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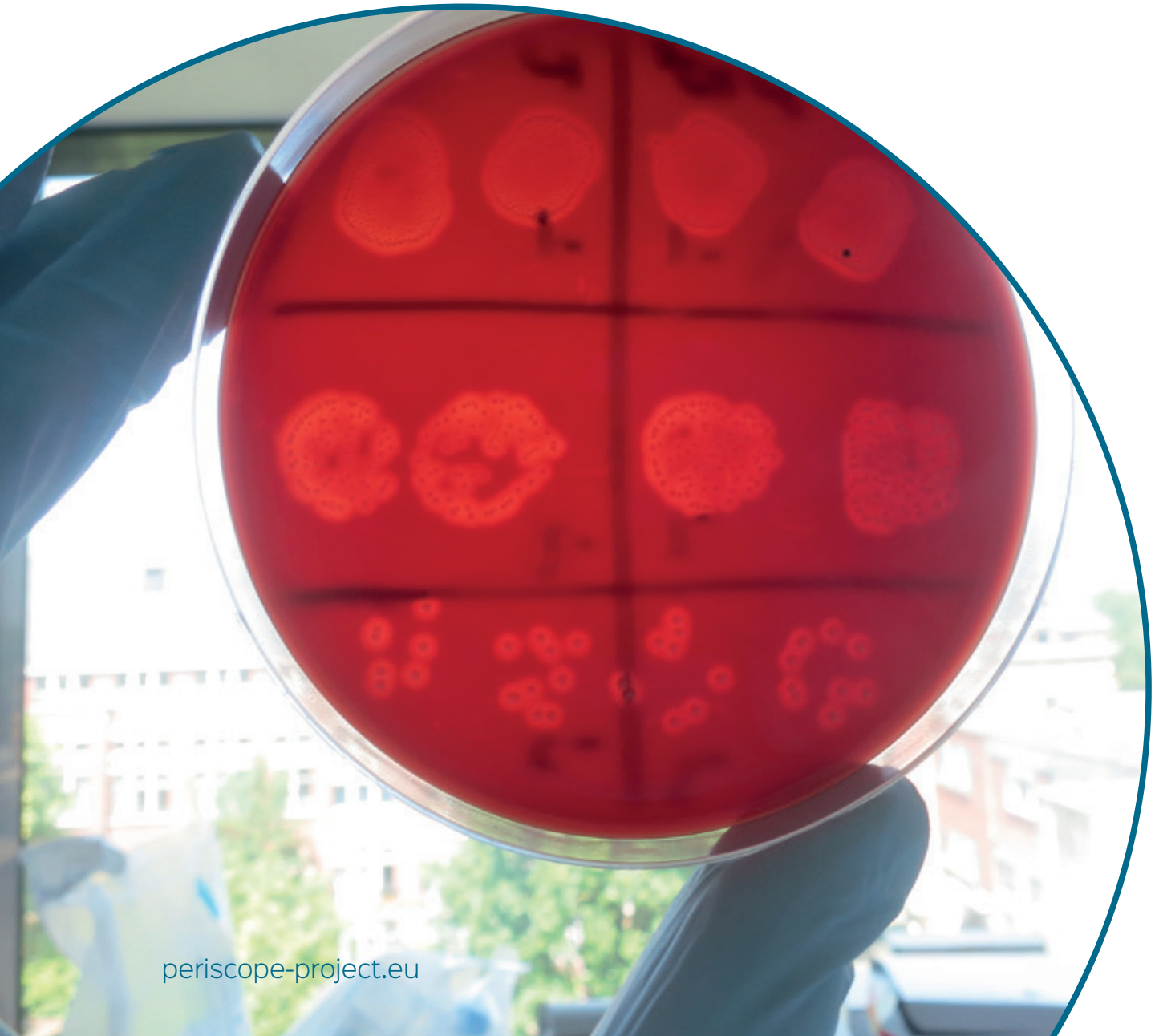
PERtussIS COrrelates of Protection Europe

Newsletter Issue 10 - June 2021



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Editorial

Dear colleagues and followers of the PERISCOPE Newsletters,

The Covid-19 pandemic has had a significant impact on the activities of the PERISCOPE consortium in Europe and in Africa. Indeed, many academic and EFPIA partners have slowed down their pertussis-related research projects in order to join the global effort to fight the Covid-19 pandemic.

With the establishment of efficient health measures and the rapid development of effective vaccines against the SARS-CoV2 virus, we are now in a position to slowly return to the main objective of this consortium: to fill the gaps in current knowledge and technologies in pertussis research in order to accelerate the development of innovative vaccines against pertussis.

Despite the delays due to the COVID-19 pandemic, we will be able to reach our goals thanks to the support of IMI which recently granted us an 18-month no-cost extension.

We would also like to inform you that Patricia Londono-Hayes, Sanofi Pasteur, has resigned as EFPIA coordinator of the consortium. She has been involved in the conception and management of the consortium from its start and we warmly thank her for her tremendous contributions to the consortium. The new EFPIA coordinator is Martina Ochs, Sanofi Pasteur.

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 combine 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) No cost extension until 31/08/2022
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 seeks to create an environment conducive to 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.

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 by investigating of the immune response generated by infection and colonization of *Bordetella pertussis* and 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 toolbox 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.

An update on AWARE study!

The team at the Oxford Vaccine Group commenced enrolment to the AWARE study in early March 2021 after a long period of uncertainty caused by the Covid-19 pandemic.

The objectives of the AWARE study are:

- To understand how the infant immune system responds after the administration of either a whole cell or acellular pertussis vaccine.
- To understand the genes that are involved in this response to either of the vaccines

Between March and June, the Oxford team succeeded to enroll 114 infants born from mother who received a pertussis vaccine during their pregnancy. The children received either a whole-cell pertussis vaccine or an acellular pertussis vaccine at 2 and 4 months of age alongside their other routine vaccinations. All children (ie. both groups), will then receive the acellular vaccine at 12 months of age. Immune responses will be monitored in the blood and nasal secretions

What opportunities does PERISCOPE offer to young scientists ?

Education of young scientists in vaccinology, especially targeting pertussis, and in the use of state-of-the-art technological tools to discover biomarkers of protection is an important priority for the PERISCOPE consortium. Many training courses (e.g. workshops on specific assays, EuroFlow training courses) have been and continue to be organized by PERISCOPE members

We asked two junior scientists involved in the project, what opportunities the PERISCOPE consortium offered them to develop their expertise and networks.

Lisa Borkner, Research fellow, Trinity College Dublin, Ireland

"The multi-angle approach to identifying correlates for protective immunity against pertussis in the PERISCOPE project unites many international groups with different research focuses towards a common goal. This wide variety gave me the chance to gain insights into aspects of infection and the immune response that I did not have personal experience in. On the other hand, I had the opportunity to offer my own expertise to collaborators in the consortium and contribute to publications outside my own group. I especially enjoyed the annual meetings in various cities across Europe where I could meet other researchers in person. It was fascinating to hear about the developments in PERISCOPE, and to understand how the different projects within the consortium built onto each other. The workshops for young researchers which gave insight into the pharmaceutical industry were very useful with regards to future career deliberations. The PERISCOPE project was the first time for me to work in a big consortium with funding from many different sources such as the EU, international sponsors, and industrial partners. I found it very informative to learn about the organizational efforts involved in such a huge project, and the need for accountability and accurate reporting, as this is also part of the work of a scientist."

Haddijatou Jobe, Scientific Officer, Gambian Pertussis Study (GaPs), MRC Unit The Gambia

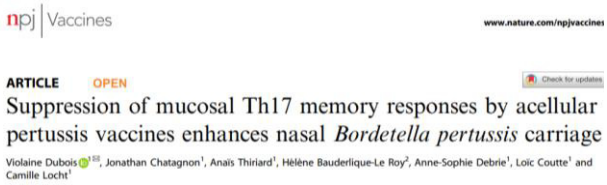
"During my time within the PERISCOPE consortium, I have had the chance to be at the forefront of leading research into whooping cough, which remains a key cause of vaccine preventable death in children worldwide. It is also a topic which lacks data in low-income countries such as The Gambia. Working on the Gambian Pertussis Study (GaPs), the Sub-Saharan African arm of the PERISCOPE consortium, has provided a useful insight into effective collaboration and the importance of aligning methodologies, including laboratory techniques, data collection and analytical approach, across different participant cohorts and settings. In particular, I learned how specific immunological readouts are developed and kept consistent across sites; as part of the GaPs team, I contributed to the preliminary work that facilitated the use of the whole blood T-cell assay (supernatant readout), particularly in an infant cohort, which has been a highlight of my work so far.

Furthermore, working on the GaPs study has provided multiple training opportunities for me. At the beginning of the trial, I helped to set up and train the field team to collect mucosal lining fluid from our study infants, applying a novel technique that has not been used in this setting previously. I am also helping to run the

B-cell ELISPOTs and T-cell assays which will inform our understanding of vaccine responses induced by the whole-cell compared to the acellular pertussis vaccine, as well as the impact of pertussis immunisation in pregnancy. Finally, over the coming year, I plan to support the development of a Luminex assay and flow cytometric readouts to further evaluate pertussis-specific T-helper cell profiles in Gambian infants following different primary immunisation schedules.

I hope that the skills and training I acquire throughout my time within GaPs and PERISCOPE will provide the ideal stepping stone to successfully embark on a PhD in the future. Thank you for the fantastic experience so far ! “

Scientists from the PERISCOPE consortium published in NPJ Vaccines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ARTICLE OPEN

Suppression of mucosal Th17 memory responses by acellular pertussis vaccines enhances nasal *Bordetella pertussis* carriage

Violaine Dubois[1✉], Jonathan Chatagnon[1], Anaïs Thiriard[1], Hélène Bauderlique-Le Roy[2], Anne-Sophie Debrie[1], Loïc Coutte[1] and Camille Locht[1]

Recent studies suggest that suboptimal and fast waning immunity induced by the alum adjuvanted acellular pertussis (aP) vaccines may have largely contributed to pertussis resurgence in industrialized countries. Dr. Violaine Dubois and her colleagues examined protective and long-term immune responses following immunization with aP vaccines in Th2-prone (BALB/c) mice and found that, unlike the whole cell (wP) pertussis vaccines, aP vaccines, while protective against lung colonization by *Bordetella pertussis* (Bp), did not protect BALB/c mice from nasal colonization. Instead, aP vaccination substantially prolonged nasal carriage by preventing the natural induction of nasal Th17 T_{RM} cells. In non-aP vaccinated BALB/c mice $CD4^+$ T_{RM} cells are gradually induced in the nose of Bp-infected mice, and they found that these cells are the main source of IL-17 involved in the adaptive immune responses. Using IL-17 KO mice, we discovered that IL-17 is required for nasal clearance of Bp. Adoptive cell transfer of IL-17-producing $CD4^+$ T_{RM} cells resulted in protection against nasal carriage. These cells mediated the recruitment of neutrophils, leading to decreased bacterial burden in the nose, suggesting that Th17 T_{RM} cells confer protection against nasal colonization by allowing neutrophil influx, which is inhibited by prior aP immunization. Therefore, aP vaccines may have augmented the Bp reservoir since its introduction.

PERISCOPE Stakeholder and annual meeting 2021 in Ghent, Belgium

Due to the Covid-19 pandemic, we had to postpone the 2020 stakeholder meeting to November 16th, 2021 in Ghent, Belgium.

The topic of the 2021 stakeholder meeting will be: ***“Sustainability of PERISCOPE consortium”.***

More information coming soon.

About PERISCOPE- *Progress beyond state of the art*

Beyond the public health objectives of PERISCOPE, the project stimulates connections among 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 virtual discussion forums and meetings have been held throughout this fourth year of the 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.