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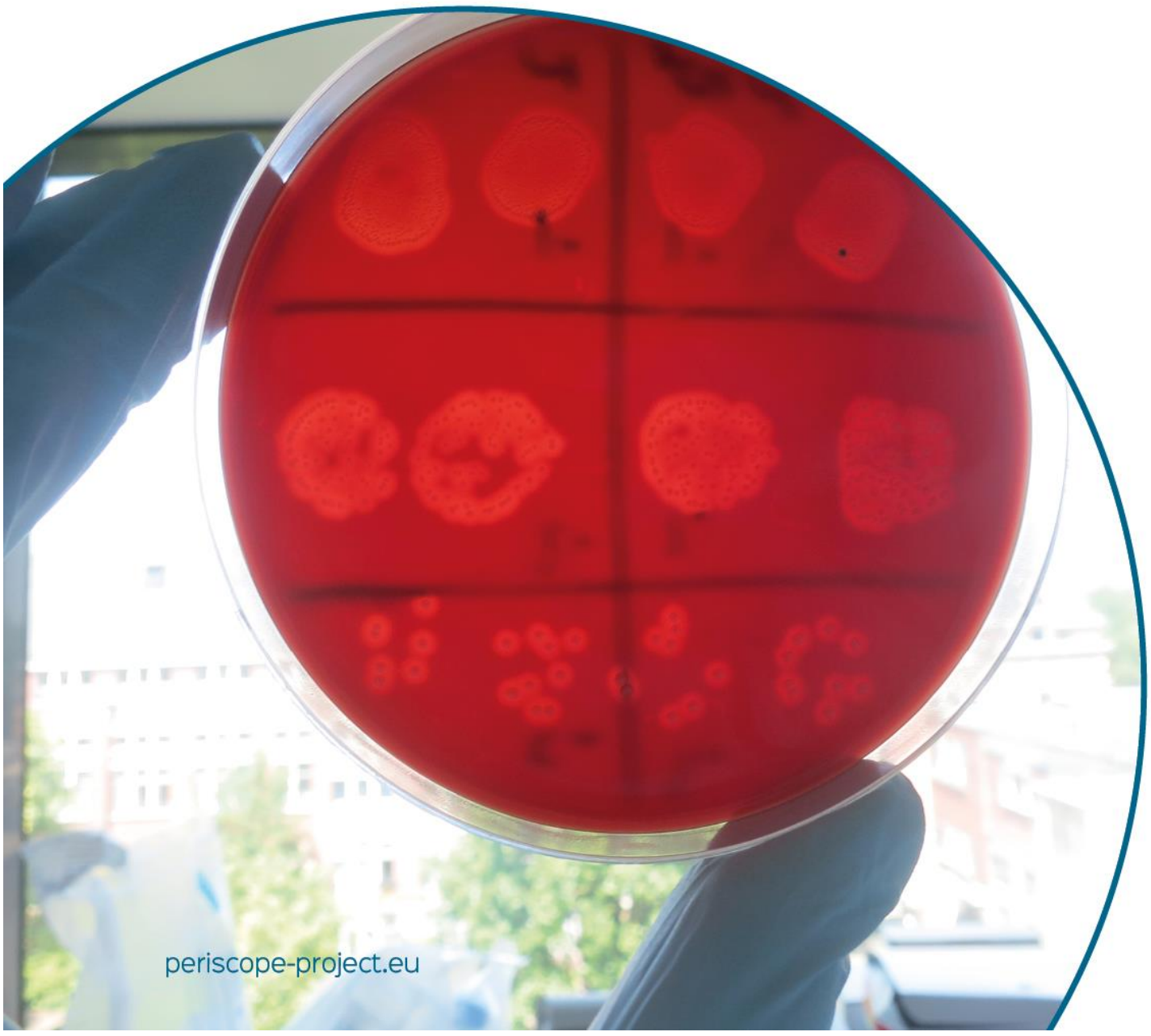

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Editorial

Dear colleagues and followers of the PERISCOPE Newsletters,

We are very pleased to present the third issue of our e-newsletter with a special focus on clinical studies that have already been initiated by 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

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This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA and BMGF.

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 initiates development of controlled Pertussis challenge model in humans

One of the key objectives of PERISCOPE is the establishment of models of pertussis infection that could help expedite the development and testing of novel or improved vaccine formulations. Notably, the development of a controlled-challenge model of *B. pertussis* colonization in humans could help researchers obtain early Proof of Concept that a novel vaccine offers protection and paved the way for large field efficacy studies.

The first clinical study called "Pertussis human challenge colonization study" was initiated on April 27th, 2017 at NIHR Wellcome Trust Clinical Research Facility in Southampton, UK, under the lead of the chief investigator Prof. Rob Read (portrait in PERISCOPE Newsletter 2). This is a controlled human infection study consisting of two phases: In phase A, a low dose of the inoculum is given intranasally to healthy participants. This dose will be escalated or de-escalated until colonisation is achieved in approximately 70% of the exposed volunteers without causing disease. The colonisation period, shedding and exploratory immunology will be assessed during a 17-day inpatient stay and follow-up over 1 year. The dose of inoculum that achieves 70% colonisation will then be confirmed in phase B, comparing healthy participants exposed to *B. pertussis* with a control group receiving a sham inoculum. The protocol of the study has been recently published in *BMJ Open*.

PERISCOPE launches its first clinical research study on Pertussis vaccination in Europe

Within the scope of PERISCOPE, nine clinical studies will be conducted with the aim to identify novel biomarkers of protection against pertussis. This objective will be reached through deep analysis of immune responses to existing pertussis vaccines (aP vs wP), as well as infection-induced immunity

The first of these clinical studies – the Booster against pertussis (BERT) study– was launched last October under the sponsorship of the Dutch Institute for Public Health and the environment (RIVM). This clinical study conducted by Dr Marlies van Houten at the Spaarne Gasthuis in Hoofddorp, The Netherlands, investigates how the immune system responds to a booster vaccination against whooping-cough. The influence of age, number of vaccinations and type of vaccines administered during childhood and prior to the booster vaccine given in this study will be investigated. In depth analysis of the induction of serum antibodies and white blood cell responses will be performed. The objective is to understand how immune responses induced by vaccination lead to a long-term memory and protection against whooping-cough. This study is part of a larger international study coordinated by the Dr. Guy Berbers (RIVM) involving three countries (The Netherlands, UK and Finland) with different epidemiological background for pertussis incidence and different primary vaccination (wP or aP) schedules.

PERISCOPE workshop on the core B-cell and T-cell assays

In order to train the laboratory personnel from the clinical sites, a 3-day workshop on the development and standardization of *B. pertussis*-specific T-cell and B-cell ELISpot assays was held in Bilthoven, The Netherlands from September 13-15, 2017.

Laboratory workers from all clinical sites (University of Oxford, University of Southampton, University of Turku and the Medical Research Council Unit the Gambia) and the task leaders were invited to join and discuss any issues related to the Standard Operating Procedures (SOP). Steps to be able to harmonize the assays have been established during this workshop.

Portraits

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

Beate Kampmann, Medical Research Council Unit The Gambia

Why do we need PERISCOPE?

"Observations made with currently used vaccines against pertussis show that protective immunity wanes with time. We need to understand why this is the case and then improve on their design for the new generation of vaccines, as whooping cough remains a serious illness, especially for very young children."

What are the main outcomes expected from the consortium?

"The consortium has a plethora of opportunities to understand correlates of protection and inform the design of new vaccines by combining basic science including work in pre-clinical and human challenge models with clinical trials including Africa and vaccines given to pregnant women. The collaboration of investigators with state of the art tools will allow us to go further than ever before in the analysis of vaccine-specific memory in search of correlates of protection."

What is your expertise and role in the consortium?

"I lead the work package in charge of the clinical trials in 3 European countries and I site in West Africa. My role is to manage these clinical studies, plus also lead the clinical trial in The Gambia. I represent the WP3 "Vaccine-induced immunity" on the steering committee and need to make sure that we are well aligned with the thoughts in other work packages, in particular WP2 , which also includes clinical studies, and WP5, which is developing the new tools and lab aspects. However, a sense of perspective and feasibility needs to prevail in order to combine the desirable with the possible. I see it as my role to mediate this perspective."

What aspect will you enjoy most working with this consortium?

"I think, we have a really unique opportunity here to gain new insights into the mechanisms of protection against *Bordetella pertussis* and hopefully ultimately come up with the key information leading to the development of a better vaccine. The multi-disciplinarity of the group is a key asset, and I enjoy the opportunity to think about how the basic science tools can be best used in the context of clinical trials."

Qiushui He
University of Turku, Finland

Why do we need PERISCOPE?

"Pertussis is a vaccine-preventable disease but resurgence and changing epidemiology of pertussis have occurred in many industrialized countries, including some European countries. Therefore, we need the PERISCOPE network in order to combine our efforts to accelerate the development of improved vaccination strategies."

What are the main outcomes expected from the consortium?

"Although pertussis vaccines have been used for many years, no surrogate of protection defined for either whole cell or acellular vaccines has been established. In PERISCOPE, different pre-clinical and clinical studies will be conducted and many advanced technologies will be used,that we do hope can help us identify the biomarker(s) of protection against pertussis."

What is your expertise and role in the consortium?

"I am a clinical microbiologist and immunologist with a long experience of pertussis research including vaccine trials and clinical studies. In PERISCOPE we are involved in the work of WP2 "Immunity to infection", WP3 "Vaccine-induced immunity" and WP5 "Biomarker discovery platform". Together with Jussi Mertsola, I am in charge of the work being conducted in Finland."

What aspect will you enjoy most working with this consortium?

"In Finland, we are active in international collaborations. Since 2005, together with Jussi Mertsola I have been leading a European network EUpertstrain in which national pertussis reference laboratories from 11 European countries are involved to compare circulating *Bordetella pertussis* strains in these countries with different vaccination programs and to evaluate impact of bacterial changes on effectiveness of vaccines and disease incidence. Since 2009 I have been the leader

of ECDC-funded project "EUPert-LabNet" to develop a laboratory-based surveillance of pertussis in whole Europe. This consortium consists of many experts in different aspects of pertussis research from Europe as well as from manufacturers. I really enjoy working together with new and old colleagues in this exciting consortium ."

PERISCOPE publications

De Graaf H, Gbesemete D, Gorringe AR, *Diavatopoulos DA, Kester KE, Faust SN and Read RC.* **Investigating *Bordetella pertussis* colonisation and immunity: protocol for an inpatient controlled human infection model.** *BMJ Open* 2017;**7:**e018594.

Borkner L and KHG Mills. **Treatment with azithromycin clears respiratory infection with *Bordetella pertussis* and attenuates innate and adaptive immune responses in a mouse model.** Proceedings of the 47th Annual Meeting of the German Society for Immunology, 2017, Erlangen, Germany.

Next PERISCOPE annual meeting

From March 8th to 9th, 2018, the PERISCOPE consortium will gather in Lyon, France to share project activities, progress and future collaborations.

About PERISCOPE

A new generation of pertussis vaccines or improved vaccination schedules is needed to combat the still persistent burden of pertussis disease around the world.

The PERISCOPE consortium has been established to steer collaboration between Pertussis stakeholders, particularly from vaccines manufacturing and the academic and public research communities in Europe. The key objective of PERISCOPE 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 *i.* the immune response generated by infection and colonization of *Bordetella pertussis, ii.* comparing the immune response to 1st (whole-cell) and 2nd generation (acellular) Pertussis vaccines in humans and *iii.* investigating the impact of maternal Pertussis immunization on the immune status of newborns. An extensive tool box of novel bioassays will be developed for used as immunological read-outs in the studies. Analysis of the data generated using *state of the art* bioinformatics platforms will ultimately allow the vaccine-developing community to define the immunological profile, or *signature,* that vaccines need to generate in humans for them to become effective at preventing infection in a durable manner.

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

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.