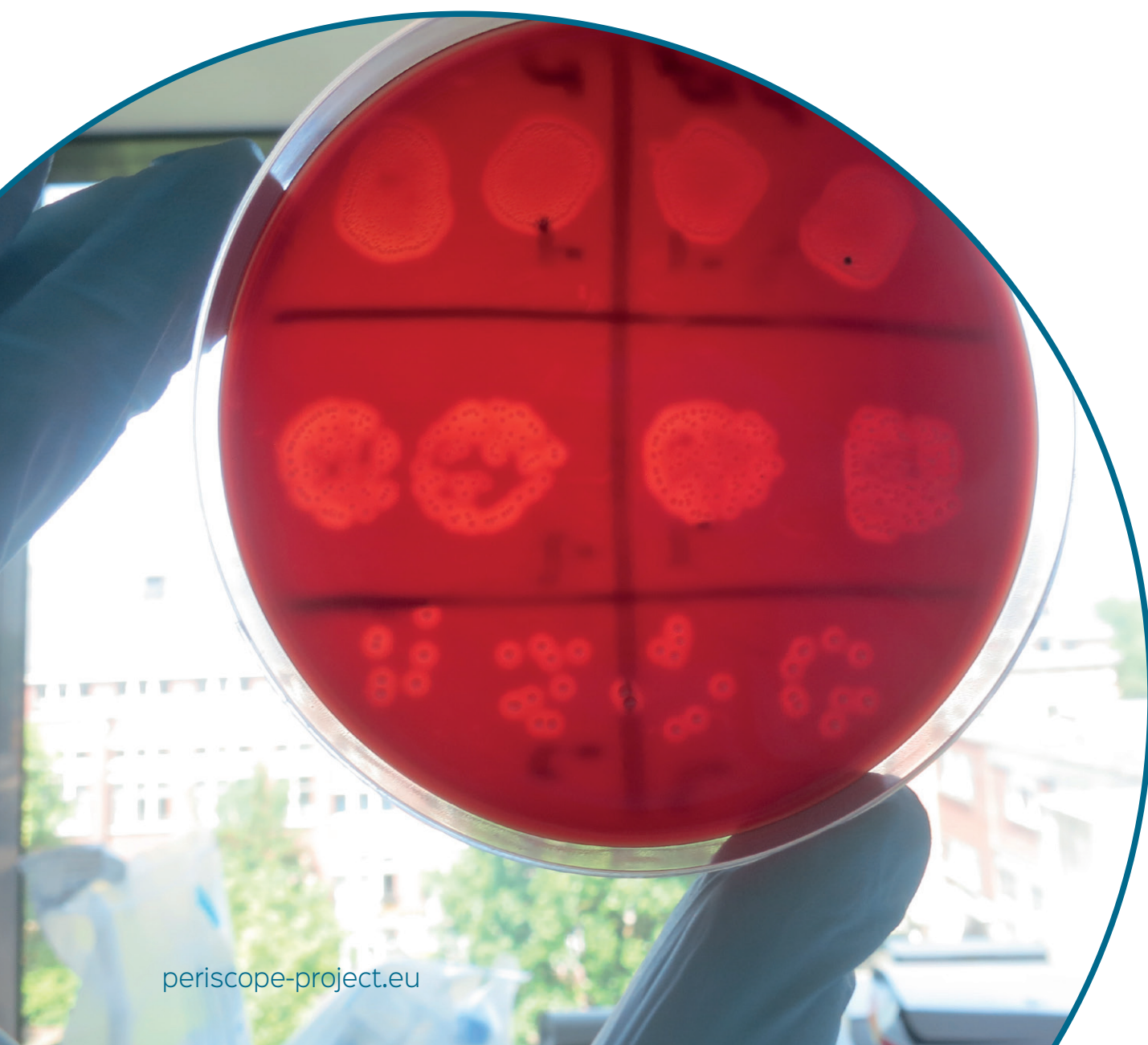


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PERtussIS CORrelates of Protection Europe

Newsletter Issue 1



Editorial

Welcome to the first issue of our Newsletter!

We are very pleased to present the first e-newsletter of the PERISCOPE (Pertussis Correlates of Protection Europe) consortium. We will issue a semi-annual document to keep you updated on the latest progress of this 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)
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Partners:	22
Website:	www.periscope-project.eu

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

The ambition of PERISCOPE

Despite the availability of effective prophylactic vaccines against pertussis, there has been a rise in the incidence of pertussis, with epidemics in Europe, Australia and the US in the last decade. As well as being a particular problem in vulnerable infants, with devastating consequences in developing countries, the incidence of pertussis is also increasing in adolescents and adults, particularly in industrialized countries. Hence, pertussis continues to be a major public health concern worldwide.

Important knowledge gaps still remain, in particular, relating to human immunity to Bp and whether observations in animal models translate to clinical practice. This paucity of knowledge hampers the development and registration of improved vaccines and the design of better vaccination strategies against pertussis in infants, adolescents and adults. PERISCOPE's ambition is to aid the development and licensing of the next generation of improved vaccines through:

Identification of biomarkers of protection

PERISCOPE adopts two parallel strategies to develop immunological read-outs that can be assessed for use as biomarkers of lasting immunity and/or vaccine-mediated protection against pertussis.

The first strategy investigates the predictive power of functional Bp (antigen)-specific immune responses generated by vaccination. PERISCOPE develops a set of core immunological read-outs to measure the quantity and functional activity of pertussis-specific circulating antibodies in human blood. The second strategy focuses on the exploration of novel immunological technologies, systems biology tools and computational modelling to identify response patterns (both innate and adaptive) to vaccination and infection, and ultimately discover if discrete immune signatures may be used as markers and

eventually surrogates of effective and long lasting vaccination.

Application of (Pre-)clinical studies and models to identify biomarkers of protection

To identify potential biomarkers of lasting immunity to pertussis, our experienced clinical partners will perform multi-centre vaccine trials in infants to compare immune responses to primary vaccination with acellular (aP) and whole-cell pertussis (wP) vaccines. These studies are performed both in Europe as well as in the Gambia and will provide information on immunity to Bp in populations with different epidemiologic and genetic backgrounds.

A human challenge model of B. pertussis

PERISCOPE will ensure the availability of reliable preclinical models in Europe, in which to test the immunogenicity and efficacy of novel vaccine formulations. This will increase the ability of academic researchers, biotechnology and pharmaceutical companies all over the world to study and screen vaccine candidates and select the most successful for clinical development. The consortium will also strengthen the technological means of testing and screening novel vaccine candidates in humans with the establishment of a human model of pertussis infection via control challenge studies in volunteers. This could permit the early evaluation of experimental vaccines for protective efficacy and ultimately accelerate the development and availability of novel and improved vaccine formulations.

Investigating the effect of maternal antibodies on response of infants to primary immunization

By applying the core immunological assays to investigate the functional humoral and cellular responses to pertussis in these infants, we are able to address the question if and how maternal antibodies to antigens included in the booster vaccine affect the development and maintenance of immunity to Bp vaccination in infants, as well as to other vaccines in the EPI

(Expanded Programme on Immunization) schedule. These studies are pivotal to accelerate implementation of immunization with aP during pregnancy.

Our public-private consortium of industrial and academic stakeholders constitutes a unique platform for interaction and consultation with Regulatory Authorities and Public Health Institutions. The validation and acceptance of new biomarkers and new disease models will be a critical step in implementing the results of this project for the benefit of public health. PERISCOPE will reach out to regulatory experts and authorities to ensure the development of a road map to ensure the biomarkers identified are ultimately validated and acceptable for inclusion in regulatory documentation and guidelines.

Portraits

In each newsletter, we will portray individual PERISCOPE members. In this first issue, we are happy to introduce the two PERISCOPE coordinators and their views on the project.



**Ronald de
Groot,
Coordinator**

Why do we need PERISCOPE?

RdG: “Despite the availability of effective prophylactic vaccines against pertussis, there has been a substantial increase in the incidence of pertussis in many countries and continents. This is not only a particular problem for vulnerable infants, but this increase is also seen in adolescents and adults. An additional concern is the large number of infections by aP-antigen deficient strains in countries using aP vaccination. Studies in humans and in animal models have indicated that vaccination with aP and wP results in different profiles of reactogenicity, immunogenicity and duration of

immunity. The immune mechanisms underlying protection against Bp are not well understood. In this respect better diagnostic tools which may be able to predict long-term protection against disease and colonization are urgently needed, since good correlates of protection are missing. Although maternal immunization provides an effective protection against disease in infants, questions remain regarding the duration of protection and the impact on the primary infant vaccination series. This all underlines the need for a new generation of improved pertussis vaccines and/or vaccine strategies. PERISCOPE represents a concerted human-centric effort aiming to accelerate the development of improved vaccination strategies against infections by Bp that will ensure long-lasting protection against disease.”

What are the main outcomes expected from the consortium?

RdG: “There are 5 main outcomes of PERISCOPE. First: PERISCOPE seeks to detect biomarkers of protection against disease and colonization based on cellular responses and/or functional antibodies. Correlates of protection will be studied through a systematic comparison of aP, wP and infection induced immunity in a large number of clinical and preclinical studies. We will develop a novel set of core assays to measure functional antibodies and T-cell responses to infection by Bp. This will facilitate the development and licensing of future new vaccines. Second: PERISCOPE will develop a human challenge model and a preclinical challenge model for infection with Bp. These models will in the future allow study of the effects of novel vaccines and provide an early indication of vaccine efficacy. Third: PERISCOPE seeks to increase the in-depth understanding of the cellular, humoral and mucosal immune response after vaccination or challenge with Bp and to discover novel biomarkers of long-lasting protective immunity to be used in the future development and registration process of novel vaccines. Fourth:

PERISCOPE will increase the understanding of the impact of maternal antibodies on infant vaccination, which will facilitate implementation of maternal vaccination in both low and high-income countries. Lastly, PERISCOPE will establish a multidisciplinary state of the art clinical and laboratory network including a bioinformatics analysis platform and a biobank to foster the capacity to evaluate novel pertussis vaccines.”

What is your expertise and role in the consortium?

RdG: “My expertise and background is in pediatric infectious diseases and immunology with a focus on clinical and translational research on the pathogenesis of a number of bacterial and viral infections. As a member of the Health Council of the Netherlands and previous president of the ESPID I have a lifelong interest and involvement in vaccination to prevent infectious diseases. My challenging role in PERISCOPE as a coordinator will be together with my 2 colleagues of the management group to bring together and further enhance the collaboration between a fantastic group of scientists with a widely varying background, to guarantee the best possible collegial atmosphere within PERISCOPE, to ensure that activities between the individual work packages are optimally aligned, to accomplish the deliverables in time and to create an atmosphere in which young and established investigators work together to reach the aims of the project, which is unique in its integrated approach to solve the problem of pertussis by using a vaccinology platform in young infants.”

What aspect will you enjoy most working with this consortium?

RdG: “It is a tremendous honor to be part of an exciting and brilliant group of investigators, which will undoubtedly lay the foundation for a better understanding and prevention of disease by Bp.”



**Patricia
Londono-
Hayes, EFPIA
Coordinator**

Why do we need PERISCOPE?

PLH: “Vaccine manufacturers are committed to continuous innovation and to responding to new challenges in infectious disease. A new generation of pertussis vaccines or vaccination schedules is needed to meet the persistent burden of Pertussis infection in developing countries and the recently observed changes in pertussis epidemiology in industrialized countries. In order to meet these challenges, it is essential for industry to use an open innovation model that facilitates collaboration with all Pertussis stake holders, and in particular experts in the academic community. Only by putting our resources and expertise together we will be able to understand what are the signatures of the protective immunological mechanisms generated by currently available vaccines or by natural infection, so we can better define the target immunological profile that novel vaccines or vaccination regimes need to generate to confer protection.

These signatures, or biomarkers, will become read-outs in the preclinical and clinical screening of novel vaccine formulations, thus accelerating and de-risking the product development process.”

What are the main outcomes expected from the consortium?

PLH: “There are 5 tangible operational objectives, as described very well by Ronald. Beyond these, the goal overall is to galvanize, revitalize and connect the Pertussis research community in Europe and beyond so there is an active network of stakeholders contributing to the development of novel vaccines and

immunization methodologies beyond the life of the program. The expectation is that the outcome of PERISCOPE will be much greater than the sum of its parts.”

What is your expertise and role in the consortium?

PLH: “I am an immunologist and microbiologist by training with extensive expertise on translational, preclinical and clinical research. I have been working on vaccine development for almost 20 years, directing product development programs, global teams and partnerships at the scientific, strategic and operational levels. In my 8 years at Sanofi Pasteur I am proud to have contributed to the development and registration of a number of products, among them Hexaxim, our hexavalent combination vaccine targeting Pertussis, and five other infections. My current role at Sanofi Pasteur focuses on external scientific affairs, in particular catalyzing and managing R&D alliances and partnerships in the European ecosystem. My role in the PERISCOPE consortium is as EFPIA Coordinator, which means that I represent the two industrial partners in the Consortium's Management Team and have overall responsibility for coordination of all aspects of the program. I am committed to ensuring a smooth interface between EFPIA and public partners, so we work synergistically to achieve the program's objectives.”

What aspect will you enjoy most working with this consortium?

PLH: “The commitment, energy and determination of all the partners is very inspirational. The level of scientific, technical and operational expertise is as high as needed to achieve the ambitious goals we have set for the program. But again, beyond the tangible aspects, I find the opportunity to bring together the industrial and academic mind sets and working practices very exciting and educational. We are learning a lot from each other, not only about what we do, but also how we do it. Last but not least, I cherish having the support of the Bill and Melinda Gates Foundation, not only because of their financial contribution, but also because of the engagement of their scientific team and valuable advice.”

PERISCOPE Kick-off in Dublin

From March 2nd to 4th, 2016, the PERISCOPE consortium came together in Dublin, Ireland for officially starting project activities that will now be continued for a total duration of 60 months. The Kick-off Meeting was hosted by PERISCOPE partner Kingston Mills from Trinity College Dublin.

The meeting was opened by PERISCOPE coordinator Professor Ronald de Groot from Radboud University Medical Center (RUMC) in Nijmegen. He welcomed our external guest, Tod Merkel, from the US Food and Drug Administration as well as Angela Wittelsberger



The PERISCOPE Consortium at a Reception in Trinity College Dublin

and Desmond Barry representing the Innovative Medicines Initiative (IMI).

After some opening remarks, all work package leaders shortly presented the planned work and objectives within the different work packages of the project, followed by several group discussions on pressing issues for the successful set-up of all project activities. The second meeting day served necessary break-out discussions on key elements within the project that ultimately led to several agreements on next steps in project implementation. The day was rounded off with a reception at the Trinity Biomedical Sciences Institute on invitation of the Dean and Vice President of Research of the Trinity College Dublin, Professor John J. Boland. The last meeting day was dedicated to discussing the set-up of clinical trials and materials necessary for the work within the

different project tasks. The meeting was concluded on midday with a summary and some closing remarks by Professor Roland de Groot.

Altogether, the meeting was of utmost importance for a smooth start of project activities with intense discussions laying the ground for good collaboration and exchange within the consortium throughout the lifetime of the project.

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.

