childINNOVAC

European Network on Nasal Vaccination against Respiratory Infections in Young Children

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childINNOVAC is a European research network (Collaborative Project) supported by the European Commission under the Health Cooperation Work Programme of the 7th Framework Programme.

Context

Despite the great advances in the prevention and treatment of infectious diseases, respiratory infections remain the most frequent cause of childhood morbidity and mortality worldwide. Although licensed vaccines targeting several of these diseases exist and are widely used, respiratory pathogens still cause more than four million deaths per year. Most of these deaths occur in young children. For many respiratory pathogens no satisfactory vaccine is available. For others, classical parenteral immunisation remains insufficiently effective.

The childINNOVAC project aims at developing novel, nasal vaccines against two major respiratory pathogens, *Bordetella pertussis* and Respiratory Syncytial Virus (RSV). RSV and *Bordetella pertussis* are among the most frequent and severe respiratory pathogens in young children. Both have a world-wide distribution and pose significant direct burdens on health systems in Europe, in neighbouring developing countries and in migrant communities.

Although efficacious vaccines against pertussis are widely used, roughly 40 million cases and 200,000-400,000 pertussis-linked deaths are recorded annually, mostly in infants aged 0-6 months, not yet sufficiently protected by the current vaccines and schedules. Hence, pertussis vaccines are needed that induce individual protection soon after birth to protect the youngest and most vulnerable children.

RSV is the first cause of bronchiolitis in infants and wheezy lower respiratory tract illness in early childhood. Virtually all children are infected by the age of three, and no vaccine is yet available against RSV. There is now a consensus that mucosally delivered live vaccines are strong candidates for future RSV vaccines .

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Objectives

The childINNOVAC project has been conceived as a response by academic and industrial scientists in Europe to confront both pathogens with a new, innovative vaccine approach: this consortium will yield proof of principle and provide prototypes of multivalent nasal vaccines based on attenuated *B. pertussis*. The concept is based on the fact that early in life, infants can mount strong anti-*B. pertussis* B and T cell responses upon natural infection in contrast to vaccination.

The live attenuated *B. pertussis* called “BPZE1” has already been constructed and shown to be much more protective in infant mice after a single nasal dose than two doses of current pertussis vaccines. In addition, this vaccine strain can be engineered into a poly-valent vaccine, to also hopefully protect against RSV.

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Our objectives will be thus of three kinds:

OBJECTIVE 1:

The main objective of childINNOVAC is to provide a proof of principle of the concept of a pre-clinically tested live attenuated *B. pertussis* vaccine, including first phase I clinical trials (to be done in adults), to pave the way towards further phase I, phase II and phase III trials, which ultimately should target the infant population.

OBJECTIVE 2:

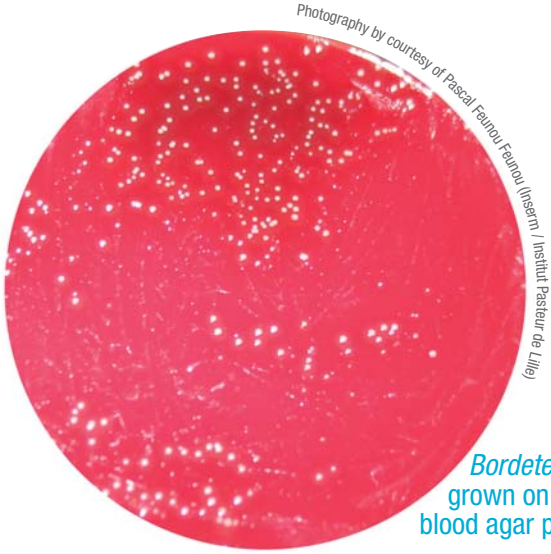
The second goal is to improve knowledge on long-term B and T cell memory after *B. pertussis* infection or current pertussis vaccination, which includes the development of standardized assessment methods. These tests will be useful for further evaluation of nasal pertussis vaccines and will add value to the requirement for the evaluation of current vaccines and booster programs.

OBJECTIVE 3:

The third goal of this project is to develop attenuated *B. pertussis* as a nasal vector to simultaneously deliver antigens derived from several pathogens. *B. pertussis*-based multivalent live vaccines would ultimately reduce the number of separate vaccinations needed in children. The heterologous model system proposed in this project is RSV.

Strategy

As the childINNOVAC project aims at the development of novel vaccination strategies in infants to induce early and long lasting protection, it involves research, development, innovation, as well as management activities. Thus, this project should lay the groundwork for nasal vaccination approaches against multiple pathogens, and in particular determine the feasibility of using live attenuated *B. pertussis* as a basis to not only immunise against whooping cough, but also against other respiratory pathogens. The overall project is based on integrating knowledge on the human B and T cell responses to infection and vaccination, with special emphasis on memory, and on the vaccine strain characteristics, with the preparation and execution of first human phase I trials (in adults) and the construction of novel, recombinant multivalent vaccine strains for future development.



Photography by courtesy of Pascal Fauroux Fauroux (Inserm / Institut Pasteur de Lille)

Bordetella pertussis colonies grown on Bordet-Gengou blood agar plates

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childINNOVAC Workpackages and Partners' Contributions

MICE

Investigation on the protective immune response — Inserm

Assessment of the safety of BPZE1 — NUI Maynooth

Evaluation of BPZE1 stability — Inserm

Construction & evaluation of a recombinant RSV-BPZE1 strain — Imperial College London; Inserm

HUMANS

***in vitro* immune responses to BPZE1** — Istituto Superiore di Sanità

Memory immune responses to infection & vaccination — Istituto Superiore di Sanità; rivm; ULB; NVI

Phase 1 safety trials in adults — ULB; Istituto Superiore di Sanità; Smittskyddsinstitutet

Clinical GMP grade lots of BPZE1 — GENimmune

Live attenuated *B. pertussis* BPZE1 strain

COORDINATION / MANAGEMENT

Inserm; InsermTransfert

Expected outcomes

One of the major impacts of childINNOVAC is to provide a solution to the problem of inducing protection against respiratory pathogens early in life, possibly at birth, with novel, single-dose nasal vaccines, based on *B. pertussis* BPZE1.The ultimate aim is to protect infants in the most vulnerable age group, before the regular vaccination schedule using already available vaccines is applied. Classical vaccination schedules would then constitute important booster immunisations.Since *B. pertussis* can accommodate large DNA inserts encoding foreign proteins, the potential of BPZE1 as a multivalent vaccine vector is enormous. childINNOVAC will provide the proof of principle in mice using the RSV model. However, it is likely that recombinant BPZE1 derivatives can be designed to target other respiratory infections, both viral and bacterial, including pneumococcal, meningococcal and *Haemophilus influenzae* infections. The development of such recombinant multivalent nasal vaccines will thus have an obvious enormous impact on the protection of infants world-wide against the major respiratory infections.

AccuSpray nasal delivery device

Photography by courtesy of Becton Dickinson and Company

childINNOVAC is a European research network (Collaborative Project) coordinated by the **French Institute of Health and Medical Research** (Inserm, Dr. Camille Locht, Lille - FRANCE). This consortium brings together 10 partners, including 2 private companies and 8 laboratories, from 7 Member States of the EU. It is supported by the European Commission under the Health Cooperation Work Programme of the 7th Framework Programme.

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GENimmune

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Principal Investigator : *Dr. Cecile A.C.M. van Els**

National Institute for Public Health and the Environment

Laboratory for Infectious Diseases and Perinatal Screening

Principal Investigator : *Dr. Anne-Marie Buisman**

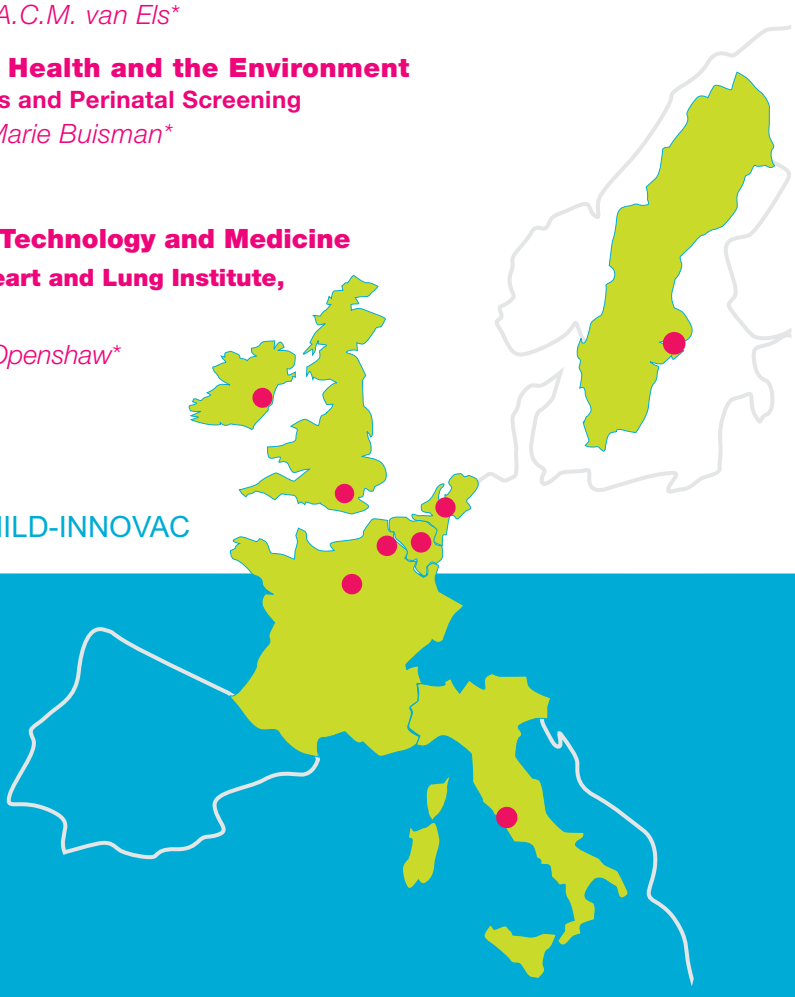
UNITED-KINGDOM

Imperial College of Science, Technology and Medicine

Faculty of Medicine, National Heart and Lung Institute,

Respiratory Medicine

Principal Investigator : *Prof. Peter Openshaw**



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