOPE Newsletters,

We are very pleased to present the fifth 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 what is currently 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 *B. pertussis* infection and disease in humans.

PERISCOPE position paper released!

The position paper entitled "PERISCOPE; Road towards effective control of pertussis" by Diavatopoulos *et al.* has been published in *the Lancet Infectious Diseases (published online Nov 28, 2018)*. The aim of this position paper is to raise awareness of the existing gaps to control pertussis and the approaches undertaken within the PERISCOPE consortium to solve these issues.

PERISCOPE member receives International Investigators Award

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Hans de Graaf from the University of Southampton (US) was honoured with the IDWeek 2018 International Investigators Award. He received the prize in recognition of excellence in his abstract submitted to IDWeek 2018: "A *Bordetella pertussis* Human Challenge Model Induces Immunizing Colonization in the Absence of Symptoms". This clinical study aims to develop a safe controlled human *Bp* infection model and to define natural immune responses against wild type *Bp* in order to facilitate the development of bioassays and next generation pertussis vaccines.

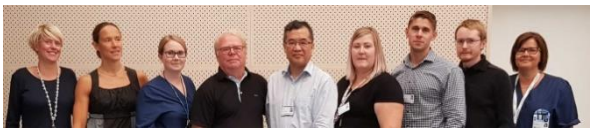
Update on the BERT study

Within the scope of PERISCOPE, nine clinical studies will be conducted.

Among them, the **B**ooster P**ert**ussis vaccine (BERT) study is currently on-going and involves 366 healthy volunteers from 3 different European countries (The Netherlands, Finland and United-Kingdom) with a different epidemiological background for pertussis incidence. The main purpose of the BERT study is to investigate the effects of an aP booster vaccination in children, young adults and elderly with different epidemiological and priming backgrounds for pertussis on the magnitude, quality and persistence of immunological memory against *B. pertussis*.

The analysis of immune responses in this study will allow us to assess biomarkers that can be used to detect early signs of the waning of immunological memory to pertussis and biomarkers that can be used to assess long lasting immunological memory to pertussis.

The Dutch team



The Finnish team

The Oxford team

Portraits

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

Cécile van Els, National Institute for Public Health and the Environment (RIVM), Bilthoven, The Netherlands

Why do we need PERISCOPE?

"Pertussis is difficult to control despite vaccination, calling for solutions including the development of improved pertussis vaccines.

Current acellular pertussis vaccines, while safer than the whole cell vaccines they replaced, seem less effective in the long term. This is thought to reflect different wiring of the induced immune response. To accelerate the development of the next generation of pertussis vaccines, key knowledge is required on the mechanisms correlating with protection against pertussis, including models and assays for evaluating such correlates. PERISCOPE brings together outstanding basic and clinical researchers and vaccinologists who as a team can bring this field forward."

What is your expertise and role in the consortium?

"I am an immunologist by training. My group has a longstanding track record on correlates of protection research in pre-clinical models and clinical cohorts in the context of a wide range of pathogens, including *B. pertussis*. We have a research line to elucidate processing and MHC display of antigen to T cells by antigen presenting cells. Knowledge on targeted antigenic sites may guide detection and profiling of *B. pertussis*-specific T cells as we showed in human and preclinical studies. With this background my primary role in PERISCOPE is to lead task 5.12. In this task we develop or fine-tune, together with other partners, methods for in depth exploration of biomarkers for superior *B. pertussis*-specific T cell immunity in variously primed PERISCOPE samples. Other responsibilities are delivering a natural infection cohort (Immfact-study) for task 2.5, developing and evaluating with my group and other partners a novel whole blood T-cell assay for task 5.7, and coordinating Periscope antigen-distribution."

What aspect will you enjoy most working with this consortium?

"It is a privilege to work with so many experts from various disciplines on the correlates of protection for pertussis. PERISCOPE is quite an ambitious project but very timely (well done initiators Ronald de Groot, Dimitri Diavatopoulos and others). To me working on a topic with such a high public health impact in our very motivated local team in Bilthoven and with new and old collaborators throughout PERISCOPE is very enjoyable. So far groups invested in setting up studies, assays, building capacity and communication. Yet the first important PERISCOPE results are emerging, such as the implementation of the experimental infection models in preclinical setting and humans, clinical studies and assays in progress, posters and papers written and accepted, and much more to come. Exciting! "

Ulrich Heininger, University of Basel Children's Hospital, Switzerland

Why do we need PERISCOPE?

"Pertussis research has been fragmented and spread all over the world in the past. Rarely has research on pertussis been supported in a way that activities by different research groups were coordinated to build up on each other. This, however, is urgently needed to avoid duplications of efforts caused by lack of coordination and harmonization. PERISCOPE now fulfills this need. Pertussis is not one of the major infectious diseases in terms of fatalities. However, it is ubiquitous all over the world and hardly any other vaccine-preventable disease than pertussis causes so much trouble to health care professionals and the public with regards to its recognition, diagnosis, treatment and last but not least prevention. Better vaccines than those currently used are therefore urgently needed. I am convinced that PERISCOPE will deliver results which can pave the way towards totally new, better acting pertussis vaccines than those currently available."

What is your expertise and role in the consortium?

"I had the privilege to coordinate one of the large acellular pertussis vaccine trials that were performed in the early 1990s. These trials were

very challenging and time consuming. They contributed a lot to our current knowledge on the performance of acellular and conventional whole cell pertussis vaccines and also allowed the discovery of some universal phenomenons which are widely neglected but important when it comes to the interpretation of vaccine study results, e.g. the so called "observer bias" (Cherry JD et al, Pediatrics. 1998; 102:909-12). Ever since, I continued to study pertussis as a disease, its epidemiology and challenges of immunization with all of its fascinating facets. This has given me broad experience in various aspects of pertussis which I am happy to share with my colleagues and thus contribute to the success of PERISCOPE. Here, my specific roles are a) leading WP4 (interaction with regulatory authorities and other stakeholders), b) critically discussing study protocols and procedures in my role as a steering committee member and c) leading the Publication Committee which is needed to guarantee fair interactions between all consortium members when it comes to publications of PERISCOPE findings."

What aspect will you enjoy most working with this consortium?

"PERISCOPE allows me to spend a significant amount of my time for dealing with the disease that I have found most fascinating and attractive in my career so far, i.e. pertussis. This consortium puts me in a position where I can interact with what I trust are the most prominent and talented experts in various fields of pertussis research, both from the pharmaceutical industry and the academic institutions involved in PERISCOPE. This is rewarding and it is a real privilege to be part of this spear-heading research consortium. "

Andrew Preston, University of Bath, United Kingdom

Why do we need PERISCOPE?

"In recent years it has become apparent that current pertussis vaccines have shortcomings but that it is going to be *very* difficult to bring a new vaccine to the point of being licensed for use. Periscope directly addresses this by aiming to develop new ways of testing novel vaccines to reach the point that we can have sufficient confidence to take them into use in humans. This includes developing new pre-clinical models and identifying measurable markers of protective immunity against which a new vaccine can be tested."

What is your expertise and role in the consortium?

"I am a molecular microbiologist who has researched fundamentals of *Bordetella pertussis* biology for 20 years. At the heart of PERISCOPE are assays and experiments involving growth and manipulation of *B. pertussis.* My group provides expertise in working with *B. pertussis* to these studies; development of novel *B. pertussis* reagents and we are investigating specific aspects of *B. pertussis* pathogenesis."

What aspect will you enjoy most working with this consortium?

"The PERISCOPE consortium includes many long-standing members of the *B. pertussis* research community. The project enables us to work together even more closely than before on matters that are important to us. It includes members new to the field of pertussis who bring a fresh perspective. Together, PERISCOPE

is a real opportunity to do genuinely novel and important research."

PERISCOPE annual meeting 2019 in Salamanca, Spain

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

You could meet us at the coming meetings:

February 10-14th; 2019: Two partners of the PERISCOPE consortium (RIVM and LUMC) have submitted an abstract to the Keystone meeting J6, B-cell T-cell interactions, Colorado, USA

Our recent publications:

Borkner L, Misiak A, Wilk MM, Mills KHG (2018) Azithromycin clears *Bordetella pertussis* infection in mice but also modulates innate and adaptive immune responses and T Cell memory. *Front Immunol* 9:1764.

Denoel P, Londoño-Hayes P, Chlebus M, de Azero MR (2018) Impact of the Innovative Medicines Initiative on vaccine development. *Nat Rev Drug Discov* 17:769-770.

Diavatopoulos D, *et al* (2018) PERISCOPE: Road towards effective control of pertussis. *Lancet Infect Dis. Published online Nov 28, 2018.*

Naninck T, Coutte L, Mayet C, Contreras V, Locht C, Le Grand R, Chapon C (2018) *In vivo* imaging of bacterial colonization of the lower respiratory tract in a baboon model of *Bordetella pertussis* infection and transmission. *Sci Rep* 8:12297.

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.