

TBVAC-HORIZON: Investigating lung immunity to accelerate the development of innovative tuberculosis vaccines

Helen McShane¹, Steffen Stenger², Nacho Aguilo³, Andrea M Cooper⁴, Hazel M Dockrell⁵, Simone A Joosten⁶, Olivier Neyrolles⁷, Eugenia Puentes⁸, Jelle Thole, Frank AW Verreck⁹, Robert Golinski¹⁰, Marit Holleman¹⁰, TBVAC-HORIZON Consortium

¹The Jenner Institute, University of Oxford, Oxford, UK; ²Medical Microbiology and Infection Control, Ulm University, Ulm, Germany; ³Department of Microbiology Pediatrics, University of Zaragoza, Madrid, Spain; ⁴Leicester TB Research Group, University of Leicester, Leicester, UK; ⁵Department of Infection Biology, London School of Hygiene and Tropical Medicine, London, UK; ⁶Leiden University Medical Center, Leiden, Netherlands; ⁷Institut de Pharmacologie et de Biologie Structurale, IPBS - CNRS, Toulouse, Midi-Pyrenees, France; ⁸Biofabri, S.L., Porriño (Pontevedra), Spain; ⁹Dpt of Parasitology. BPRC, Rijswijk, Netherlands; ¹⁰TuBerculosis Vaccine Initiative, Lelystad, Netherlands

Background/Introduction: TBVAC-HORIZON is a research project in the Horizon Europe (HE) program of the European Union (EU). It aims to increase understanding of immune protection in the lung in *M. tuberculosis* (Mtb) infection and to develop mucosal vaccination strategies for translation towards clinical evaluation. The Consortium's activities range from pre-clinical research to aligned studies with humans, non-human primates (NHP) and mice. The goal is to fill the vaccine pipeline to accelerate availability of more effective TB vaccines. The project is linking 19 institutions and builds on over 25 years of EU-funded collaborations.

Objectives & Methods:

Activities cover four main areas:

- Investigation of the composition, spatial organisation and functioning of immune responses in the Mtb-infected lung on the single cell level. Focus lies on T and B cell functions during early infection, impact of vaccination on cell migration and the influence of the hypoxic microenvironment on immune responses. Experiments are performed with mice and evaluated in a coordinated way across the Consortium, including in vivo multi-photon microscopy of immune cell interaction with infected cells.
- Evaluation if mucosal revaccination with BCG and other live attenuated vaccines improves protective efficacy against Mtb infection. These studies (humans, NHP and mice) have aligned designs to maximise their scientific value.
- Identification of host immune profiles and biomarkers/correlates of natural and vaccine-induced immune protection in the lung. This work builds on the outcomes of the aligned studies and includes co-morbidity induced immune modulations with special focus on diabetes.
- Acceleration of TB vaccine development by head-to-head testing of selected vaccine candidates in standardised animal models (mice), and innovation by establishment of novel delivery systems and adjuvant formulations and a new GMP platform for live attenuated vaccines.

Funding Sources

TBVAC-HORIZON is funded from the EU's HE programme under grant agreement #101080309 and co-funded by the UKRI of the Department for Science, Innovation and Technology (DSIT) and the Swiss State Secretariat for Education, Research and Innovation (SERI).

Conflicts of Interest

None



