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Press information

A good outcome for the CHILD-INNOVAC project: successful test in humans of a nasal vaccine against pertussis

The CHILD-INNOVAC European research programme, coordinated by Inserm, has enabled the development of an innovative vaccine that can be administered intranasally, to combat pertussis, which has shown a resurgence in developed countries in recent years. The research consortium, headed by Camille Locht, Director of the Centre for Infection and Immunity of Lille (a joint Unit involving Inserm, CNRS, Institut Pasteur de Lille and University of Lille Nord de France), today published promising results from Phase I clinical trials of the vaccine in human subjects in the online journal *PLOS ONE*.

See the video of the discovery : *http://youtu.be/RWmxtTXpBjU*

Researchers from the CHILD-INNOVAC European project, which brought together 10 European partners*, evaluated the efficacy and safety of a new concept in intranasal vaccination against pertussis. They also carried out clinical trials in humans, which provided conclusive results.

Pertussis is a wrongly “forgotten” disease, according to Camille Locht, a Research Director at Inserm and Director of Scientific Affairs of the Institut Pasteur de Lille. The disease currently affects several tens of millions of individuals, and kills approximately 300,000 children annually worldwide. The associated morbidity and mortality are increasing throughout the world. Its resurgence has become a matter for major concern since 2010 in some developed countries, such as the USA, Australia, the UK, the Netherlands and France.

The CHILD-INNOVAC project is more specifically focused on combating two major respiratory pathogens: *Bordetella pertussis* (the bacterium that causes whooping cough) and respiratory syncytial virus (which causes bronchiolitis in infants). These pathogens mainly affect infants aged 0 to 6 months, who are poorly protected by the vaccines presently available. The project also provides proof of concept that this vaccine may be applied to other respiratory infections.

The researchers from the CHILD-INNOVAC project have succeeded in testing in humans, for the first time, a live bacterial vaccine, genetically attenuated and specially designed for intranasal administration to combat major respiratory pathogens. *“This original method of administration will make the vaccine accessible to greater numbers of people at a smaller cost,”* explains the project coordinator, Camille Locht.

CHILD-INNOVAC:
a European success

The main success of this European project is the achievement of a vaccine for which the immunogenicity and safety could be tested in humans in only two and a half years (compared with 5-7 years for most projects of this type). This is a very short time, which Camille Locht explains is due to *“the skills and motivation of the consortium, which brought together experts in their respective areas of specialisation from seven European countries. It was possible to relay the data in a flexible and efficient manner at the different stages of the project.”* The project received a budget of €5 million, awarded by the European Commission under FP7.

The Phase I trials in humans allowed the immunogenicity and safety of the vaccine to be measured in comparison with a placebo, under double-blind conditions. They took place in Sweden, which has the most "naive" population with respect to vaccination against pertussis, given that vaccination was abandoned in that country for several years, for reasons of inefficacy.
The main objective of these trials was to record all possible adverse events, namely cough, sneezing, nasal discharge, effects on general health, etc. These measurements were examined by an independent data monitoring committee.
The second objective was to assess colonisation of the nasal mucosa by the vaccine, and the triggering of an immune response.
It was possible to test three different doses of the vaccines: a low, intermediate and high dose.
Results obtained after monitoring the vaccinated subjects for 6 months, and analysing 60,000 data points, showed that the vaccine induced no adverse events compared with the placebo, even at the high dose. The vaccine colonised the nasal mucosa best at the high dose. Moreover, immune responses were triggered in all subjects whom the vaccine had colonised. *"It is of special interest that a single nasal administration was able to induce an immune response that was maintained for at least 6 months, i.e. for the duration of the study,"* comments Camille Locht.

The next step will involve administering higher volumes in an effort to increase the level of colonisation of the nasal mucosa by the vaccine. Camille Locht and his collaborators also hope to improve the stability of vaccine over time, with a view to industrial development in the near future.

Inserm Transfert, in charge of the valorization of the IP portfolio related to the BPZE-based technology, recently entered into an agreement with a biotech partner to further develop the technology.

Sources

"A phase I clinical study of a live attenuated Bordetella pertussis vaccine – BPZE1; A single centre, double-blind, placebo-controlled, dose-escalating study of BPZE1 given intranasally to healthy adult male volunteers"

Rigmor Thorstensson[1], Birger Trollfors[1], Nabil Al-Tawil[2], Maja Jahnmatz[1,3], Jakob Bergström[1], Margaretha Ljungman[1], Anna Törner[1], Lena Wehlin[1], Annie Van Broekhoven[4], Fons Bosman[4], Anne-Sophie Debrie[5,6,7,8], Nathalie Mielcarek[5,6,7,8] and Camille Locht[5,6,7,8]

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PLOS ONE **:** http://dx.plos.org/10.1371/journal.pone.0083449 ***, 08 January 2014***

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CHILD-INNOVAC

The CHILD-INNOVAC project was aimed at developing innovative intranasal vaccines against the two main respiratory pathogens, pertussis and respiratory syncytial virus (RSV). The project has provided prototypes for polyvalent vaccines that can be administered intranasally, based on attenuated *B. pertussis*. The immunity induced by the BPZE1 vaccine was studied in detail, together with its genetic and biological stability and safety.

CHILD-INNOVAC began in 2008, and was supported by the EU (FP7) for 4 years. It was coordinated by Inserm, along with 27 other European projects. The project involved 10 partners, including 2 private companies and 8 laboratories, based in 7 European countries:

See video

Inserm (coordinator), France: http://www.inserm.fr/
Inserm Transfert, France: http://www.inserm-transfert.fr/
Université Libre de Bruxelles, Belgium: http://www.ulb.be/
Innogenetics, Belgium: http://www.innogenetics.com
National University of Ireland, Maynooth: www.immunology.nuim.ie
Istituto Superiore Di Sanità, Italy: http://www.iss.it/
Swedish Institute for Communicable Disease Control: http://www.smittskyddsinstitutet.se/in-english/
Netherlands Vaccine Institute: http://www.nvi-vaccin.nl/
National Institute for Public Health and the Environment, the Netherlands: http://www.rivm.nl/
Imperial College of Science, Technology and Medicine, England: http:/www3.imperial.ac.uk/

Inserm is the leading provider of European "Health" projects with 21 projects coordinated by the Institute under the FP7 initiative.

Founded in 1964, the French National Health and Medical Research Institute (Inserm) is a public science and technology institute, jointly supervised by the French Ministry of Higher Education and Research and the Ministry of Health.

The mission of its scientists is to study all diseases, from the most common to the most rare, through their work in biological, medical and public health research.

With a budget of 840 million euros in 2012, Inserm supports more than 300 laboratories across France. In total, the teams include nearly 13,000 researchers, engineers, technicians and administrative staff, etc.

Inserm is a member of the National Alliance for Life and Health Sciences, founded in April 2009 with CNRS, Inserm, the CEA, INRA, INRIA, the IRD, the Pasteur Institute, the Conference of University Presidents - Conférence des Présidents d'Université (CPU) and the Conference of Chairmen of The Regional and University Hospital Centres - Conférence des directeurs généraux de centres hospitaliers régionaux and universitaires. This alliance forms part of the policy to reform the research system by better coordinating the parts played by those involved and by strengthening the position of French research in this field through a concerted plan.

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