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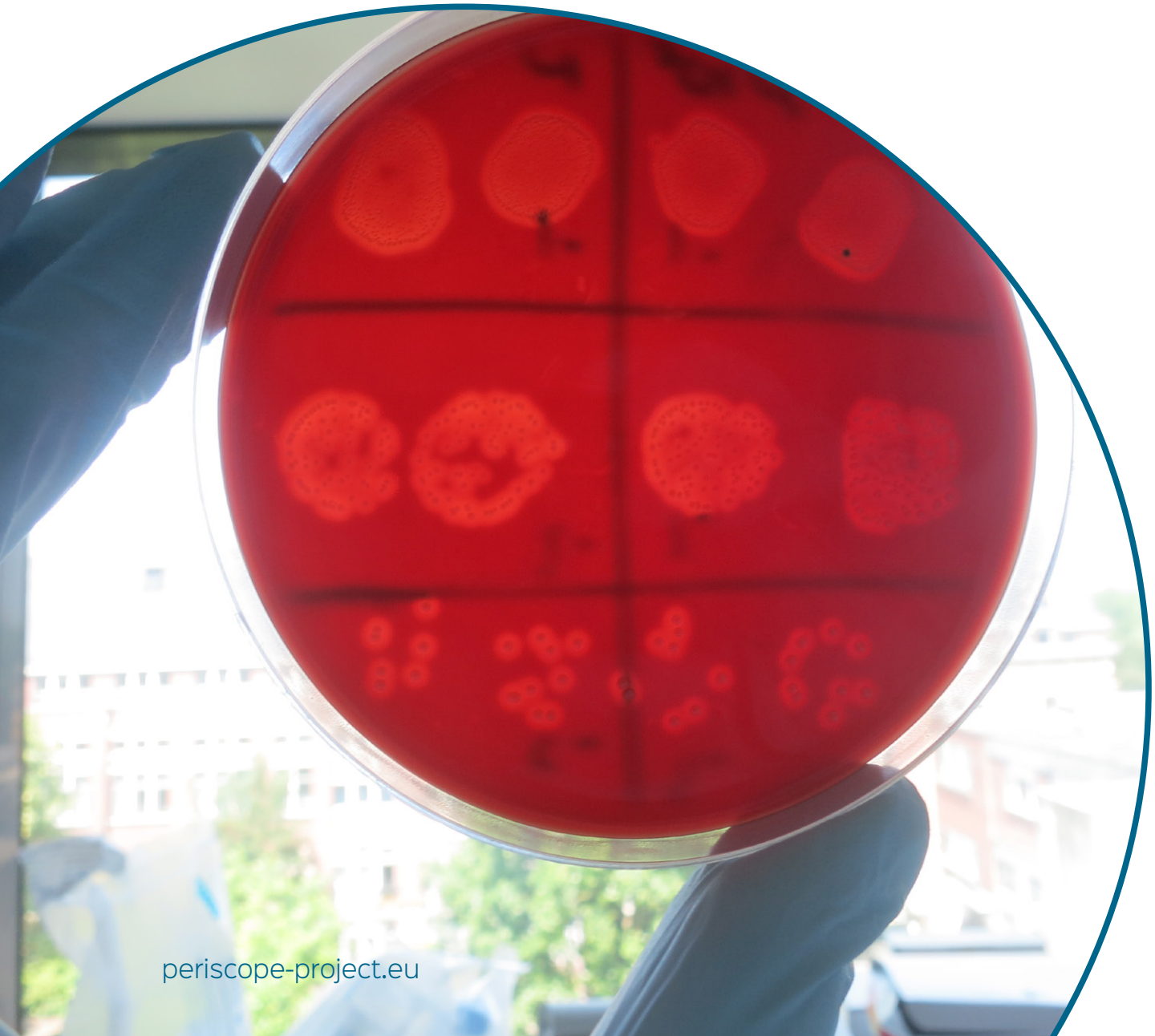
PERtussIS COrrelates of Protection Europe

Newsletter Issue 2 - May 2017



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Editorial

Dear colleagues and followers of the PERISCOPE Newsletters,

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

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.

Context and overall objectives of the project

A new generation of pertussis vaccines or improved vaccination schedules is needed to meet the persistent burden of Pertussis infection in developing countries and to reduce the risk of contracting Pertussis disease in industrialised countries, which recent observations indicate has risen in some segments of the population compared with previous estimations.

The PERISCOPE consortium was created to meet these challenges by facilitating collaboration between stakeholders in the field of pertussis, 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 1st (whole-cell) and 2nd generation (acellular) Pertussis vaccines in humans. To achieve this goal, the consortium will develop an extensive tool box of bioassays to support pan-European vaccination studies. It is hoped that the data generated from these studies will ultimately allow the vaccine-developing community to define an ideal immunological profile or signature that vaccines need to generate in humans for them to become effective at preventing infection in a durable manner.

PERISCOPE will also develop laboratory and clinical models of Pertussis infection. Once established, these models will be used to study the capacity of novel formulations of Pertussis candidate vaccines to prevent infection, with the aim of providing an early indication of their potential value as vaccines.

PERISCOPE will also increase our understanding of the benefits of Pertussis immunisation during pregnancy with regards to the immune status of newborns and infants, leading to further implementation of pregnancy vaccination programs in low, medium and high income countries.

Finally, PERISCOPE will establish a multi-disciplinary clinical and laboratory network including up-to-date bioinformatics analysis platforms and biobanks to support the various stakeholders as they study Pertussis vaccination.

The tools and networks developed by PERISCOPE should enable the development of a new generation of Pertussis vaccines and/or vaccination schedules in Europe and beyond.

Main results achieved so far

Progress has been made in designing and planning the clinical studies that will be carried out to explore immune responses to Pertussis vaccination at study sites in The Netherlands, United Kingdom, Finland and The Gambia (West Africa).

The protocol for a clinical study aimed at developing a model of Pertussis infection in human volunteers was finalised and approved by the consortium's governance bodies and local ethical committees. The required authorisations are being sought prior to setting up the study.

Advances were made towards developing a toolbox of immunological and microbiological tests to be used to explore immune responses to Pertussis vaccination and infection.

The PERISCOPE project was presented to the European Medicines Agency (EMA). This is the start of a dialogue with the regulatory authorities that will continue throughout the project.

Progress beyond the state of the art and expected potential impact

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 first 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.

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.

Scientific Advisory Board

An international Scientific Advisory Board (SAB) was set up to provide valuable insights, recommendations and expertise to the PERISCOPE project.

SAB statement of Purpose

The PERISCOPE scientific advisory board is comprised of a group of distinguished scientists, each nationally and internationally recognized for excellence in their fields of research. They bring a wide range of experiences and perspectives on board to provide independent assessments of PERISCOPE's priorities and strategies, provide practical advice to project design, and help evaluate results.

Tod Merkel, Chair of SAB

Tod Merkel is Principal Investigator in the Laboratory of Respiratory and Special Pathogens in the Center for Biologics Evaluation and Research, Food and Drug Administration (FDA), USA.

Dr. Merkel received his Ph.D. from the University of Virginia and received postdoctoral training at the National Institutes of Health before establishing a research program in the Food and Drug Administration. He brings over thirty years of experience in infectious disease research and related disciplines and fifteen years of vaccine regulatory experience to the study of bacterial pathogenesis and the evaluation of new vaccines. He has extensive experience developing and utilizing pre-clinical models of bacterial infections, including murine and non-human primate models of Pertussis, murine models of Staphylococcal infection, and murine models of Anthrax.

Portraits

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

Kent Kester

Sanofi Pasteur, USA

Why do we need PERISCOPE?

KK: "The development and deployment of

current acellular pertussis vaccines (aP) have not demonstrated optimal long term protection with wide use. The increasing numbers of cases of clinical pertussis in previously-vaccinated patients is concerning and puts the onus on vaccine developers to improve current offerings. The unique organization of a focused, disease-specific IMI consortium like Periscope brings together seasoned academic researchers and vaccine developers focused on learning more about pertussis and how best to protect against it."

What are the main outcomes expected from the consortium?

KK: "As a clinical researcher whose efforts are directed against functional assessments, like human challenge models, I'm looking for us to discern new immunological and/or other biomarkers associated with pertussis colonization/infection that will allow us to adjust vaccine development targets in order to see how best to apply these learnings to the development of better pertussis vaccines."

What is your expertise and role in the consortium?

KK: "I am an adult infectious disease physician with experience in human challenge models and the translational development of new technologies. Most of my human challenge studies have been done in the context of malaria vaccine development. In PERISCOPE, I'm helping the group focused on developing and evaluating the pertussis human challenge model, a unique and essential functional assessment that will allow us to discern new approaches to the induction of pertussis immunity."

What aspect will you enjoy most working with this consortium?

KK: "As in all international consortia, the best part for me is the opportunity to engage in novel and cutting-edge science with a variety of international subject matter experts."

Kingston Mills
Trinity College Dublin, Ireland

Why do we need PERISCOPE?

KM: "We need PERISCOPE in order to coordinate and advance the best research efforts in Europe in the area of pertussis vaccines. Pertussis is a remerging infectious diseases and most scientist and clinicians working in this area believe that the current acellular pertussis vaccines, while safe, are sub-optimal in terms of long-term efficacy and their ability to induce immunological memory. We need to put in place the assays and the guidelines to help inform the future development and testing of 3rd generation pertussis vaccines."

What are the main outcomes expected from the consortium?

KM: "We expect of have developed and/or validated pre-clinical models for testing the capacity to protect against *B. pertussis* infection, transmission and disease. We hope to identify or least validate biomarkers of protective immunity that can be used in the development and regulation of next generation pertussis vaccines."

What is your expertise and role in the consortium?

KM: "I am a cellular immunologist with a long interest in the immunology of *Bordetella pertussis*, especially cellular immunity and the role of T cell subtypes in natural and vaccine induced immunity to *B. pertussis*. I am leader of work package 1 on pre-clinical models. My lab will be responsible for a significant amount of the work on one pre-clinical model. My group is also involved in developing the T cell assays to be used in the human clinical trials."

What aspect will you enjoy most working with this consortium?

KM: "Working with new and old colleagues on an exciting project in a research area that is close to my heart."

Rob Read

University of Southampton, UK

Why do we need PERISCOPE?

RR: "Because of the occurrence of outbreaks of whooping cough even in vaccinated children and adults. It is clear that the aP vaccines do not provide the same level or kind of protection as the old whole cell vaccines even though they have been very acceptable to the public in terms of their side effect profiles. Secondly, there does appear to be a reservoir of infection in the community which we need to try to understand a little better than we currently do. In the city in which I work there was an unexpected death of a neonate a couple of years ago which really focused our attention locally on this as an emerging problem. The use of maternal vaccination has been an excellent intervention for us in the UK but there is still the potential for outbreaks in children and adults and deaths in unprotected neonates. A comprehensive study of the nature and mechanisms of natural and vaccine-induced immunity will enable us to better protect the public."

What are the main outcomes expected from the consortium?

RR: "I have to admit I am very focused on the human experimental challenge programme, which I lead here in Southampton. It has become apparent that older children and adolescents are a potential reservoir for *Bordetella pertussis* transmission to young infants who have not yet completed their primary immunization schedule.

Asymptomatic pertussis infection has been detected serologically during outbreaks which implies that there is biologically significant colonization of the nasopharynx, akin to Haemophilus, Neisseria and pneumococcal pathogenesis. So from my perspective at least (sorry to be partisan!) a major outcome will be establishing safe human experimental carriage model to enable us to study the immunological consequences of this interaction. This information should then feed into the other major components of the programme and allow us to understand natural and vaccine-induced immunity to a much better degree."

What is your expertise and role in the consortium?

RR: "I am primarily an adult infectious disease physician and look after patients with severe community-acquired infections. However, over the years I have studied the interaction of bacterial pathogens with human respiratory mucosa. This culminated in the development of a model of Neisseria carriage in human volunteers in which we showed that *Neisseria lactamica* carriage is directly protective against meningococcal carriage in University students. We are currently working hard to try and understand the mechanism of this protection, and have been funded by the UK Medical Research Council to extend the work using genetically modified strains. Altogether, my team has conducted deliberate bacterial infection of the respiratory tract in over 400 volunteers, and we are experienced in the ethical and research governance frameworks that enable this kind of research. My role is to deliver the human model of experimental

carriage by *Bordetella pertussis* on behalf of the consortium."

What aspect will you enjoy most working with this consortium?

RR: "The consortium consists of many experts from different countries in Europe and many walks of scientific life including industry and academia. As a relative newcomer to the pertussis field it has been a real pleasure to meet such an interesting and friendly (but quite seriously focused) group of scientists, not all of whom are grossly eccentric. I will really enjoy working with T cell biologists and the vaccinologists to exploit the model we generate, and sincerely hope that we can be a successful cog in the wheel."

PERISCOPE 1st annual meeting

From March 8th to 10th, 2017, the PERISCOPE consortium gathered in Prague, Czech Republic, to share project activities, progress and future collaborations.

The 2017 Annual Meeting was hosted by PERISCOPE partner Peter Sebo from Institute of Microbiology of the CAS, v. v. i. (IMIC)

The annual meeting was preceded by a stakeholder session on March 8 in the afternoon. Representatives of three IMI projects were invited to give a short presentation of their consortia and discuss the main challenges encountered and lessons learned. **Biovacsafe** was represented by the EFPIA coordinator Giuseppe Del Giudice (GSK Vaccines), **Advance** was represented by the EFPIA coordinator Vincent Bauchau (GSK Vaccines) and **SAFE-T** was represented by the coordinator Michael Merz, (Novartis) and his colleague Nicole Schneiderhan-Marra (NMI, Natural and Medical Sciences Institute at the University of Tübingen). The discussions were very constructive and helped to identify potential hurdles and possible solutions.

The following 2-day annual meeting was opened by PERISCOPE coordinator Ronald de Groot (RUMC, The Netherlands) and Angela Wittelsberger representing the Innovative Medicines Initiative (IMI). The Bill & Melinda Gates Foundation representative Hani Kim stressed the importance of pertussis vaccination research. After these openings, all work package leaders gave an update on the progress and challenges encountered by the members of their respective work package during this first year of the project. The second meeting day served necessary break-out discussions in smaller working groups on key elements, current challenges, clinical studies and data and sample management.

The meeting was rounded off with a summary and some concluding remarks by Professor Ronald de Groot, encouraging the consortium members to keep up the good work and collaboration and focus on the goals set.

The PERISCOPE consortium at the annual meeting 2017 in Prague, CZ

PERISCOPE Coordinators at the stakeholder session with invited speakers

(left to right: Patricia Londono-Hayes, Vincent Bauchau, Giuseppe del Giudice, Ronald de Groot, Michael Merz, Angela Wittelsberger, Nicole Schneiderhan-Marra)

PERISCOPE Coordinators with Karen Makar and Hani Kim, both Bill & Melinda Gates Foundation

(left to right: Karen Makar, Hani Kim, Patricia Londono-Hayes, Ronald de Groot)

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.